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PHARMACY / MEDICAL POLICY – 5.01.540

Miscellaneous Oncology Drugs

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Last Revised:	Oct. 13, 2026	None
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*View current policy here.		

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | APPENDIX | HISTORY

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Introduction

Chemotherapy, often called chemo, is cancer treatment that uses drugs. Radiation and surgery treat one area of cancer. But chemo usually travels through the bloodstream to treat the whole body. Treating the whole body is called a systemic treatment. The goal of chemo is to either treat cancer or ease its symptoms. Treating cancer can be to cure it, decrease the chance it will return, or stop or slow its growth. Easing cancer symptoms without trying to cure the cancer is called palliative therapy. Chemotherapy drugs can be used in many different ways. Chemo can make a tumor smaller before surgery or radiation, destroy cancer cells that surgery or radiation didn't treat, help other treatments work better, or kill cancer cells that have come back or spread. Chemotherapy is given in different ways. This includes by mouth (oral), through a vein (intravenous), by a shot (injection), or with a cream rubbed onto the skin (topical). In some cases, chemo is injected between the layers of tissue covering the brain and spinal cord (intrathecal), is given into the belly area (intraperitoneal), or is injected into an artery (intra-arterial). This policy gives information about many different types of chemo drugs and the criteria for when they may be medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can

be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Drug	Medical Necessity
Oral Drugs	
Hedgehog Pathway Inhibitors	
Erivedge (vismodegib) oral	**Erivedge (vismodegib) may be considered medically necessary for adult individuals when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with 1 of the following: ○ Metastatic basal cell carcinoma (BCC) **OR** ○ Locally advanced BCC that has recurred following surgery **OR** ○ Locally advanced BCC in individuals who are not candidates for surgery or radiation therapy **AND** • Dose is limited to 150 mg per day
Odomzo (sonidegib) oral	**Odomzo (sonidegib) may be considered medically necessary for adult individuals when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with 1 of the following: ○ Locally advanced basal cell carcinoma (BCC) that has recurred following surgery or radiation therapy **OR** ○ Locally advanced BCC in individuals who are not candidates for surgery or radiation therapy **AND** • Dose is limited to 200 mg per day (1 tablet daily)

Drug	Medical Necessity
Oral Drugs	
Drugs Targeting Acute Myeloid Leukemia (AML)	
Idhifa (enasidenib) oral	**Idhifa (enasidenib) may be considered medically necessary for:** • Treatment of relapsed or refractory acute myeloid leukemia (AML) in adult individuals with an isocitrate dehydrogenase-2 (IDH2) mutation
Tabloid (thioguanine) oral	**Tabloid (thioguanine) may be considered medically necessary for the treatment of acute myeloid leukemia when all the following criteria are met:** • The individual has been diagnosed with acute myeloid leukemia **AND** • Tabloid (thioguanine) will be used for remission induction or remission consolidation therapy **AND** • Dose is limited to 3 mg/kg per day **Tabloid (thioguanine) may be considered medically necessary for the treatment of acute lymphoblastic leukemia**
Tibsovo (ivosidenib) oral	**Tibsovo (ivosidenib) may be considered medically necessary for the treatment of adult individuals with newly-diagnosed acute myeloid leukemia (AML) when all the following criteria are met:** • The individual is aged 75 years or older OR has comorbidities that preclude use of intensive induction chemotherapy **AND** • Has newly diagnosed AML with a susceptible isocitrate dehydrogenase-1 (IDH1) mutation who are at least 75 years old **AND** • Tibsovo is used in combination with azacitidine or as monotherapy

Drug	Medical Necessity
Oral Drugs	
	Tibsovo (ivosidenib) may be considered medically necessary for the treatment of relapsed or refractory acute myeloid leukemia (AML) in adult individuals when all the following criteria are met: • The individual is aged 18 years or older **AND** • Has been diagnosed with relapsed or refractory AML with a susceptible IDH1 mutation **Tibsovo (ivosidenib) may be considered medically necessary for the treatment of adult individuals with previously treated, locally advanced or metastatic cholangiocarcinoma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with previously treated, locally advanced, or metastatic cholagniocaricnoma with a susceptible IDH1 mutation **Tibsovo (ivosidenib) may be considered medically necessary for the treatment of adult individuals with relapsed or refractory myelodysplastic syndromes when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with relapsed or refractory myelodysplastic syndromes with a susceptible IDH1 mutation
Daurismo (glasdegib) oral	**Daurismo (glasdegib) may be considered medically necessary for newly-diagnosed acute myeloid leukemia (AML) when all the following criteria are met:** • The individual is aged 75 years or older OR has comorbidities that preclude use of intensive induction chemotherapy **AND**

Drug	Medical Necessity
Oral Drugs	
	• Daurismo is used in combination with low-dose cytarabine
Poly (ADP-ribose) Polymerase (PARP) Inhibitors	
Lynparza (olaparib) oral	**Lynparza (olaparib) may be considered medically necessary for the maintenance treatment of adult individuals with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has a deleterious or suspected deleterious BRCA mutation (as confirmed by genetic testing) **AND** • Is in complete or partial response to first-line platinum-based chemotherapy **Lynparza (olaparib) may be considered medically necessary in combination with bevacizumab for the maintenance treatment of adult individuals with advanced epithelial ovarian, fallopian tube or primary peritoneal cancer when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Is in complete or partial response to first-line platinum-based chemotherapy **AND** • The cancer is associated with homologous recombination deficiency (HRD)-positive status defined by: o A deleterious or suspected deleterious BRCA mutation (as confirmed by genetic testing) **AND/OR** o Microsatellite instability or SNP analysis (loss of heterozygosity) **AND**

Drug	Medical Necessity
Oral Drugs	
	• Lynparza is used in combination with bevacizumab for maintenance treatment **Lynparza (olaparib) may be considered medically necessary for the maintenance treatment of adult individuals with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, who are in a complete or partial response to platinum-based chemotherapy.** **Lynparza (olaparib) may be considered medically necessary for the treatment of adult individuals with advanced ovarian cancer unresponsive to platinum-based chemotherapy when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has a deleterious or suspected deleterious **germline** BRCA-mutation (gBRCAm) (as confirmed by genetic testing) **AND** • Has been treated with at least 3 prior lines of chemotherapy **Lynparza (olaparib) may be considered medically necessary for the adjuvant treatment of adult individuals with high risk early breast cancer when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has HER2-negative high risk early breast cancer **AND** • Has a deleterious or suspected deleterious BRCA-mutation or a PALB2 mutation (as confirmed by genetic testing) **AND** • Has been treated with chemotherapy in the neoadjuvant or adjuvant setting

Drug	Medical Necessity
Oral Drugs	
	Note: Early breast cancer is distinguished from locally advanced and metastatic disease. Early breast cancer includes Stages 0 to IIB or T0 to T2 and N0 to N1. Locally advanced breast cancer includes stages IIIA to IIIC or T3N0 and Tx N2-3. Metastatic breast cancer is Tx Nx M1 or Stage IV. **Lynparza (olaparib) may be considered medically necessary for the treatment of adult individuals with metastatic breast cancer when all the following are true:** • The individual is aged 18 years or older **AND** • Has HER2-negative metastatic breast cancer **AND** • Has a deleterious or suspected deleterious BRCA mutation or a PALB2 mutation (as confirmed by genetic testing) **AND** • Has been treated with chemotherapy in the neoadjuvant, adjuvant or metastatic setting **AND** • If hormone receptor (HR)-positive, individual should have been treated with a prior endocrine therapy or be considered inappropriate for endocrine therapy **Lynparza (olaparib) may be considered medically necessary for the maintenance treatment of adult individuals with metastatic pancreatic adenocarcinoma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has a deleterious or suspected deleterious **germline** BRCA-mutation (gBRCAm) (as confirmed by genetic testing) **AND** • The disease has not progressed on at least 16 weeks of a first-line platinum-based chemotherapy regimen

Drug	Medical Necessity
Oral Drugs	
	Lynparza (olaparib) may be considered medically necessary for the treatment of adult individuals with metastatic castration-resistant prostate cancer (mCRPC) when all the following criteria are met: • The individual is aged 18 years or older **AND** • 1 of the following situations is true: ○ For the treatment of deleterious or suspected deleterious germline or somatic homologous recombination repair (HRR) gene-mutated (see **Appendix** for biomarker testing) metastatic castration-resistant prostate cancer (mCRPC) who have progressed following prior treatment with Xtandi (enzalutamide) or abiraterone. **OR** ○ In combination with abiraterone and prednisone or prednisolone, for the treatment of deleterious or suspected deleterious BRCA-mutated (BRCAm) (see **Appendix** for biomarker testing) metastatic castration-resistant prostate cancer (mCRPC)
Rubraca (rucaparib) oral	**Rubraca (rucaparib) may be considered medically necessary for the treatment of adult individuals when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with 1 of the following: ○ BRCA mutation (germline and/or somatic)-associated epithelial ovarian, fallopian tube, or primary peritoneal cancer who have been treated with 2 or more chemotherapies (as confirmed by genetic testing) **OR**

Drug	Medical Necessity
Oral Drugs	
	○ Recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy as maintenance treatment **OR** ○ BRCA mutation (germline and/or somatic)-associated metastatic castration-resistant prostate cancer (mCRPC) who have been treated with androgen receptor-directed therapy (e.g., abiraterone, enzalutamide) (as confirmed by genetic testing)
Talzenna (talazoparib) oral	**Talzenna (talazoparib) may be considered medically necessary for adult individuals when all the following criteria are met:** • The individual is aged 18 years or older **AND** • 1 of the following situations is true: ○ Talzenna is used as a single agent, for the treatment of germline BRCA-mutated, HER2-negative locally advanced or metastatic breast cancer (as confirmed by genetic testing) **OR** ○ Is used in combination with enzalutamide, for the treatment of HRR gene-mutated metastatic castration-resistant prostate cancer (mCRPC) (see **Appendix**)
Zejula (niraparib) oral	**Zejula (niraparib) may be considered medically necessary for the maintenance treatment of adults with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer if all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer **AND**

Drug	Medical Necessity
Oral Drugs	
	• Are in complete or partial response to first-line platinum-based chemotherapy **AND** • Cancer is associated with homologous recombination deficiency (HRD)-positive status defined by 1 of the following: ○ A deleterious or suspected deleterious *BRCA* mutation ○ Genomic instability **AND** • Dose is limited to 300 mg daily **Zejula (niraparib) may be considered medically necessary for the maintenance treatment of adults with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer if all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer **AND** • Has deleterious or suspected deleterious germline *BRCA*-mutation **AND** • Are in complete response or partial response to platinum-based chemotherapy **AND** • Dose is limited to 300 mg daily
Cyclin-Dependent Kinases 4 and 6 (CDK4/6) Inhibitors	

Drug	Medical Necessity
Oral Drugs	
Ibrance (palbociclib) oral	**Ibrance (palbociclib) may be considered medically necessary for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer when all the following are met:** • The individual has tried and had an inadequate response or intolerance to Kisqali (ribociclib) or Verzenio (abemaciclib) **AND** • Ibrance (palbociclib) is used in combination with 1 of the following: ○ An aromatase inhibitor as initial endocrine based therapy ○ Faslodex (fulvestrant) in individuals with disease progression following endocrine therapy **Ibrance (palbociclib) may be considered medically necessary for the treatment of adult individuals with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer when all the following criteria are met:** • The individual has not had disease progression after chemotherapy plus HER2-targeted therapy (e.g., trastuzumab) **AND** • Ibrance (palbociclib) will be used as maintenance treatment in combination with HER2-targeted and endocrine therapies **Ibrance (palbociclib) may be considered medically necessary for the treatment of adult individuals with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-positive, locally advanced or metastatic breast cancer when the following criteria are met:** • The individual is aged 18 years or older **AND**

Drug	Medical Necessity
Oral Drugs	
	• Has been diagnosed with HR-positive, HER2-positive locally advanced or metastatic breast cancer **AND** • Ibrance (palbociclib) is used in combination with trastuzumab, with or without pertuzumab, and endocrine therapy for maintenance treatment following induction treatment **Ibrance (palbociclib) may be considered medically necessary for the treatment of adults with endocrine-resistant *PIK3CA*-mutated, hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, locally advanced or metastatic breast cancer when the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with HR-positive, HER2-negative locally advanced or metastatic breast cancer with *PIK3CA* mutation **AND** • Has disease progression following at least 1 line of endocrine therapy in the metastatic setting OR recurrence on or within 12 months of completing adjuvant therapy **AND** • Will be given in combination with Itovebi (inavolisib) and fulvestrant as first-line therapy **AND** • Has not experienced disease progression on or following other phosphatidylinositol 3-kinase (PI3K) inhibitors
Kisqali (ribociclib) oral	**Kisqali (ribociclib) may be considered medically necessary when all the following are met:** • The individual is aged 18 years or older **AND** • Meets 1 of the following: ○ Used in combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of

Drug	Medical Necessity
Oral Drugs	
	premenopausal or postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer **OR** ○ Used for initial treatment or following disease progression on endocrine therapy, for postmenopausal with HR+, HER2- advanced or metastatic breast cancer, in combination with Faslodex (fulvestrant) **OR** ○ Used in combination with an aromatase inhibitor for the adjuvant treatment of individuals with HR-positive, HER2-negative stage II and III early breast cancer at high risk of recurrence **Use as maintenance therapy following response to chemotherapy regimens is considered not medically necessary.**
Verzenio (abemaciclib) oral	**Verzenio (abemaciclib) may be considered clinically necessary for the treatment of postmenopausal women, or pre/perimenopausal women whose estrogen levels are suppressed on GnRH (gonadotrophin releasing hormone) therapy, who meet 1 of the following indications:** • In combination with endocrine therapy (tamoxifen or an aromatase inhibitor) for the adjuvant treatment of adult individuals with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive, early breast cancer at high risk of recurrence **OR** • In combination with an aromatase inhibitor as initial endocrine-based therapy for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer

Drug	Medical Necessity
Oral Drugs	
	OR • In combination with fulvestrant for the treatment of hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer in women with disease progression following endocrine therapy **OR** • In combination with imlunestrant for the treatment of adults with estrogen receptor (ER)-positive, HER2-negative, estrogen receptor-1 (ESR1)-mutated advanced or metastatic breast cancer with disease progression following at least 1 line of endocrine therapy **OR** • As monotherapy for the treatment of HR-positive, HER2 – negative advanced or metastatic breast cancer in individuals with disease progression following endocrine therapy and prior chemotherapy in the metastatic setting
Nuclear Export Inhibitors	
Xpovio (selinexor) oral	**Xpovio (selinexor) may be considered medically necessary for treatment of adult individuals with multiple myeloma who have received at least 1 prior therapy when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Xpovio is used in combination with bortezomib and dexamethasone **Xpovio (selinexor) may be considered medically necessary for treatment of adult individuals with relapsed or refractory multiple myeloma (RRMM) who have received at least 4 prior therapies when all the following criteria are met:** • The individual is aged 18 years or older **AND**

Drug	Medical Necessity
Oral Drugs	
	• Has received at least 4 prior therapies and whose disease is refractory to: ○ At least 2 proteasome inhibitors (i.e., bortezomib, carfilzomib, ixazomib) **AND** ○ At least 2 immunomodulatory agents (i.e., lenalidomide, pomalidomide, thalidomide) **AND** ○ An anti-CD-38 monoclonal antibody (i.e., daratumumab, isatuximab-irfc) **AND** • Xpovio is used in combination with dexamethasone
Inhibitor of Tropomyosin Receptor Tyrosine Kinases	
Rozlytrek (entrectinib) oral	**Rozlytrek (entrectinib) may be considered medically necessary for the treatment of:** • Adult individuals with metastatic non-small cell lung cancer (NSCLC) whose tumors are *ROS1*-positive **OR** • Adult and pediatric individuals aged 1 month and older with solid tumors that: ○ Have a neurotrophic tyrosine receptor kinase (NTRK) gene fusion without a known acquired resistance mutation **AND** ○ Are metastatic or where surgical resection is likely to result in severe morbidity **AND** ○ Have no satisfactory alternative treatments or that have progressed following treatment
Vitrakvi (larotrectinib) oral	**Vitrakvi (larotrectinib) may be considered medically necessary for the treatment of adult and pediatric individuals with solid tumors that:** • Have a neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion without a known acquired resistance mutation

Drug	Medical Necessity
Oral Drugs	
	AND • Are metastatic or where surgical resection is likely to result in severe morbidity **AND** • Have no satisfactory alternative treatments or that have progressed following treatment
Nitrosoureas	
• **Gleostine (lomustine) oral** • **Generic lomustine oral**	**Gleostine (lomustine) and generic lomustine may be considered medically necessary for the treatment of individuals with any of the following:** • Primary and metastatic brain tumors following appropriate surgical and/or radiotherapeutic procedures **OR** • Hodgkin's lymphoma whose disease has progressed following initial chemotherapy when used as a component of combination chemotherapy
Janus-Associated Kinase Inhibitors	
• **Jakafi (ruxolitinib)** • **Jakafi XR (ruxolitinib extended-release)**	**Jakafi (ruxolitinib) and Jakafi XR (ruxolitinib extended-release) may be considered medically necessary for the treatment of individuals when all of the following criteria are met:** • The individual meets 1 of the following: ○ Myelofibrosis in adults aged 18 years or older **OR** ○ Polycythemia vera in adults aged 18 years or older, after an inadequate response or intolerance to hydroxyurea **OR** ○ Steroid-refractory acute graft-versus-host disease in adult and pediatric individuals aged 12 years and older **OR** ○ Chronic graft-versus-host disease after an inadequate response to 1 or 2 lines of systemic therapy in adult and pediatric individuals aged 12 years and older **AND**

Drug	Medical Necessity
Oral Drugs	
	• The dose is limited to: ○ Jakafi (ruxolitinib): 50 mg daily ○ Jakafi XR (ruxolitinib extended-release): 55 mg daily
Ojjaara (momelotinib) oral	**Ojjaara (momelotinib) may be considered medically necessary for adults when all of the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with intermediate or high-risk myelofibrosis (MF), including primary MF or secondary MF (post-polycythemia vera and post-essential thrombocythemia) **AND** • Has been diagnosed with transfusion-dependent anemia associated with MF **AND** • Dose is limited to 200 mg daily
Vonjo (pacritinib) oral	**Vonjo (pacritinib) may be considered medically necessary for adults with intermediate or high-risk primary or secondary myelofibrosis when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has intermediate or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis with a platelet count below 50 × 10^9/L **AND** • Dose is limited to 400 mg per day (taken as 200 mg twice daily) **Note:** Documentation for intermediate or high-risk primary myelofibrosis should include a statement about risk stratification and/or genetically inspired prognostic scoring system (GIPSS) of >2 or a GIPSS of 1-2 plus MIPPS70 of >4. Documentation of intermediate or high-risk secondary myelofibrosis should include a statement about risk stratification and record of post-polycythemia vera or post-essential thrombocythemia.

Drug	Medical Necessity
Oral Drugs	
RET Inhibitors	
Gavreto (pralsetinib) oral	**Gavreto (pralsetinib) may be considered medically necessary when:** • Individual meets 1 of the following: ○ Adult individuals with metastatic RET fusion-positive non-small cell lung cancer (NSCLC) **OR** ○ Adult and pediatric individuals aged 12 years and older with advanced or metastatic RET fusion-positive thyroid cancer who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) **AND** • The dose (for all indications) is limited to 400 mg once daily
Retevmo (selpercatinib) oral	**Retevmo (selpercatinib) may be considered medically necessary when:** • The individual meets 1 of the following: ○ Adult individuals with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a *rearranged during transfection (RET)* gene fusion ○ Adult and pediatric individuals aged 2 years and older with advanced or metastatic medullary thyroid cancer (MTC) with a *RET* mutation who require systemic therapy ○ Adult and pediatric individuals aged 2 years and older with advanced or metastatic thyroid cancer with a *RET* gene fusion who require systemic therapy and who are radioactive iodine-refractory (if radioactive iodine is appropriate) ○ Adult and pediatric individuals aged 2 years and older with locally advanced or metastatic solid tumors with a *RET* gene fusion that have progressed on or following prior systemic treatment or who have no satisfactory alternative treatment options

Drug	Medical Necessity
Oral Drugs	
	AND • The dose (for all indications) is limited to: ○ 120 mg twice daily if less than 50 kg ○ 160 mg twice daily if at least 50 kg
Nucleoside Metabolic Inhibitors	
Onureg (azacitidine) oral	**Onureg (azacitidine) may be considered medically necessary for the treatment of adults individuals with acute myeloid leukemia (AML) when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has AML and achieved first complete remission (CR) or complete remission with incomplete blood count recovery (CRi) following intensive induction chemotherapy and are not able to complete intensive curative therapy. **AND** • Dose is limited to 300 mg once daily for 14 consecutive days followed by 14 days off therapy in 28-day cycles
Purixan (mercaptopurine) oral	**Purixan (mercaptopurine) may be considered medically necessary for the treatment of individuals with acute lymphoblastic leukemia (ALL) as part of a combination chemotherapy maintenance regimen.**
Hypoxia-Inducible Factor Inhibitor	
Welireg (belzutifan) oral	**Welireg (belzutifan) may be considered medically necessary for the treatment of adult individuals with von Hippel-Lindau (VHL) disease when all of the following are met:** • The individual is aged 18 years or older **AND** • Has 1 of the following associated with VHL disease: ○ Renal cell carcinoma (RCC) ○ Central nervous system (CNS) hemangioblastomas ○ Pancreatic neuroendocrine tumors (pNET) **AND** • Is not requiring immediate surgery

Drug	Medical Necessity
Oral Drugs	
	AND • Diagnosis of VHL disease is confirmed by a germline alteration in the VHL gene **AND** • Dose is limited to 120 mg once daily **Welireg (belzutifan) may be considered medically necessary for the treatment of adult individuals with renal cell carcinoma with a clear cell component (ccRCC) when all of the following are met:** • The individual is aged 18 years or older **AND** • Meets 1 of the following: ○ Used in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, for the adjuvant treatment of adult individuals with ccRCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions ○ Has been diagnosed with advanced ccRCC previously treated with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor, AND a vascular endothelial growth factor (VEGF) tyrosine kinase inhibitor **AND** • The dose is limited to 120 mg once daily **Welireg (belzutifan) may be considered medically necessary for the treatment of individuals with locally advanced, unresectable, or metastatic pheochromocytoma or paraganglioma (PPGL) when all of the following are met:** • The individual is aged 12 years or older

Drug	Medical Necessity
Oral Drugs	
	AND • Has been diagnosed with locally advanced, unresectable, or metastatic pheochromocytoma or PPGL **AND** • Dose is limited to 120 mg once daily
Isocitrate Dehydrogenase-1 (IDH1) Inhibitor	
Rezlidhia (olutasidenib) oral	**Rezlidhia (olutasidenib) may be considered medically necessary for the treatment of adult individuals with relapsed or refractory acute myeloid leukemia (AML) when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has a susceptible isocitrate dehydrogenase-1 (IDH1) mutation.
Isocitrate Dehydrogenase-1 (IDH1) and Isocitrate Dehydrogenase-2 (IDH2) Inhibitor	
Voranigo (vorasidenib) oral	**Voranigo (vorasidenib) may be considered medically necessary for the treatment of Grade 2 astrocytoma or oligodendroglioma when all the following criteria are met:** • The individual is aged 12 years or older **AND** • Has been diagnosed with Grade 2 astrocytoma or oligodendroglioma **AND** • Has a susceptible IDH1 or IDH2 mutation **AND** • Voranigo (vorasidenib) is used following surgery including biopsy, sub-total resection, or gross total resection **AND** • Voranigo (vorasidenib) is prescribed by or in consultation with an oncologist **AND** • Dose is limited to 40 mg daily
Menin Inhibitor Oral Agents	

Drug	Medical Necessity
Oral Drugs	
Komzifti (ziftomenib) oral	**Komzifti (ziftomenib) may be considered medically necessary for the treatment of adult individuals with relapsed or refractory acute myeloid leukemia (AML) when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with relapsed or refractory acute myeloid leukemia (AML) with a susceptible nucleophosmin 1 (NPM1) mutation **AND** • There are no satisfactory alternative treatment options **AND** • Medication is prescribed by or in consultation with an oncologist or hematologist **AND** • The dose is limited to 600 mg daily
Revuforj (revumenib) oral	**Revuforj (revumenib) may be considered medically necessary for the treatment of acute leukemia when all the following are met:** • The individual is aged 1 year or older **AND** • Meets 1 of the following: ○ Has been diagnosed with relapsed or refractory acute leukemia with a lysine methyltransferase 2A gene (KMT2A) translocation **OR** ○ Has been diagnosed with acute myelocytic leukemia with a lysine methyltransferase 2A gene (KMT2A) translocation **AND** • Dose is limited to 540 mg daily

Drug	Medical Necessity
Oral Drugs	
	Revuforj (revumenib) may be considered medically necessary for the treatment of acute myeloid leukemia (AML) when all the following are met: • The individual is aged 1 year or older **AND** • Has been diagnosed with relapsed or refractory AML with a susceptible nucleophosmin 1 (NPM1) mutation **AND** • There are no satisfactory alternative treatment options **AND** • Dose is limited to 540 mg daily
Miscellaneous Oral Agents	
Balversa (erdafitinib) oral	**Balversa (erdafitinib) may be considered medically necessary for treatment of adult individuals with locally advanced or metastatic urothelial carcinoma (mUC) when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has locally advanced or metastatic urothelial carcinoma that has susceptible FGFR3 (fibroblast growth factor receptor) genetic alterations **AND** • Has progressed during or following at least 1 line of prior systemic therapy
Inqovi (decitabine and cedazuridine) oral	**Inqovi (decitabine and cedazuridine) may be considered medically necessary for any of the following:** • Treatment of adult individuals with myelodysplastic syndromes (MDS), including previously treated and untreated, de novo and secondary MDS **OR** • In combination with venetoclax for the treatment of newly diagnosed acute myeloid leukemia (AML) in adult individuals

Drug	Medical Necessity
Oral Drugs	
	aged 75 years or older, OR who have comorbidities that preclude use of intensive induction chemotherapy
Inrebic (fedratinib) oral	**Inrebic (fedratinib) may be considered medically necessary for treatment of adult individuals with intermediate-2 or high-risk primary or secondary (post-polycythemia vera or post-essential thrombocythemia) myelofibrosis (MF) when:** • The dose is limited to 400 mg daily **Note:** Documentation for intermediate-2 or high-risk primary myelofibrosis should include a statement about risk stratification and/or genetically inspired prognostic scoring system (GIPSS) of ≥2. Documentation of intermediate-2 or high-risk secondary myelofibrosis should include a statement about risk stratification and record of post-polycythemia vera or post-essential thrombocythemia.
Iwilfin (eflornithine) oral	**Iwilfin (eflornithine) may be considered medically necessary for the treatment of adult and pediatric individuals with high-risk neuroblastoma when all of the following are met:** • The individual is diagnosed with high-risk neuroblastoma **AND** • Has demonstrated at least a partial response to prior multiagent, multimodality therapy including anti-GD2 immunotherapy (e.g., naxitamab-gqgk or dinutuximab) **AND** • Dose is limited to 768 mg twice daily
Krazati (adagrasib) oral	**Krazati (adagrasib) may be considered medically necessary for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with KRAS G12C-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) **AND** • Has received at least 1 prior systemic therapy

Drug	Medical Necessity
Oral Drugs	
	AND • Dose is limited to 1,200 mg per day (taken as 600 mg twice daily)
Leukeran (chlorambucil) oral	**Leukeran (chlorambucil) may be considered medically necessary of adult individuals when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with 1 of the following: ○ Chronic lymphatic (lymphocytic) leukemia ○ Malignant lymphomas including lymphosarcoma, giant follicular lymphoma, and Hodgkin's disease **AND** • Dose is limited to 0.2 mg/kg daily
Lifyorli (relacorilant)	**Lifyorli (relacorilant) may be considered medically necessary for the treatment of adult individuals with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer **AND** • Has received 1 to 3 prior systemic treatment regimens that included a bevacizumab-containing regimen **AND** • Lifyorli (relacorilant) is used in combination with nab-paclitaxel (paclitaxel protein-bound)
Lonsurf (trifluridine and tipiracil) oral	**Lonsurf (trifluridine and tipiracil) may be considered medically necessary for treatment of adult individuals with metastatic colorectal cancer as a single agent or in combination with bevacizumab in those who have been:** • Previously treated with fluoropyrimidine, oxaliplatin, and irinotecan-based chemotherapy

Drug	Medical Necessity
Oral Drugs	
	AND • Previously treated with an anti-VEGF biological therapy **AND** • If the tumor is RAS wild-type, previously treated with an anti-EGFR therapy **Lonsurf (trifluridine and tipiracil) may be considered medically necessary for treatment of adult individuals with metastatic gastric or gastroesophageal junction adenocarcinoma who have been:** • Treated with at least 2 prior lines of chemotherapy that included a fluoropyrimidine, a platinum, either a taxane or irinotecan **AND** • If appropriate, HER2/neu-targeted therapy* * Individuals with HER2/neu-positive tumors must have received prior HER2/neu-targeted therapy. Example of HER2/neu-targeted therapy is Herceptin (trastuzumab).
Lumakras (sotorasib) oral	**Lumakras (sotorasib) may be considered medically necessary for the treatment of locally advanced or metastatic non-small cell lung cancer (NSCLC) when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with KRAS G12C-mutated locally advanced or metastatic NSCLC, as determined by an FDA-approved test **AND** • Has received at least 1 prior systemic therapy **AND** • Dose is limited to 960 mg per day

Drug	Medical Necessity
Oral Drugs	
	Lumakras (sotorasib) may be considered medically necessary for the treatment of KRAS G12C-mutated metastatic colorectal cancer (mCRC) when all the following criteria are met: • The individual is aged 18 years or older **AND** • Has been diagnosed with KRAS G12C-mutated mCRC **AND** • Has received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy **AND** • Will be used in combination with Vectibix (panitumumab) **AND** • Dose is limited to 960 mg per day
Lysodren (mitotane) oral	**Lysodren (mitotane) may be considered medically necessary for the treatment of inoperable, functional or nonfunctional, adrenal cortical carcinoma.**
Lytgobi (futibatinib) oral	**Lytgobi (futibatinib) may be considered medically necessary for the treatment of previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with previously treated, unresectable, locally advanced or metastatic intrahepatic cholangiocarcinoma **AND** • Is harboring fibroblast growth factor receptor 2 (FGFR2) gene fusions or other rearrangements **AND** • Dose is limited to 20 mg per day
Matulane (procarbazine hydrochloride) oral	**Matulane (procarbazine hydrochloride) may be considered medically necessary when all the following are met:**

Drug	Medical Necessity
Oral Drugs	
	• The individual is diagnosed with stage III or IV Hodgkin's disease **AND** • Matulane (procarbazine hydrochloride) is used in combination with other anticancer drugs
Modeyso (dordaviprone) oral	**Modeyso (dordaviprone) may be considered medically necessary for the treatment of diffuse midline glioma when all the following are met:** • The individual is aged 1 year or older **AND** • Has been diagnosed with diffuse midline glioma harboring an H3 K27M mutation **AND** • Has experienced disease progression following prior therapy **AND** • Dose is limited to 625 mg weekly
Ninlaro (ixazomib) oral	**Ninlaro (ixazomib) may be considered medically necessary for the treatment of individuals with multiple myeloma when all the following criteria are met:** • The individual has received at least 1 prior therapy **AND** • Ninlaro is used in combination with lenalidomide and dexamethasone
Ogsiveo (nirogacestat) oral	**Ogsiveo (nirogacestat) may be considered medically necessary when all of the following are met:** • The individual is aged 18 years or older **AND** • Is diagnosed with progressing desmoid tumors that require systemic treatment **AND** • Has tried and had an inadequate response or intolerance to generic sorafenib **AND**

Drug	Medical Necessity
Oral Drugs	
	• Dose is limited to 150 mg twice daily
Pemazyre (pemigatinib) oral	**Pemazyre (pemigatinib) may be considered medically necessary for the treatment of:** • Adults with previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with a fibroblast growth factor receptor 2 (FGFR2) fusion or other rearrangement as detected by an FDA-approved test **AND** • The dose is limited to 13.5 mg once daily for 14 consecutive days followed by 7 days off therapy in 21-day cycles **Pemazyre (pemigatinib) may be considered medically necessary for the treatment of:** • Adults with relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with fibroblast growth factor receptor 1 (FGFR1) rearrangement **AND** • The dose is limited to 13.5 mg once daily
Romvimza (vimseltinib) oral	**Romvimza (vimseltinib) may be considered medically necessary for the treatment of tenosynovial giant cell tumor (TGCT) when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with symptomatic TGCT **AND** • Surgical resection will potentially cause worsening functional limitation or severe morbidity **AND** • Romvimza (vimseltinib) is prescribed by or in consultation with an oncologist **AND** • Dose is limited to 30 mg twice weekly

Drug	Medical Necessity
Oral Drugs	
Rydapt (midostaurin) oral	**Rydapt (midostaurin) may be considered medically necessary for the treatment of adult individuals with:** • Newly diagnosed acute myeloid leukemia (AML) that is FLT3 mutation-positive as detected by an FDA-approved test, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation ○ Documentation of genetic testing is required for coverage consideration • Aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN), or mast cell leukemia (MCL) **Note:** Rydapt is not indicated as a single-agent induction therapy for the treatment of individuals with AML
Generic temozolomide oral	**Generic temozolomide may be considered medically necessary for the treatment of adult individuals when all of the following are met:** • The individual is aged 18 years or older **AND** • Meets 1 of the following: ○ Is diagnosed with glioblastoma and generic temozolomide will be used concomitantly with radiotherapy, and then as maintenance treatment **OR** ○ Is diagnosed with anaplastic astrocytoma and temozolomide is used as first-line therapy **OR** ○ Is diagnosed with refractory anaplastic astrocytoma
Thalomid (thalidomide) oral	**Thalomid (thalidomide) may be considered medically necessary for the treatment of individuals with:** • Newly diagnosed multiple myeloma when used in combination with dexamethasone **OR**

Drug	Medical Necessity
Oral Drugs	
	• Cutaneous manifestations of moderate to severe erythema nodosum leprosum (ENL)
Vistogard (uridine triacetate) oral	**Vistogard (uridine triacetate) may be considered medically necessary for the emergency treatment of adult and pediatric individuals:** • Fluorouracil or capecitabine overdose regardless of the presence of symptoms **OR** • Early-onset, severe or life-threatening toxicity affecting cardiac or central nervous system OR early-onset, unusually severe adverse reactions (e.g., gastrointestinal toxicity or neutropenia) within 96 hours (4 days) following the end of fluorouracil or capecitabine administration
Vitrakvi (larotrectinib) oral	**Vitrakvi (larotrectinib) may be considered medically necessary for the treatment of adult and pediatric individuals with solid tumors that:** • Have a neurotrophic receptor tyrosine kinase (*NTRK*) gene fusion without a known acquired resistance mutation **AND** • Are metastatic or where surgical resection is likely to result in severe morbidity **AND** • Have no satisfactory alternative treatments or that have progressed following treatment
Xeloda (capecitabine) oral	**Xeloda (capecitabine) may be considered medically necessary for the treatment of adults when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with 1 of the following: ○ Breast cancer ○ Colon cancer ○ Esophageal and esophagogastric junction cancer ○ Gastric cancer

Drug	Medical Necessity
Oral Drugs	
	○ Pancreatic adenocarcinoma **AND** • Has tried and had an inadequate response or intolerance to generic capecitabine

Drug	Medical Necessity
Interferon Agents	
Intron A (interferon alfa-2b) IL, IM, IV, SC	**Intron A (interferon alfa-2b) may be considered medically necessary for the treatment of individuals with:** • Hairy cell leukemia and are aged 18 years or older (route is IM, SC) • Malignant melanoma as adjuvant to surgical treatment in individuals aged 18 years and older who are free of disease but at high risk for systemic recurrence within 56 days of surgery (route is IV, SC) • Clinically aggressive follicular Non-Hodgkin's Lymphoma in conjunction with anthracycline-containing combination chemotherapy in individuals aged 18 years and older (route is SC) • Condylomata acuminata involving external surfaces of the genital and perianal areas for intralesional treatment of individuals aged 18 years and older (route is intralesional [IL]) • AIDS Related Kaposi's Sarcoma in individuals aged 18 years and older (route is IM, SC) • Chronic hepatitis C in individuals aged 18 years and older with compensated liver disease who have a history of blood or blood-product exposure and/or are HCV antibody positive (route is IM, SC) • Chronic hepatitis C, when used in combination with ribavirin, in individuals 3 years of age and older with compensated liver disease previously untreated with alpha interferon therapy and

Drug	Medical Necessity
	in individuals aged 18 years and older who have relapsed following alpha interferon therapy (route is IM, SC) • Chronic hepatitis B in individuals aged 1 year and older with compensated liver disease and who have been serum HBsAg positive for at least 6 months and have evidence of HBV replication (serum HBeAg positive) with elevated serum ALT (route is IM, SC)
Sylatron (peginterferon alfa-2b) SC	**Sylatron (peginterferon alfa-2b) may be considered medically necessary for the treatment of adult individuals for:** • The adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
• **Abraxane (paclitaxel protein-bound particles) IV** • **Brand paclitaxel protein-bound particles (American Regent-unbranded) IV** • **Brand paclitaxel protein-bound particles (Teva-unbranded) IV**	**Abraxane (paclitaxel protein-bound particles), brand paclitaxel protein-bound particles (American Regent – unbranded), and brand paclitaxel protein-bound particles (Teva – unbranded) may be considered medically necessary for the treatment of individuals in one of the following situations:** • Metastatic breast cancer, after failure of combination chemotherapy for metastatic disease or relapse within 6 months of adjuvant chemotherapy. Prior therapy must include an anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin) unless clinically contraindicated **OR** • Locally advanced or metastatic non-small cell lung cancer (NSCLC), as first-line treatment in combination with carboplatin, in individuals who are not candidates for curative surgery or radiation therapy **OR** • Metastatic adenocarcinoma of the pancreas as first-line treatment, in combination with gemcitabine

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	OR • Adult individuals with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received 1 to 3 prior systemic treatment regimens, which included a bevacizumab-containing regimen, and when used in combination with Lifyorli (relacorilant) **OR** • As an alternative to paclitaxel when there has been a documented paclitaxel infusion reaction
Amtagvi (lifileucel) IV	**Amtagvi (lifileucel) may be considered medically necessary for the treatment of individuals with unresectable or metastatic melanoma when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with unresectable or metastatic melanoma **AND** • Has been treated with a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) blocking antibody such as pembrolizumab, nivolumab, or atezolizumab **AND** • Is *BRAF* V600 mutation-positive, the individual has been treated with a BRAF inhibitor with or without a MEK inhibitor **AND** • Has not been previously treated with Amtagvi (lifileucel) **AND** • Amtagvi (lifileucel) is prescribed by or in consultation with an oncologist
Aphexda (motixafortide) SC	**Aphexda (motixafortide) may be considered medically necessary to mobilize hematopoietic stem cells for collection and subsequent autologous transplantation in individuals with multiple myeloma when all the following are met:** • The individual has been histologically diagnosed with multiple myeloma

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	AND • Is eligible for autologous hematopoietic stem cell transplant **AND** • Documentation of a valid medical rationale is provided for why the individual is not able to use generic plerixafor
Arranon (nelarabine) IV, Generic nelarabine IV	**Arranon (nelarabine) and generic nelarabine may be considered medically necessary for the treatment of individuals with T-cell acute lymphoblastic leukemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL) in adult and pediatric individuals age 1 year and older whose disease has not responded to or has relapsed following treatment with at least 2 chemotherapy regimens OR as first-line therapy when added to the ABFM (augmented Berlin-Frankfurter Muenster) regimen in intermediate to high-risk individuals or ABFM regimen induction failures.** **Note**: The ABFM induction therapy consists of vincristine, daunorubicin, prednisone, asparaginase, intrathecal cytarabine, and intrathecal methotrexate.
Asparlas (calaspargase pegol - mknl) IV	**Asparlas (calaspargase pegol - mknl) may be considered medically necessary as a component of a multi-agent chemotherapeutic regimen for the treatment of:** • Acute lymphoblastic leukemia in pediatric and young adult individuals aged 1 month to 21 years
• **Beizray (docetaxel) IV** • **Docivyx (docetaxel) IV**	**Beizray (docetaxel) and Docivyx (docetaxel) may be considered medically necessary when used:** • As a single agent for locally advanced or metastatic breast cancer after chemotherapy failure • In combination with doxorubicin and cyclophosphamide as adjuvant treatment of operable node-positve breast cancer • In combination with carboplatin, trastuzumab with/without pertuzumab as neoadjuvant or adjuvant therapy for previously untreated, recurrent, or metastatic HER2-positive breast cancer

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• As a single agent for locally advanced or metastatic non-small cell lung cancer (NSCLC) after platinum therapy failure • In combination with cisplatin for unresectable, locally advanced or metastatic untreated NSCLC • In combination with prednisone in metastatic castration-resistant prostate cancer • In combination with cisplatin and fluorouracil for untreated, advanced gastric adenocarcinoma, including the gastroesophageal junction • In combination with cisplatin and fluorouracil for induction treatment of locally advanced squamous cell carcinoma of the head and neck
• **Brand bendamustine IV** • **Belrapzo (bendamustine) IV** • **Bendeka (bendamustine) IV** • **Treanda (bendamustine) IV** • **Vivimusta (bendamustine) IV**	**Brand bendamustine, Belrapzo (bendamustine), Bendeka (bendamustine), Treanda (bendamustine), and Vivimusta (bendamustine) may be considered medically necessary for the treatment of individuals with:** • Chronic lymphocytic leukemia (CLL) • Indolent B-cell non-Hodgkin lymphoma (NHL) that has progressed during or within 6 months of treatment with rituximab or a rituximab-containing regimen • Follicular lymphoma when used in combination with rituximab • Previously untreated mantle cell lymphoma (MCL) in individuals who are ineligible for autologous hematopoietic stem cell transplantation (HSCT) and bendamustine is being used in combination with Calquence (acalabrutinib) and rituximab
Blenrep (belantamab mafodotin-blmf) IV	**Blenrep (belantamab mafodotin-blmf) may be considered medically necessary for the treatment of adult individuals with relapsed or refractory multiple myeloma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has received at least 2 prior lines of therapy including a proteasome inhibitor (PI) (i.e., bortezomib, carfilzomib,

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	ixazomib) and an immunomodulatory agent (i.e., lenalidomide, pomalidomide, thalidomide) **AND** • Do not currently have a documented corneal epithelial disease **AND** • Blenrep is used in combination with bortezomib and dexamethasone for the first 8 cycles, then continued as monotherapy
• **Generic clofarabine IV** • **Clolar (clofarabine) IV**	**Generic clofarabine and Clolar (clofarabine) may be considered medically necessary in individuals aged 1 to 21 years with relapsed or refractory acute lymphoblastic leukemia after at least two prior regimens.**
Cosela (trilaciclib) IV	**Cosela (trilaciclib) may be considered medically necessary to decrease the incidence of chemotherapy-induced myelosuppression in adult individuals when administered prior to a platinum (e.g., cisplatin, carboplatin, oxaliplatin)/etoposide-containing regimen or topotecan containing regimen for extensive-stage small cell lung cancer.**
Dacogen (decitabine) IV	**Dacogen (decitabine) may be considered medically necessary for the treatment of adults with myelodysplastic syndromes (MDS) when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with MDS* **AND** • Has tried and had an inadequate response to generic decitabine **Note:** Including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups **Dacogen (decitabine) may be considered medically necessary for the treatment of acute myeloid leukemia when the individual has tried and had an inadequate response to generic decitabine**
• **Cosmegen (dactinomycin) IV** • **Dactinomycin IV**	**Cosmegen (dactinomycin) and dactinomycin may be considered medically necessary for the treatment of:** • Wilms tumor when used in combination with other anticancer drugs • Rhabdomyosarcoma when used in combination with other anticancer drugs • Ewing sarcoma when used in combination with other anticancer drugs • Metastatic, nonseminomatous testicular cancer when used in combination with other anticancer drugs • Post-menarchal individuals with gestational trophoblastic neoplasia, as a single agent or in combination with other anticancer drugs • Adults with locally recurrent or locoregional solid malignancies, as a component of palliative or adjunctive regional perfusion
Danyelza (naxitamab-gqgk) IV	**Danyelza (naxitamab-gqgk), in combination with GM-CSF (e.g., sargramostim), may be considered medically necessary for the treatment of pediatric individuals 1 year of age and older and adult individuals with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy.**
Darzalex (daratumumab) IV	**Darzalex (daratumumab) may be considered medically necessary for the treatment of adult individuals with high-risk smoldering multiple myeloma when all the following are met:**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• The individual is aged 18 years or older **AND** • Percentage of clonal plasma cells in bone marrow of at least 10% **AND** • 1 of the following risk factors: ○ Serum M-protein level of at least 30 g/L ○ IgA smoldering multiple myeloma ○ Immunoparesis with reduced levels of two uninvolved immunoglobulin isotypes ○ Ratio of involved free light chains to uninvolved free light chains (FLC ratio) in serum of 8 to 99 ○ Percentage of clonal plasma cells in bone marrow of 51% to 59% **Darzalex (daratumumab) may be considered medically necessary for the treatment of adult individuals with multiple myeloma when used:** • In combination with lenalidomide and dexamethasone as first-line therapy and in individuals with relapsed or refractory multiple myeloma who have received at least 1 prior therapy • In combination with bortezomib, melphalan and prednisone as first-line therapy • In combination with bortezomib, thalidomide, and dexamethasone as first-line therapy in individuals who are eligible for autologous stem cell transplant • In combination with Kyprolis (carfilzomib), lenalidomide, and dexamethasone as first-line treatment • In combination with bortezomib and dexamethasone in individuals who have received at least 1 prior therapy • In combination with Kyprolis (carfilzomib) and dexamethasone in individuals with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• In combination with pomalidomide and dexamethasone in individuals who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor (i.e., bortezomib, carfilzomib, ixazomib) • As monotherapy, in individuals who have received at least 3 prior lines of therapy including a proteasome inhibitor (PI) (i.e., bortezomib, carfilzomib, ixazomib) and an immunomodulatory agent (i.e., lenalidomide, pomalidomide, thalidomide) or who are refractory to a PI and an immunomodulatory agent
Darzalex Faspro (daratumumab and hyaluronidase-fihj) SC	**Darzalex Faspro (daratumumab and hyaluronidase-fihj) may be considered medically necessary for the treatment of adult individuals with light chain (AL) amyloidosis when used:** • In combination with bortezomib, cyclophosphamide, and dexamethasone as first-line therapy **Darzalex Faspro (daratumumab and hyaluronidase-fihj) may be considered medically necessary for the treatment of adult individuals with high-risk smoldering multiple myeloma when all the following are met:** • The individual is aged 18 years or older **AND** • Percentage of clonal plasma cells in bone marrow of at least 10% **AND** • 1 of the following risk factors: ○ Serum M-protein level of at least 30 g/L ○ IgA smoldering multiple myeloma ○ Immunoparesis with reduced levels of two uninvolved immunoglobulin isotypes ○ Ratio of involved free light chains to uninvolved free light chains (FLC ratio) in serum of 8 to 99 ○ Percentage of clonal plasma cells in bone marrow of 51% to 59%

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	Darzalex Faspro (daratumumab and hyaluronidase-fihj) may be considered medically necessary for the treatment of adult individuals with multiple myeloma when used: • In combination with bortezomib, lenalidomide, and dexamethasone for induction and consolidation in newly diagnosed individuals who are eligible for autologous stem cell transplant • In combination with bortezomib, lenalidomide, and dexamethasone in newly diagnosed individuals who are ineligible for autologous stem cell transplant • In combination with lenalidomide and dexamethasone as first-line therapy and in individuals with relapsed or refractory multiple myeloma who have received at least 1 prior therapy • In combination with bortezomib, melphalan and prednisone as first-line therapy • In combination with bortezomib, thalidomide, and dexamethasone as first-line therapy in individuals who are eligible for autologous stem cell transplant • In combination with bortezomib and dexamethasone in individuals who have received at least 1 prior therapy • In combination with pomalidomide and dexamethasone in individuals who have received at least 1 prior line of therapy including lenalidomide and a proteasome inhibitor (PI) (i.e., bortezomib, carfilzomib, ixazomib) • In combination with Tecvayli (teclistamab-cqyv) in individuals with relapsed or refractory multiple myeloma who have received at least 1 prior line of therapy including a proteasome inhibitor (PI) (i.e., bortezomib, carfilzomib, ixazomib) and an immunomodulatory agent (i.e., lenalidomide, pomalidomide, thalidomide)

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• In combination with Kyprolis (carfilzomib) and dexamethasone in individuals with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy • As monotherapy, in individuals who have received at least 3 prior lines of therapy including a proteasome inhibitor (PI) (i.e., bortezomib, carfilzomib, ixazomib) and an immunomodulatory agent (i.e., lenalidomide, pomalidomide, thalidomide) or who are refractory to a PI and an immunomodulatory agent
Generic decitabine IV	**Generic decitabine may be considered medically necessary for the treatment of adults with myelodysplastic syndromes (MDS) when all the following are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with MDS* * Including previously treated and untreated, de novo and secondary MDS of all French-American-British subtypes (refractory anemia, refractory anemia with ringed sideroblasts, refractory anemia with excess blasts, refractory anemia with excess blasts in transformation, and chronic myelomonocytic leukemia) and intermediate-1, intermediate-2, and high-risk International Prognostic Scoring System groups **Generic decitabine may be considered medically necessary for the treatment of acute myeloid leukemia**
Decnupaz (pivekimab sunirine-pvzy) IV	**Decnupaz (pivekimab sunirine-pvzy) may be considered medically necessary for the treatment of adult individuals with blastic plasmacytoid dendritic cell neoplasm (BPDCN) when the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with CD-123 expressing BPDCN **AND** • Does not have:

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	○ Central nervous system (CNS) involvement ○ Veno-occlusive disease of the liver **AND** • Decnupaz (pivekimab sunirine-pvzy) will not be used in combination with Elzonrys (tagraxofusp-erzs) **AND** • Medication is prescribed by or in consultation with a hematologist or oncologist **AND** • The dose is limited to 0.045 mg/kg every 3 weeks
• **Doxil (doxorubicin hydrochloride liposome) IV** • **Generic doxorubicin hydrochloride liposome IV**	**Doxil (doxorubicin hydrochloride liposome) and generic doxorubicin hydrochloride liposome may be considered medically necessary when:** • The individual meets 1 of the following: ○ Ovarian cancer after failure of platinum-based chemotherapy **OR** ○ AIDS-related Kaposi's sarcoma after failure of prior systemic chemotherapy **OR** ○ Multiple myeloma in combination with bortezomib in individuals who have not previously received bortezomib AND have received at least one prior therapy **AND** • Dose is limited to the following: ○ 50 mg/m^2 every 4 weeks for ovarian cancer ○ 20 mg/m^2 every 3 weeks for AIDS-related Kaposi's sarcoma ○ 30 mg/m^2 every 3 weeks for multiple myeloma
Elitek (rasburicase) IV	**Elitek (rasburicase) may be considered medically necessary for the initial management of plasma uric acid levels in individuals with leukemia, lymphoma, or solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis and subsequent elevation of plasma uric acid**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
Elzonris (tagraxofusp-erzs) IV	**Elzonris (tagraxofusp-erzs) may be considered medically necessary for the treatment of individuals with blastic plasmacytoid dendritic cell neoplasm (BPDCN) when the following criteria are met:** • The individual is aged 2 years and older **AND** • Has been diagnosed with BPDCN **AND** • Elzonrys (tagraxofusp-erzs) will not be used in combination with Decnupaz (pivekimab sunirine-pvzy) **AND** • Medication is prescribed by or in consultation with a hematologist or oncologist
Empliciti (elotuzumab) IV	**Empliciti (elotuzumab) may be considered medically necessary:** • In combination lenalidomide and dexamethasone for the treatment of adult individuals with multiple myeloma who have received 1 to 3 prior therapies • In combination with pomalidomide and dexamethasone for the treatment of adult individuals with multiple myeloma who have received at least 2 prior therapies including lenalidomide and a proteasome inhibitor (i.e., bortezomib, carfilzomib, ixazomib)
Erwinaze (asparaginase *Erwinia chrysanthemi*) IM, IV	**Erwinaze (asparaginase *Erwinia chrysanthemi*) may be considered medically necessary as a component of a multi-agent chemotherapeutic regimen for the treatment of individuals with acute lymphoblastic leukemia (ALL) who have developed hypersensitivity to *E. coli*-derived asparaginase (e.g., Oncaspar [pegaspargase], Asparlas [calaspargase pegol – mknl])**
Evomela (melphalan) IV	**Evomela (melphalan) may be considered medically necessary for use as a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation.**
Floxuridine intra-arterial	**Floxuridine may be considered medically necessary for the palliative management of gastrointestinal adenocarcinoma**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	metastatic to the liver in individuals who are considered incurable by surgery or other means.
Gazyva (obinutuzumab) IV	**Gazyva (obinutuzumab) may be considered medically necessary:** • In combination with chlorambucil, for previously untreated chronic lymphocytic leukemia (CLL) • In combination with venetoclax for CLL • In combination with bendamustine followed by Gazyva monotherapy, for relapsed or refractory follicular lymphoma, following a rituximab-containing regimen • In combination with chemotherapy followed by Gazyva monotherapy in individuals achieving at least a partial remission, for the treatment of adult individuals with previously untreated stage II bulky, III or IV follicular lymphoma • In combination with zanubrutinib in adults diagnosed with relapsed or refractory follicular lymphoma who have received 2 or more lines of systemic therapy **Gazyva (obinutuzumab) may be considered medically necessary for the treatment of adult individuals with active lupus nephritis when the following criteria are met:** • The individual is aged 18 years or older **AND** • Has a diagnosis of SLE confirmed using either the American College of Rheumatology (**ACR** or **EULAR/ACR**) or Systemic Lupus International Collaborating Clinics (**SLICC**) criteria **AND** • Gazyva (obinutuzumab) will be used in combination with mycophenolate, cyclophosphamide, azathioprine, or an immunosuppressant AND a corticosteroid **AND** • Has class III (focal proliferative), class IV (diffuse proliferative), and/or class V (membranous) lupus nephritis

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	AND • No previous use of dialysis in the past 12 months **AND** • Gazyva (obinutuzumab) is not used concurrently with Lupkynis (voclosporin) or Benlysta (belimumab) for the treatment of active lupus nephritis **AND** • Gazyva (obinutuzumab) is prescribed by or in consultation with a nephrologist or rheumatologist
Grafapex (treosulfan) IV	**Grafapex (treosulfan) may be considered medically necessary if all of the following are met:** • The individual is aged 1 year or older **AND** • Has a diagnosis of acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) **AND** • Is in complete hematological remission (first or consecutive) **AND** • Has not had a previous allogeneic hematopoietic stem cell transplantation (alloHSCT) **AND** • Confirmed availability of a matched-related donor or matched-unrelated donor identified by molecular typing (one antigen [class I] OR one allele [class II] disparity, or both, accepted) **AND** • Grafapex (treosulfan) is given as part of a conditioning regimen with fludarabine for alloHSCT **AND** • Prescribed by, or in consultation with, an oncologist or hematologist **AND** • Dose is limited to 10 g/m^2 given daily for 3 days

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
• **Generic eribulin mesylate** • **Halaven (eribulin mesylate) IV**	**Generic eribulin mesylate and Halaven (eribulin mesylate) may be considered medically necessary for the treatment of individuals with:** • Metastatic breast cancer who have previously received at least 2 chemotherapeutic regimens for the treatment of metastatic disease. Unless clinically contraindicated prior therapy must include an anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin) and a taxane (e.g., docetaxel, paclitaxel) in either the adjuvant or metastatic setting • Unresectable or metastatic liposarcoma who have received a prior anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin) containing regimen
Hepzato Kit (melphalan hepatic delivery system) intra-arterial	**Hepzato Kit (melphalan hepatic delivery system) may be considered medically necessary if all of the following are met:** • The individual is aged 18 years or older **AND** • Has a diagnosis of unresectable or metastatic uveal melanoma **AND** • Has histologically or cytologically-proven ocular melanoma metastases affecting less than 50% of the parenchyma of the liver **AND** • Has disease that is limited to the bone, lymph, nodes, subcutaneous tissues, or lung and is amenable to resection or radiation **AND** • Has at least 100,000 platelets/μL at the time of treatment **AND** • Has an absolute neutrophil count (ANC) of at least 1,500 cells/μL at the time of treatment **AND** • Has not received more than six treatments

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
Inlexzo (gemcitabine intravesical system) Intravesical	**Inlexzo (gemcitabine intravesical system) may be considered medically necessary for the treatment of Bacillus Calmette-Guérin (BCG)-unresponsive, non-muscle invasive bladder cancer (NMIBC) when all the following are met:** • The individual is aged 18 years or older **AND** • Has a diagnosis of BCG-unresponsive NMIBC with carcinoma *in situ* (CIS) with or without papillary tumors **AND** • Dose is limited to 225 mg every 3 weeks up to 6 months followed by once every 12 weeks
IVRA (melphalan) IV	**IVRA (melphalan) may be considered medically necessary for the palliative treatment of individuals with multiple myeloma for whom oral therapy is not appropriate.**
Ixempra (ixabepilone) IV	**Ixempra (ixabepilone) may be considered medically necessary when used in combination with capecitabine for the treatment of metastatic or locally advanced breast cancer when all the following are met:** • The individual has been diagnosed with metastatic or locally advanced breast cancer **AND** • Cancer is resistant to treatment with an anthracycline and a taxane OR cancer is taxane resistant and anthracycline therapy is contraindicated **AND** • Will be used in combination with capecitabine **AND** • Dose is limited to 40 mg/m^2 every 3 weeks **Ixempra (ixabepilone) may be considered medically necessary as a single agent for the treatment of metastatic or locally advanced breast cancer when all the following are met:**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• The individual has been diagnosed with metastatic or locally advanced breast cancer **AND** • Had an inadequate response to an anthracycline, a taxane, and capecitabine **AND** • Will be used as a single agent **AND** • Dose is limited to 40 mg/m^2 every 3 weeks
Jelmyto (mitomycin) Intravesical	**Jelmyto (mitomycin) may be considered medically necessary for the treatment of adult individuals with low-grade upper tract urothelial cancer (LG-UTUC).**
Kepivance (palifermin) IV	**Kepivance (palifermin) may be considered medically necessary to decrease the incidence and duration of severe oral mucositis if all the following are met:** • The individual has hematologic malignancies and is receiving myelotoxic therapy in the setting of autologous hematopoietic stem cell support **AND** • Dose is limited to 60 mcg/kg/day for 3 consecutive days before and 3 consecutive days after myelotoxic therapy for a total of 6 doses
Khapzory (levoleucovorin) IV	**Khapzory (levoleucovorin) may be considered medically necessary when:** • The individual meets 1 of the following: ○ Rescue after high-dose methotrexate therapy in individuals with osteosarcoma **OR** ○ Diminishing the toxicity associated with overdosage of folic acid antagonists or impaired methotrexate elimination **OR** ○ Adults with metastatic colorectal cancer in combination with fluorouracil

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	AND • The individual has tried and had an inadequate response or intolerance to generic levoleucovorin
Kimmtrak (tebentafusp-tebn) IV	**Kimmtrak (tebentafusp-tebn) may be considered medically necessary for the treatment of HLA-A*02:01-positive adult individuals with unresectable or metastatic uveal melanoma.**
Kyprolis (carfilzomib) IV	**Kyprolis (carfilzomib) may be considered medically necessary for the treatment of adult individuals when used:** • As first-line treatment for individuals with multiple myeloma when used in combination with daratumumab, lenalidomide, and dexamethasone **OR** • For the treatment of individuals with relapsed or refractory multiple myeloma who have received 1 to 3 lines of therapy In combination with: ○ Dexamethasone ○ Lenalidomide plus dexamethasone ○ Darzalex (daratumumab) plus dexamethasone ○ Darzalex Faspro (daratumumab and hyaluronidase-fihj) plus dexamethasone ○ Isatuximab plus dexamethasone **OR** • As a single agent for the treatment of individuals with relapsed or refractory multiple myeloma who have received 1 or more lines of therapy
Leukine (sargramostim) IV, SC	**Leukine (sargramostim) may be considered medically necessary for:** • Acute myeloid leukemia following induction chemotherapy • Mobilization and following transplantation of autologous peripheral blood progenitor cells • Myeloid reconstitution after (allogenic or autologous) bone marrow transplantation

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• Bone marrow transplantation (allogenic or autologous) failure or engraftment delay • Exposure to myelosuppressive doses of radiation (Hematopoietic Syndrome of Acute Radiation Syndrome) • In combination with Danyelza (naxitamab-gqgk) for the treatment of pediatric individuals aged 1 year and older and adult individuals with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy) • In combination with Unituxin, for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy **Leukine (sargramostim) may be considered medically necessary as second-line therapy for the treated of individuals taking myelosuppressive anti-cancer regimens, at risk of severe febrile neutropenia** to decrease the incidence of infection when documentation for 1 of the following is provided:** • Granix (tbo-filgrastim) or Nivestym (filgrastim-aafi) has been tried and failed **OR** • There is a contraindication to the use of Granix (tbo-filgrastim) and Nivestym (filgrastim-aafi) ****The following types of individuals are considered to be at risk of severe febrile neutropenia:** • Have experienced febrile neutropenia during a previous cycle of treatment with the current chemotherapy regimen **OR**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• Receiving chemotherapy regimen that is expected to result in a 20 % or higher incidence of FN, based on guidelines from the American Society of Clinical Oncology **OR** • With bone marrow impairment **OR** • Have received 2 or more prior chemotherapy regimens or extensive radiation **OR** • With other serious comorbidities (reviewed on a case basis)
Nipent (pentostatin) IV	**Nipent (pentostatin) may be considered medically necessary as a single agent treatment for both untreated and alpha-interferon-refractory hairy cell leukemia in individuals with active disease as defined by clinically significant anemia, neutropenia, thrombocytopenia, or disease related symptoms.**
Oncaspar (pegaspargase) IM/IV	**Oncaspar (pegaspargase) may be considered medically necessary for:** • The first-line treatment of individuals with acute lymphoblastic leukemia (ALL) • The treatment of ALL in individuals with a hypersensitivity to asparaginase
Onivyde (irinotecan liposome injection) IV	**Onivyde (irinotecan liposome injection) may be considered medically necessary for the treatment of adults with:** • Metastatic adenocarcinoma of the pancreas when combined with fluorouracil and leucovorin following disease progression on gemcitabine-based therapy • Metastatic adenocarcinoma of the pancreas when combined with oxaliplatin, fluorouracil, and leucovorin as first-line treatment • Metastatic cholangiocarcinoma when combined with fluorouracil and leucovorin following disease progression on gemcitabine plus cisplatin

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
Portrazza (necitumumab) IV	**Portrazza (necitumumab) may be considered medically necessary for the treatment of adult individuals when all the following are met:** • The individual is aged 18 years or older **AND** • Has a diagnosis of metastatic squamous non-small cell lung cancer **AND** • Medication is used as first-line treatment in combination with gemcitabine and cisplatin **AND** • Dose is limited to 800 mg on Days 1 and 8 of each 3-week cycle
Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn) IM	**Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn) may be considered medically necessary as a component of a multi-agent chemotherapeutic regimen for the treatment of acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL) in individuals who have developed hypersensitivity to *E. coli*-derived asparaginase (e.g., Oncaspar [pegaspargase], Asparlas [calaspargase pegol – mknl])**
Rytelo (imetelstat) IV	**Rytelo (imetelstat) may be considered medically necessary for the treatment of adults with low- to intermediate-1 risk myelodysplastic syndromes (MDS) with transfusion-dependent anemia when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with low- to intermediate-1 risk MDS (**Related Information**) **AND** • Has transfusion-dependent anemia defined as requiring transfusion of at least 4 red blood cell units over an 8-week period **AND**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• Has not responded to or have lost response to or are ineligible for an erythropoiesis-stimulating agent (ESA) **AND** • Has tried and had an inadequate response or intolerance to Reblozyl (luspatercept-aamt) **AND** • Does not have deletion 5q [del(5q)] cytogenic abnormalities **AND** • Will not be used in combination with an erythropoiesis-stimulating agent or luspatercept **AND** • Rytelo (imetelstat) is prescribed by or in consultation with an oncologist or hematologist **AND** • Dose is limited to 7.1 mg/kg every 4 weeks
Sarclisa (isatuximab-irfc) IV	**Sarclisa (isatuximab-irfc) may be considered medically necessary for the treatment of multiple myeloma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Meets 1 of the following: ○ Sarclisa (isatuximab-irfc) is given in combination with pomalidomide and dexamethasone and the individual has received at least 2 prior therapies including lenalidomide and a proteasome inhibitor (i.e., bortezomib, carfilzomib, ixazomib) **OR** ○ Sarclisa (isatuximab-irfc) is given in combination with Kyprolis (carfilzomib) and dexamethasone and the individual has received 1 to 3 prior lines of therapy **OR** ○ Sarclisa (isatuximab-irfc) is given in combination with bortezomib, lenalidomide, and dexamethasone for newly

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	diagnosed multiple myeloma and the individual is not eligible for autologous stem cell transplant (ASCT)
Sarclisa Escena (isatuximab-irfc)	**Sarclisa Escena (isatuximab-irfc) may be considered medically necessary for the treatment of multiple myeloma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Meets 1 of the following: ○ In combination with pomalidomide and dexamethasone, for the treatment of individuals with multiple myeloma who have received at least 1 prior line of therapy including lenalidomide and a proteasome inhibitor (i.e., bortezomib, carfilzomib, ixazomib) **OR** ○ In combination with carfilzomib and dexamethasone for the treatment of individuals with relapsed or refractory multiple myeloma who have received 1 to 3 prior lines of therapy **OR** ○ In combination with bortezomib, lenalidomide, and dexamethasone for newly diagnosed multiple myeloma and the individual is not eligible for autologous stem cell transplant (ASCT)
Tecelra (afamitresgene autoleucel) IV	**Tecelra (afamitresgene autoleucel) may be considered medically necessary for the treatment of individuals with unresectable or metastatic synovial sarcoma when all the following criteria are met:** • The individual is aged 12 years or older **AND** • Has been diagnosed with unresectable or metastatic synovial sarcoma **AND** • Is HLA-A*02:01P, -A*02:02P, -A*02:03P, or -A*02:06P positive and MAGE-A4 antigen positive

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	AND • Has progressed following at least 1 prior systemic chemotherapy **AND** • Tecelra (afamitresgene autoleucel) is prescribed by or in consultation with an oncologist
Temodar (temozolomide) IV	**Temodar (temozolamide) may be considered medically necessary for the treatment of adult individuals when all of the following are met:** • The individual is aged 18 years or older **AND** • Meets 1 of the following: ○ Is diagnosed with glioblastoma and Temodar (temozolomide) IV will be used concomitantly with radiotherapy, and then as maintenance treatment **OR** ○ Is diagnosed with anaplastic astrocytoma and Temodar (temozolomide) is used as first-line therapy **OR** ○ Is diagnosed with refractory anaplastic astrocytoma
Tepylute (thiotepa) IV	**Tepylute (thiotepa) may be considered medically necessary for the treatment of individuals with adenocarcinoma of the breast or ovary.**
Trisenox (arsenic trioxide) IV	**Trisenox (arsenic trioxide) may be considered medically necessary for the treatment of:** • The individual meets 1 of the following: ○ Adults with newly-diagnosed low-risk acute promyelocytic leukemia (APL) whose APL is characterized by the presence of the t(15;17) translocation or PML/RAR-alpha gene expression when used in combination with tretinoin **OR** ○ Induction of remission and consolidation in individuals with APL who are refractory to, or have relapsed from, retinoid

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	and anthracycline chemotherapy, and whose APL is characterized by the presence of the t(15;17) translocation or PML/RAR-alpha gene expression **AND** • Dose is limited to 0.15 mg/kg/day
Trodelvy (sacituzumab govitecan-hziy) IV	**Trodelvy (sacituzumab govitecan-hziy) may be considered medically necessary for the treatment of adult individuals when:** • Used as a single agent for the first-line treatment of adult individuals with unresectable locally advanced or metastatic triple negative breast cancer (TNBC) who are not candidates for PD-1 or PD-L1 inhibitor-based therapy • In combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph for the first-line treatment of adult individuals with unresectable locally advanced or metastatic TNBC whose tumors express PD-L1 (CPS at least 10) • Unresectable locally advanced or metastatic triple-negative breast cancer (mTNBC) who have received 2 or more prior systemic therapies, at least 1 of them for metastatic disease • Unresectable locally advanced or metastatic hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative (IHC 0, IHC 1+ or IHC 2+/ISH–) breast cancer who have received endocrine-based therapy and at least 2 additional systemic therapies in the metastatic setting • Locally advanced or metastatic urothelial cancer (mUC) who have previously received a platinum-containing chemotherapy and either programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-L1) inhibitor
Unituxin (dinutuximab) IV	**Unituxin (dinutuximab) may be considered medically necessary for the treatment of high-risk neuroblastoma in pediatric individuals when:**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• The individual is using Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA) **AND** • Has achieved at least a partial response to prior first-line multiagent, multimodality therapy
• **Generic bortezomib SC/IV** • **Brand bortezomib SC/IV** • **Boruzu (bortezomib) SC/IV** • **Velcade (bortezomib) SC/IV**	**Generic bortezomib, brand bortezomib, Boruzu (bortezomib), and Velcade (bortezomib) may be considered medically necessary for the treatment of adult individuals with any of the following:** • Multiple myeloma • Mantle cell lymphoma
Vyloy (zolbetuximab-clzb) IV	**Vyloy (zolbetuximab-clzb) may be considered medically necessary for the treatment of adults with locally advanced unresectable or metastatic human epidermal growth factor receptor 2 (HER2)-negative gastric or gastroesophageal junction adenocarcinoma when all the following criteria are met:** • The individual is aged 18 years or older **AND** • Has been diagnosed with HER2-negative gastric or gastroesophageal junction adenocarcinoma that is documented as CLDN18.2+ positive defined as moderate to high overexpression in at least 75% of tumor cells **AND** • Will be used in combination with fluoropyridimine- and platinum-containing chemotherapy for first-line treatment **AND** • Vyloy (zolbetuximab-clzb) is prescribed by or in consultation with an oncologist
Vyxeos (cytarabine-daunorubicin) IV	**Vyxeos (cytarabine-daunorubicin) may be considered medically necessary for the treatment of acute myeloid leukemia (AML) when all the following are met:**

Drug	Medical Necessity
Miscellaneous Intramuscular/Intravenous/Subcutaneous Agents	
	• The individual is aged 1 year or older **AND** • Individual is newly diagnosed therapy-related AML or AML with myelodysplasia-related changes
• **Evdi (trabectedin) IV** • **Yondelis (trabectedin) IV**	**Evdi (trabectedin) and Yondelis (trabectedin) may be considered medically necessary for the treatment of individuals with unresectable or metastatic liposarcoma or leiomyosarcoma who received a prior anthracycline (e.g., daunorubicin, doxorubicin, epirubicin, idarubicin, valrubicin) containing regimen.**
Zepzelca (lurbinectedin) IV	**Zepzelca (lurbinectedin) may be considered medically necessary for the treatment of adult individuals with:** • Extensive-stage small cell lung cancer (ES-SCLC) whose disease has not progressed after first-line induction therapy with atezolizumab or atezolizumab and hyaluronidase-tqjs, carboplatin and etoposide, and Zepzelca (lurbinectedin) is being used as maintenance treatment in combination with atezolizumab or atezolizumab and hyaluronidase-tqjs
Zusduri (mitomycin) Intravesical	**Zusduri (mitomycin) may be considered medically necessary for the treatment of adult individuals with recurrent low-grade intermediate-risk non-muscle invasive bladder cancer (LG-IR-NMIBC).**

Drug	Investigational
As listed	**The medications listed in this policy are subject to the product's US Food and Drug Administration (FDA) dosage and administration prescribing information.** **All other uses of the medications listed in this policy are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**All drugs listed in the policy may be approved up to 6 months.**
Re-authorization criteria	**All drugs listed in the policy may be approved up to 12 months as long as the drug-specific coverage criteria are met and chart notes demonstrate that the individual continues to show a positive clinical response to therapy.**

Documentation Requirements
The individual's medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include the following: • Office visit notes that contain the diagnosis, relevant history, physical evaluation and medication history

Coding

Code	Description
HCPCS	
C9399	Unspecified drugs or biologicals (use to report: Hepzato, Tecelra, Zusduri, Inlexzo and Modeyso)
J0614	Injection, treosulfan (Grafapex), 50 mg
J0870	Injection, imetelstat (Rytelo), 1 mg
J0893	Injection, decitabine (Sun Pharma), not therapeutically equivalent to J0894, 1 mg
J0894	Injection, decitabine (Dacogen), 1 mg
J1326	Injection, zolbetuximab-clzb (Vyloy), 2 mg
J1448	Injection, trilaciclib (Cosela), 1 mg
J2277	Injection, motixafortide (Aphexda), 0.25 mg
J2425	Injection, palifermin (Kepivance), 50 mc
J2783	Injection, rasburicase (Elitek), 0.5 mg

Code	Description
J2820	Injection, sargramostim (GM-CSF) (Leukine), 50 mcg
J3590	Unclassified biologics (use to report: Amtagvi, Evdi andSylatron)
J9017	Injection, arsenic trioxide (Trisenox), 1 mg
J9019	Injection, asparaginase (Erwinaze), 1,000 IU (code termed 01/01/26)
J9021	Injection, asparaginase, recombinant (Rylaze), 0.1 mg
J9027	Injection, clofarabine (Clolar), 1 mg
J9033	Injection, bendamustine HCl (Treanda), 1 mg
J9034	Injection, bendamustine HCl (Bendeka), 1 mg
J9036	Injection, bendamustine HCl, (Belrapzo/bendamustine), 1 mg
J9041	Injection, bortezomib (Velcade), 0.1 mg
J9046	Injection, bortezomib (Dr. Reddy's), not therapeutically equivalent to J9041, 0.1 mg
J9047	Injection, carfilzomib (Kyprolis), 1 mg
J9048	Injection, bortezomib (Fresenius Kabi), not therapeutically equivalent to J9041, 0.1 mg
J9049	Injection, bortezomib (Hospira), not therapeutically equivalent to J9041, 0.1 mg
J9051	Injection, bortezomib (Maia), not therapeutically equivalent to J9041, 0.1 mg
J9053	Injection, belantamab mafodotin-blmf (Blenrep), 0.1 mg (new code effective 07/01/26)
J9054	Injection, bortezomib (Boruzu), 0.1 mg
J9056	Injection, bendamustine HCl (Vivimusta), 1 mg
J9118	Injection, calaspargase pegol-mknl (Asparlas), 10 units
J9120	Injection, dactinomycin (Cosmegen), 0.5 mg
J9144	Injection, daratumumab, 10 mg and hyaluronidase-fihj (Darzalex Faspro)
J9145	Injection, daratumumab (Darzalex), 10 mg
J9153	Injection, liposomal, 1 mg daunorubicin and 2.27 mg cytarabine (Vyxeos)
J9172	Injection, docetaxel (Docivyx), 1 mg

Code	Description
J9174	Injection, docetaxel (Beizray), 1 mg
J9176	Injection, elotuzumab (Empliciti),1 mg
J9179	Injection, eribulin mesylate (Halaven and generic eribulin mesylate) 0.1 mg
J9183	Gemcitabine intravesical system, 225 mg (new code effective 04/01/26)
J9200	Injection, floxuridine, 500 mg
J9205	Injection, irinotecan liposome (Onivyde), 1 mg
J9207	Injection, ixabepilone (Ixempra), 1 mg
J9214	Injection, interferon, alfa-2b, recombinant (Intron A), 1 million units
J9223	Injection, lurbinectedin (Zepzelca) 0.1 mg
J9227	Injection, isatuximab-irfc (Sarclisa) 10 mg
J9246	Injection, melphalan (Evomela), 1 mg
J9248	Injection, melphalan (Hepzato), 1 mg
J9249	Injection, melphalan (Apotex), 1 mg (use to report: IVRA infusion)
J9258	Injection, paclitaxel protein-bound particles (Teva), not therapeutically equivalent to J9264, 1 mg
J9261	Injection, nelarabine (Arranon), 50 mg
J9264	Injection, paclitaxel protein-bound particles (Abraxane), 1 mg
J9266	Injection, pegaspargase (Oncaspar), per single dose vial
J9268	Injection, pentostatin (Nipent), 10 mg
J9269	Injection, tagraxofusp-erzs (Elzonris), 10 mcg
J9274	Injection, tebentafusp-tebn (Kimmtrak), 1 mcg
J9281	Mitomycin, pyelocalyceal instillation (Jelmyto), 1 mg
J9282	Mitomycin, intravesical instillation (Zusduri), 1 mg
J9295	Injection, necitumumab (Portrazza), 1 mg
J9301	Injection, obinutuzumab (Gazyva), 10 mg

Code	Description
J9317	Injection, sacituzumab govitecan-hziy (Trodelvy), 2.5 mg
J9328	Injection, temozolomide (Temodar), 1 mg
J9341	Injection, thiotepa (Tepylute), 1 mg
J9348	Injection, naxitamab-gqgk (Danyelza), 1 mg
J9352	Injection, trabectedin (Yondelis), 0.1 mg (code termed 09/30/26)
J9362	Injection, trabectedin (Yondelis), 0.01mg (new code effective 10/01/26)
J9999	Not otherwise classified, antineoplastic drugs (use to report: Decnupaz and Sarclisa Escena and)
Q2050	Injection, doxorubicin HCl, liposomal, not otherwise specified (Doxil and generic Doxil), 10 mg
Q2057	Afamitresgene autoleucel, including leukapheresis and dose preparation procedures (Tecelra), per therapeutic dose

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Consideration of Age

Age limits specified in this policy are determined according to the US Food and Drug Administration (FDA) -approved indications, where applicable.

Benefit Application

The drugs in this policy that are administered orally are managed through the pharmacy benefit. Drugs administered via IV infusion or intravesical instillation are managed through the medical benefit. Darzalex Faspro (daratumumab and hyaluronidase-fihj) and Oncaspar (pegaspargase) are also managed through the medical benefit.

Table 1. Revised International Prognostic Scoring System (IPSS-R) in Myelodysplastic Syndrome

Prognostic Variable	Score						
	0	0.5	1.0	1.5	2.0	3.0	4.0
Cytogenetics*	Very good		Good		Intermediate	Poor	Very poor
Bone marrow blast (%)	≤2		>2 to <5		5 to 10	>10	
Hemoglobin (g/dL)	≥10		8 to <10	<8			
Platelets (cells/mcL)	≥100	50 to 100	<50				
Absolute neutrophil count (cells/mcL)	≥0.8	<0.8					

*Cytogenetic definitions: Very good: -Y, del(11q); Good: Normal, del(5q), del(12p), del(20q), double including del(5q); Intermediate: del(7q), +8, +19, i(17q), any other single, double not including del(5q) or -7/del(7q), or independent clones; Poor: -7, inv(3)/t(3q)/del(3q), double including -7/del(7q), complex: 3 abnormalities; Very poor: Complex: >3 abnormalities

Risk Group	IPSS-R Score
Very low	≤1.5
Low	>1.5 to 3.0
Intermediate	>3 to 4.5
High	>4.5 to 6
Very high	>6

Evidence Review

Amtagvi (lifileucel)

The approval of Amtagvi was based on results from the prospective, interventional multicenter Phase 2 C-144- 01 trial. Among the primary efficacy analysis set of 73 individuals in Cohort 4 who received Amtagvi at the recommended dose, the objective response rate (ORR) was 31.5% and the median duration of response (DOR) was not reached at 18.6 months follow-up. Among a pooled efficacy set of 153 individuals from Cohorts 2 and 4 who received the recommended Amtagvi dose, the ORR was 31.4% and the median DOR was not reached at 21.5 months follow-up. The prescribing information for Amtagvi includes a Boxed Warning regarding the risk of treatment-related mortality, prolonged severe cytopenia, severe infection, and cardiopulmonary and renal impairment.

Balversa (erdafitinib)

Balversa (erdafitinib) a kinase inhibitor that binds to and inhibits enzymatic activity of FGFR1, FGFR2, FGFR3 and FGFR4 based on *in vitro* data. Balversa also binds to RET, CSF1R, PDGFRA, PDGFRB, FLT4, KIT, and VEGFR2. Balversa inhibited FGFR phosphorylation and signaling and decreased cell viability in cell lines expressing FGFR genetic alterations, including point mutations, amplifications, and fusions. Balversa is the first targeted therapy for metastatic bladder cancer approved by the FDA. This drug is currently fulfilling a previous unmet space in therapy for the most common type of bladder cancer; transitional cell carcinoma (urothelial carcinoma). The overall response rate of the participants in the clinical trial was 32.2% with 2.3% having a complete response. Warning and precautions regarding Balversa includes ocular disorders (central serous retinopathy/retinal pigment epithelial detachment) resulting in visual defects and hyperphosphatemia (76% in treated individuals).

Darzalex (daratumumab)

Darzalex (daratumumab) is a CD38-directed cytolytic antibody indicated for the treatment of adult individuals with multiple myeloma. When used in combination treatment with lenalidomide and dexamethasone (DRd) in individuals ineligible for autologous stem cell transplant daratumumab demonstrated an improvement in Progression Free Survival (PFS) in the DRd arm as compared to the lenalidomide and low-dose dexamethasone (Rd) arm; the

median PFS had not been reached in the DRd arm and was 31.9 months in the Rd arm (hazard ratio [HR]=0.56; 95% CI: 0.43, 0.73; p<0.0001), representing 44% reduction in the risk of disease progression or death in individuals treated with DRd. When used in combination treatment with bortezomib, melphalan and prednisone (VMP) in individuals ineligible for autologous stem cell transplant daratumumab demonstrated an improvement in PFS in the D-VMP arm as compared to the VMP arm; the median PFS had not been reached in the D-VMP arm and was 18.1 months (95% CI:16.53, 19.91) in the VMP arm (HR=0.5; 95% CI: 0.38, 0.65; p<0.0001), representing 50% reduction in the risk of disease progression or death in individuals treated with D-VMP. The most frequently reported adverse reactions (incidence ≥20%) were infusion reactions, neutropenia, thrombocytopenia, fatigue, asthenia, nausea, diarrhea, constipation, decreased appetite, vomiting, muscle spasms, arthralgia, back pain, pyrexia, chills, dizziness, insomnia, cough, dyspnea, peripheral edema, peripheral sensory neuropathy, bronchitis, pneumonia and upper respiratory tract infection.

Decnupaz (pivekimab sunirine-pvzy)

Decnupaz is an interleukin-3 receptor-α (CD123)-targeting antibody and alkylating agent conjugate. The efficacacy was established in CADENZA (NCT03386513), a multicenter, open-label, single-arm, clinical trial that included 33 adult individuals with treatment-naïve BPDCN with no central nervous system (CNS) involvement. Treatment consisted of Decnupaz 0.045 mg/kg intravenously once every three weeks. The efficacy of Decnupaz in individuals with treatment-naïve BPDCN was based on the rate of complete remission or clinical complete remission (CR/CRc). The median follow-up was 21.5 months (range: 4.2, 27). The median time to CR/CRc was 1.8 months (range: <0.5 to 4). Among the 33 individuals with treatment-naïve BPDCN, 13 (39.4%) individuals were able to receive post-study treatment HSCT. CADENZA (NCT03386513) was a multicenter, open-label, single-arm, clinical trial that included 51 adult individuals with relapsed or refractory BPDCN without evidence of active CNS disease treated with Decnupaz 0.045 mg/kg intravenously once every three weeks. The efficacy of Decnupaz in individuals with relapsed/refractory BPDCN was based on the rate of CR/CRc. The median follow-up was 24.1 months (range: 0.2 to 30.4). The median time to CR/CRc was 1.7 months (range: 1 to 6). Among the 51 individuals with relapsed/refractory BPDCN, 6 (11.8%) individuals were able to receive post study treatment HSCT. Newly diagnosed BPDCN individuals treated with Decnupaz showed a composite complete response rate of 69.7% with a median duration of response of 9.7 months; 39.4% of these individuals received post-study stem cell transplants.

Individuals with relapsed or refractory disease had a composite complete response rate of 15.7% with a median duration of response of 9.2 months; 11.8% received post-study stem cell transplants.

Most common adverse reactions (≥20%) included edema, fatigue, musculoskeletal pain, hemorrhage, infusion-related reactions, nausea, and diarrhea. Decnupaz carries a boxed warning for hepatotoxicity, including hepatic veno-occlusive disease, and warnings for infusion-related reactions, edema, sulfite allergic reactions, and embryo-fetal toxicity.

Erivedge (vismodegib)

Erivedge (vismodegib) is a Hedgehog pathway inhibitor. It binds to and inhibits Smoothened, a trans-membrane protein involved in Hedgehog signal transduction. The evidence of efficacy was established in the pivotal Phase II open label trial of vismodegib 150mg once daily. This study demonstrated a statistically significant single-agent activity for both locally advanced (42.9% response rate; $p<0.0001$) and metastatic (30.3% response rate; $p=0.0011$) basal cell carcinoma (laBCC and mBCC respectively). Overall median duration of treatment for the combined cohorts ($n=104$) was 9.7 months (range 1.1 to 18.7 months). The median duration of response was 7.6 months and median progression free survival (PFS) was 9.5 months for both groups (independently). This data is pending press in the New England Journal of Medicine and is currently only available from the manufacturer. Published efficacy data is only available from the extension of the open label Phase I study currently ongoing. As of January 2010, there were 2 individuals who achieved complete remission and 17 who achieved partial response from the original 33 individuals enrolled in the study who had aBCC (overall response of 57%).

Gazyva (obinutuzumab)

Gazyva (obinutuzumab) targets the CD20 antigen expressed on the surfaces of pre-B and mature B-lymphocytes. After binding, obinutuzumab mediates B-cell lysis by engaging immune effector cells, directly activating direct cell death pathways, and/or activating the complement cascade. The immune effector cell mechanisms include antibody-dependent cellular cytotoxicity (ADCC) and antibody-dependent cellular phagocytosis.

Clinical trials explored the safety of Gazyva (obinutuzumab) in previously untreated individuals with CLL. Individuals were treated with chlorambucil alone, obinutuzumab + chlorambucil, or rituximab + chlorambucil. Adverse reactions included infusion reactions, neutropenia, thrombocytopenia, leukopenia, pyrexia, diarrhea, constipation, nasopharyngitis, and urinary tract infections. These adverse reactions are consistent with those seen comparing obinutuzumab + chlorambucil to chlorambucil alone except back pain (5% vs. 2%), anemia (12% vs. 10%) and cough (10% vs. 7%), which were observed at a higher incidence in the obinutuzumab treated individuals. The incidence of Grade 3-4 back pain (<1% vs. 0%), cough (0% vs. <1%) and anemia (5% vs. 4%) was similar in both treatment arms.

Obinutuzumab was approved on the basis of an improvement in progression-free survival (PFS) in a randomized, open-label, multicenter trial in individuals with Follicular Lymphoma, which is a type of the Non-Hodgkin Lymphoma, with no response or who have progressed within 6 months of a rituximab-containing regimen. These individuals were randomized to bendamustine alone (n = 166) or bendamustine + obinutuzumab (n = 155) for six 28-day cycles. Individuals in the combination arm who had a complete response (CR), partial response (PR), or stable disease (SD) at the end continued obinutuzumab monotherapy for two years. The primary endpoints included PFS. The median PFS in the combination arm was not reported, whereas the bendamustine arm was 13.8 months. The best overall response was 78.7% for obinutuzumab combination and 74.7% for bendamustine alone, which was defined as the best CR/PR within 12 months of initiating therapy. The most common adverse reactions (≥ 10%) were infusion reactions, neutropenia, nausea, fatigue, cough, diarrhea, constipation, pyrexia, thrombocytopenia, vomiting, upper respiratory tract infection, decreased appetite, arthralgia, sinusitis, anemia, asthenia, and urinary tract infections. The most common grade 3-4 reactions (≥ 10%) were neutropenia, thrombocytopenia, and infusion reactions. The safety profile was consistent with the overall indolent non-Hodgkin lymphoma population.

Ibrance (palbociclib)

Ibrance (palbociclib) is an orally active selective and reversible inhibitor of CDK 4/6. The agent halts the progression of the cell cycle at G1 via its selective inhibition of CDK 4/6, thereby preventing cellular proliferation. Palbociclib is indicated in combination with letrozole for the treatment of postmenopausal women with ER+/HER2- advanced breast cancer as initial endocrine-based therapy for metastatic disease.

This indication was approved under accelerated approval based on PFS and continued approval may be contingent upon verification and description of clinical benefit in a confirmatory trial. The current approval was based on data from an international, randomized, double-blind, placebo-controlled, clinical trial (PALOMA-2) that randomized 666 postmenopausal women (2:1) to palbociclib plus letrozole or placebo plus letrozole. Palbociclib 125 mg or placebo was administered orally once daily for 21 consecutive days, followed by 7 days off. Letrozole 2.5 mg was administered orally once daily. Treatment continued until disease progression or unacceptable toxicity. The median progression-free survival (PFS) was 24.8 months in the palbociclib plus letrozole arm and 14.5 months in the placebo plus letrozole arm (HR=0.576, 95% CI: 0.463, 0.718, p<0.0001). Overall survival data are immature.

Safety data was evaluated in 444 individuals who received palbociclib plus letrozole. Neutropenia was the most frequently reported adverse reaction in PALOMA-2 with an incidence of 80%. The most common adverse reactions observed in 10% or more of individuals taking palbociclib were neutropenia, infections, leukopenia, fatigue, nausea, alopecia, stomatitis, diarrhea, anemia, rash, asthenia, thrombocytopenia, vomiting, decreased appetite, dry skin, pyrexia, and dysgeusia. The most frequently reported grade 3 or greater adverse reactions in individuals receiving palbociclib plus letrozole were neutropenia, leukopenia, infections, and anemia.

Idhifa (enasidenib)

The efficacy of Idhifa (enasidenib) 100 mg was evaluated in an open-label, single-arm, multicenter, two-cohort clinical trial of 199 individuals with relapsed or refractory AML and an IDH2 mutation. IDH2 mutations were identified by a local diagnostic test and retrospectively confirmed by the Abbott RealTime IDH2 assay or prospectively identified by the Abbott RealTime IDH2 assay. Efficacy was based off of the rate of complete response (CR)/complete response with partial hematologic recovery (CR/CRh), the duration of CR/CRh, and the rate of conversion from transfusion dependence to transfusion independence. For individuals who achieved a CR/CRh, the median time to first response was 1.9 months and the median time to best response was 3.7 months. Of the 157 individuals who were dependent on red blood cell and/or platelet transfusions at baseline, 34% became independent of transfusions during any 56-day post baseline period.

Inlexzo (gemcitabine)

The approval of Inlexzo was supported by results from the single-arm, open-label Phase 2b SunRISe-1 study (NCT04640623), specifically Cohort 2, which evaluated Inlexzo monotherapy in 83 individuals with BCG-unresponsive CIS with or without papillary tumors. In the Phase 2b SunRISe-1 trial, Inlexzo achieved an 82% complete response (CR) rate, with 51% of responders maintaining CR for ≥12 months. The most common adverse reactions were urinary tract events (frequency, infection, dysuria, urgency, pain, and hematuria). Serious adverse reactions occurred in 24% of individuals, 7% discontinued treatment, and 1.2% experienced fatal events, including cognitive disorder.

Iwilfin (eflornithine)

Approval of Iwilfin was based on findings from an externally controlled trial comparing outcomes from Study 3b (investigational arm) and Study ANBL0032 (clinical trial-derived external control arm).

In Study 3b (NCT02395666), eligible individuals with high-risk neuroblastoma (HRNB) received Iwilfin orally twice daily, with dosage based on body surface area (BSA), until disease progression, unacceptable toxicity, or for a maximum of 2 years. The external control arm included individuals in the experimental arm of Study ANBL0032, which evaluated dinutuximab, granulocyte-macrophage colony-stimulating factor, interleukin-2, and cis-retinoic acid compared to cis-retinoic acid alone in pediatric individuals with HRNB.

Individuals who met the criteria for the comparative analysis of Study 3b and Study ANBL0032, with complete data for specified clinical covariates, were matched (1:3) using propensity scores. Results showed that, in the protocol-specified primary analysis, the event-free survival (EFS) hazard ratio (HR) was 0.48 and overall survival (OS) HR was 0.32. Supplementary analyses in subpopulations or using alternative statistical methods were performed because of the externally controlled study design. In these analyses, the EFS HR ranged from 0.43 to 0.59 and the OS HR ranged from 0.29 to 0.45.

Kisqali (ribociclib)

Kisqali (ribociclib) offers a favorable overall response rate of 52.7% versus 37.1% in the ribociclib plus letrozole versus the placebo plus letrozole, respectively, and a median duration of response hazard ratio of 0.59 (95% CI: 0.41,0.85, P=.002). The evidence supporting efficacy are limited to

the completed placebo-controlled and ongoing dose expansion-crossover Phase 3 trials, it does however present in favor of ribociclib when used in combination with letrozole. This drug is conveniently dosed in an oral, film-coated tablet has a diverse adverse effect profile with an increased risk of QT prolongation, hepatobiliary toxicity, neutropenia, embryo-fetal toxicity, and a warning for avoidance of the use in pregnancy. Post-marketing surveillance and close-monitoring will be critical.

Komzifti (ziftomenib)

The efficacy of Komzifti was evaluated in an open-label, single-arm, multicenter clinical trial (Study KO-MEN-001, NCT04067336; KOMET-001) in 112 adult individuals with relapsed or refractory AML with an NPM1 mutation identified using next-generation sequencing or polymerase chain reaction. Individuals with NPM1 mutations, including Type A, B, and D mutations and other NPM1 mutations likely to result in cytoplasmic localization of the NPM1 protein, were enrolled. Other eligibility criteria included creatinine clearance ≥ 30 mL/min, total bilirubin ≤ 1.5 x the upper limit of normal (ULN), aminotransferases ≤ 2 x ULN, QTcF ≤ 480 msec, and Eastern Cooperative Oncology Group performance status score of 0-2. KOMZIFTI was given orally at a dose of 600 mg once daily until disease progression or unacceptable toxicity. Individuals were permitted to resume treatment with Komzifti following hematopoietic stem cell transplant (HSCT). Four (3.6%) of the 112 individuals underwent stem cell transplantation following KOMZIFTI treatment. The rate of complete remission (CR) plus CR with partial hematologic recovery (CRh) was 21.4% (95% CI: 14.2, 30.2). The median duration of CR+CRh was 5.0 months (95% CI: 1.9, 8.1). For individuals who achieved a CR or CRh, the median time to first response was 2.7 months (range, 0.9 to 15 months). Of the 24 individuals who achieved a response of CR or CRh, 21 (88%) individuals did so within 6 months of initiating Komzifti. The most common adverse reactions (≥20%), including laboratory abnormalities, were aspartate aminotransferase increased, infection without an identified pathogen, potassium decreased, albumin decreased, alanine aminotransferase increased, sodium decreased, creatinine increased, alkaline phosphatase increased, hemorrhage, diarrhea, nausea, fatigue, edema, bacterial infection, musculoskeletal pain, bilirubin increased, potassium increased, differentiation syndrome, pruritus, febrile neutropenia, and transaminases increased. Komzifti includes a Boxed Warning for differentiation syndrome.

Lartruvo (olaratumab)

Lartruvo (olaratumab) is a human IgG1 antibody that binds platelet-derived growth factor receptor alpha (PDGFR- α). PDGFR- α is a receptor tyrosine kinase expressed on cells of mesenchymal origin. Signaling through this receptor plays a role in cell growth, chemotaxis, and mesenchymal stem cell differentiation. The receptor has also been detected on some tumor and stromal cells, including sarcomas, where signaling can contribute to cancer cell proliferation, metastasis, and maintenance of the tumor microenvironment. The interaction between olaratumab and PDGFR- α prevents binding of the receptor by the PDGF-AA and –BB ligands as well as PDGF-AA, -BB, and –CC-induced receptor activation and downstream PDGFR- α pathway signaling. Olaratumab exhibits in vitro and in vivo anti-tumor activity against selected sarcoma cell lines and disrupted the PDFGR- α signaling pathway in vivo tumor implant models.

The efficacy of Lartruvo (olaratumab) was demonstrated in Trial 1, an open-label, randomized, active-controlled study. Eligible individuals were required to have soft tissue sarcoma not amenable to curative treatment with surgery or radiotherapy, a histologic type of sarcoma for which an anthracycline-containing regimen was appropriate but had not been administered, ECOG PS of 0-2, and tumor specimen available for assessment of PDGFR-α expression by an investigational use assay. Individuals were randomized (1:1) to receive olaratumab in combination with doxorubicin or doxorubicin as a single agent. PDGFR-α expression (positive versus negative), number of previous lines of treatment (0 versus 1 or more), histological tumor type (leiomyosarcoma versus synovial sarcoma versus all others), and ECOG PS (0 or 1 versus 2) were used to allocate individuals in the randomization. olaratumab was administered at 15 mg/kg as an intravenous infusion on Days 1 and 8 of each 21-day cycle until disease progression or unacceptable toxicity. All individuals received doxorubicin 75 mg/m^2 as an intravenous infusion on Day 1 of each 21-day cycle for a maximum of eight cycles and were permitted to receive dexrazoxane prior to doxorubicin in Cycles 5 to 8. Individuals randomized to receive doxorubicin as a single agent were offered olaratumab at the time of disease progression. The efficacy outcome measures were overall survival (OS), and progression-free survival (PFS) and objective response rate (ORR) as assessed by investigator and by independent review according to RECIST v1.1. A total of 133 individuals were randomized, 66 individuals to the LARTRUVO plus doxorubicin arm and 67 individuals to the doxorubicin arm. Baseline demographics and disease characteristics were: median age of 58 years (range 22 to 86); 44% men; 86% White, 8% Black, 3% Asian, and 2% Other; 56% ECOG PS 0 and 39% ECOG PS 1; 65% no prior chemotherapy (excluding adjuvant and neoadjuvant therapy); 38% leiomyosarcoma, 1.5% synovial sarcoma, and 61% other histologies [17% liposarcoma (8% dedifferentiated, 4%

myxoid, 3% well-differentiated, 1.5% pleomorphic, 1% liposarcoma not otherwise specified (NOS)), 11% undifferentiated pleomorphic sarcoma, 5% angiosarcoma, 5% undifferentiated sarcoma NOS, 3% extraskeletal myxoid chondrosarcoma, 2% malignant peripheral nerve sheath tumor, 2% myxofibrosarcoma, 2% malignant solitary fibrous tumor, 2% endometrial stromal sarcoma, 1.5% chondrosarcoma, 1.5% epithelioid sarcoma, 1.5% fibrosarcoma, 1.5% low-grade fibromyxoid sarcoma, and 5% other histologies with one individual each]. All individuals had metastatic disease and were enrolled at US sites. Among individuals randomized to doxorubicin, 30 (45%) individuals received LARTRUVO as a single agent at the time of disease progression. Trial 1 demonstrated a significant improvement in overall survival.

Lifyorli (relacorilant)

Lifyorli (relacorilant) is a reversible glucocorticoid receptor (GR) antagonist. The efficacy of Lifyorli in combination with nab-paclitaxel was evaluated in ROSELLA (NCT05257408), a multicenter, open-label, active-controlled, randomized, two-arm, trial in individuals with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer. Individuals were permitted to receive up to three prior lines of systemic therapy and prior bevacizumab was required. The trial excluded individuals who required chronic or frequent use of glucocorticoids. A total of 381 individuals were randomized (1:1) to receive: (1) LIFYORLI 150 mg orally the day before, the day of, and the day after administration of nab paclitaxel 80 mg/m2 intravenous infusion on Days 1, 8 and 15 of each 28-day cycle (188); OR (2) nab-paclitaxel 100 mg/m2 intravenous infusion on Days 1, 8 and 15 of each 28-day cycle (193). Treatment was administered until disease progression or unacceptable toxicity. Tumor response assessments occurred every 8 weeks for the first 40 weeks and every 12 weeks thereafter. The major efficacy outcome measures were progression-free survival (PFS) assessed by blinded independent central review (BICR) and overall survival (OS). PFS was evaluated according to Response Evaluation Criteria in Solid Tumors (RECIST), version 1.1. Individuals receiving Lifyorli plus nab-paclitaxel experienced a 35% reduction in risk of death and a median overall survival of 16.0 months versus 11.9 months for nab-paclitaxel alone. There was also a 30% reduction in risk of disease progression compared to nab-paclitaxel monotherapy.

Common adverse reactions occurring in more than 20% of individuals included decreased hemoglobin, decreased neutrophils, fatigue, nausea, diarrhea, decreased platelets, rash, and decreased appetite. Warnings include neutropenia, severe infections, adrenal insufficiency, exacerbation of glucocorticoid-treated conditions, and embryo-fetal toxicity.

Lonsurf (trifluridine and tipiracil)

Lonsurf is a combination of trifluridine, a nucleoside metabolic inhibitor, and tipiracil, a thymidine phosphorylase inhibitor. Inclusion of tipiracil increases trifluridine exposure by inhibiting its metabolism by thymidine phosphorylase. Following uptake into cancer cells, trifluridine is incorporated into DNA, interferes with DNA synthesis and inhibits cell proliferation. Trifluridine/tipiracil demonstrated anti-tumor activity against KRAS wild-type and mutant human colorectal cancer xenografts in mice.

The clinical efficacy and safety of Lonsurf (trifluridine and tipiracil) were evaluated in an international, randomized, double-blind, placebo-controlled study conducted in individuals with previously treated metastatic colorectal cancer (CRC).

A total of 800 individuals were randomized 2:1 to receive Lonsurf (N=534) plus best supportive care (BSC) or matching placebo (N=266) plus BSC. Randomization was stratified by KRAS status (wild-type vs. mutant), time since diagnosis of first metastasis (<18 months vs. ≥ 18 months), and region (Japan vs. US, Europe and Australia). Key eligibility criteria included prior treatment with at least 2 lines of standard chemotherapy for metastatic CRC, ECOG 0-1, absence of brain metastasis, and absence of ascites requiring drainage in the past four weeks. Individuals received 35 mg/m2 Lonsurf or matching placebo orally twice daily after meals on Days 1 - 5 and 8 – 12 of each 28-day cycle until disease progression or unacceptable toxicity. The major efficacy outcome measure was overall survival (OS), and an additional efficacy outcome measure was progression-free survival (PFS). The median age was 63 years, 61% were male, 58% and 35% were White and Asian respectively, and all individuals had baseline ECOG Performance Status (PS) of 0 or 1. The primary site of disease was colon (62%) or rectum (38%). KRAS status was wild-type (49%) or mutant (51%) at study entry. All individuals received prior treatment with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy. All but one individual received bevacizumab, and all but two individuals with KRAS wild-type tumors received panitumumab or cetuximab. A statistically significant improvement in overall survival and progression-free survival were demonstrated in individuals in the Lonsurf plus BSC arm compared to those who received placebo plus BSC.

Lynparza (olaparib)

There is limited evidence from a non-randomized open-label study in individuals with deleterious or suspected deleterious gBRCAm-associated advanced ovarian cancer. All individuals (N=193) were treated with Lynparza (olaparib) with an objective response rate of 31% and a median duration of response of 7.4 months.[5] In the subgroup of individuals who had 3 or more lines of prior chemotherapy (n=137), ORR was 34%, mostly classified as partial response (CR 2%, PR 32%). Median duration of response was 7.9 months. A separate randomized open-label study showed similar progression free survival (8.8 vs. 7.1 months) and objective response rate (31% vs. 18%, NS) after treatment with olaparib or pegylated liposomal doxorubicin, respectively, in 97 gBRCAm individuals. Over half of the individuals had received 3 or more prior chemotherapy regimens.[9] The use of olaparib as a maintenance agent following objective response to chemotherapy was not well supported by current evidence and not approved by the FDA. No evidence of real-world effectiveness was found at the time of review. An indirect comparison of response rates for olaparib (from the single pivotal trial) to historically reported response rates of other therapeutic agents in heavily pretreated advanced ovarian cancer individuals was performed by the FDA. Estimated response rate to 4th- line alternative chemotherapy regimens is 10-20%,[2] but it is expected gBRCAm individuals would have a higher response rate. Olaparib appears to provide at least a similar to a more favorable response rate in this heavily pretreated population, with a response rate of 34% from the pivotal trial.

The incidence of myelodysplastic syndrome and/or acute myeloid leukemia (MDS/AML) in olaparib clinical trials is higher than that reported generally in ovarian cancer individuals, 0.8% to 3.1% vs. 0.0033% respectively.[2] Seventeen of the 22 cases found in olaparib clinical trials were fatal. Post-marketing surveillance and monthly monitoring of complete blood count is warranted. Other serious concerns include potential development of secondary malignancy and pneumonitis. Common adverse events include mostly gastrointestinal complaints and fatigue. Anemia is the most frequently reported serious adverse event. In the comparative trial against liposomal doxorubicin, olaparib is associated with numerically less serious adverse events than liposomal doxorubicin. The most reported serious adverse events were anemia for olaparib and palmar-plantar erythrodysesthesia syndrome for liposomal doxorubicin.

Ovarian cancer (OC) is the leading cause of death in women with gynecological cancer and is the 5th most common cause of cancer mortality in women. Most individuals are diagnosed at advanced stage (stage III or above) with a median age of diagnosis at 63. Epithelial ovarian cancer accounts for the majority (90%) of OC cases. The incidence rate for ovarian cancer

between 2006 and 2010 was 12.5 cases per 100,000 women. Women with a family history of ovarian cancer, such as first-degree family members with ovarian cancer and BRCA1 or BRCA2 mutation, are at increased risk of developing advanced OC. Other risk factors for ovarian cancer include nulliparity, older age at pregnancy and first birth, hormone therapy, pelvic inflammatory disease, etc.

Possible causes of OC include incessant ovulation, increasing age and hormonal exposure. Epithelial OC comprises the majority of primary OC. Histologically, serous tumors account for the majority and are typically associated with a poorer prognosis. Due to deleterious mutations of a tumor suppressor BRCA genes, about 10-15% of epithelial OC and up to 50% of high-grade serous tumors are affected by homologous DNA repair defects. The enzymes poly (ADP-ribose) polymerase (PARP) are required for efficient DNA repair. Inhibition of PARP ensures that DNA breaks cannot be repaired and thus results in cell death. Lynparza (olaparib) is an inhibitor of PARP enzymes, including PARP1, PARP2, and PARP3. PARP enzymes are involved in normal cellular homeostasis, such as DNA transcription, cell cycle regulation, and most notably DNA repair. Olaparib disrupts cellular homeostasis and induces cell death by inhibiting PARP enzymatic activity. In the presence of deleterious BRCA mutation, DNA single strand breaks occur which would require PARP enzymes for repair. PARP inhibitors disable this repair pathway rendering cell death.

Current standard treatment for advanced OC include cytoreductive surgery followed by chemotherapy with platinum and taxane based agents. However, there is a high risk for recurrence and developing drug resistance. Individuals who relapse within 6 months after initial chemotherapy are termed platinum-resistant. Platinum resistance is associated with lower subsequent response rate to subsequent regimens and lower survival.

The efficacy and safety of Lynparza in combination with abiraterone and prednisone or prednisolone in individuals with mCRPC was evaluated in a randomized, double-blind, placebo-controlled, multi-center trial "PROpel". In this trial, 796 individuals with mCRPC were randomized 1:1 to receive either Lynparza and abiraterone or placebo and abiraterone. All individuals received either prednisone or prednisolone, a GnRH analog or prior bilateral orchiectomy. The major efficacy endpoint was Radiological Progression-Free Survival (rPFS) and Overall Survival (OS). In the individuals with BRCAm, rPFS was 30% in the treatment group compared to 74% in the placebo group, with the hazard ratio of 0.24 (0.12, 0.45). The overall survival was 28% in the treatment group compared to 66% in the placebo group, with the hazard ratio of 0.30 (0.15, 0.59).

Lysodren (mitotane)

Lysodren is an adrenal cytotoxic agent which is indicated for the treatment of inoperable, functional or nonfunctional, adrenal cortical carcinoma. The mechanism of action of mitotane is unknown. Mitotane modifies the peripheral metabolism of steroid and directly suppresses the adrenal cortex.

The most common adverse reactions are nausea, vomiting, diarrhea, anorexia, dizziness, depression, vertigo and rash.

Ninlaro (ixazomib)

Ninlaro (ixazomib) is a reversible proteasome inhibitor. It preferentially binds and inhibits the chymotrypsin-like activity of the beta 5 subunit of the 20S proteasome. Lxazomib induced apoptosis of multiple myeloma cell lines in vitro. It demonstrated in vitro cytotoxicity against myeloma cells from individuals who had relapsed after multiple prior therapies, including bortezomib, lenalidomide, and dexamethasone. The combination of ixazomib and lenalidomide demonstrated synergistic cytotoxic effects in multiple myeloma cell lines. In vivo, ixazomib demonstrated antitumor activity in a mouse multiple myeloma tumor xenograft model.

The efficacy and safety of Ninlaro in combination with lenalidomide and dexamethasone was evaluated in a randomized, double-blind, placebo-controlled, multicenter study in individuals with relapsed and/or refractory multiple myeloma who had received at least one prior line of therapy. Individuals who were refractory to lenalidomide or proteasome inhibitors were excluded from the study. A total of 722 individuals were randomized in a 1:1 ratio to receive either the combination of Ninlaro, lenalidomide and dexamethasone (N=360; Ninlaro regimen) or the combination of placebo, lenalidomide and dexamethasone (N=362; placebo regimen) until disease progression or unacceptable toxicity. Randomization was stratified according to number of prior lines of therapy (1 versus 2 or 3), myeloma International Staging System (ISS) (stage I or II versus III), and previous therapy with a proteasome inhibitor (exposed or naïve). Twenty three percent (N=166) of the individuals had light chain disease and 12% (N=87) of individuals had free light chain-measurable only disease. Thromboprophylaxis was recommended for all individuals in both treatment groups according to the lenalidomide prescribing information. Antiemetics were used in 19% of individuals in the Ninlaro regimen and

12% of individuals in the placebo regimen; antivirals in 64% and 60%, respectively, and antihistamines in 27% and 19%, respectively. These medications were given to individuals at the physician's discretion as prophylaxis and/or management of symptoms. Individuals received Ninlaro 4 mg or placebo on Days 1, 8, and 15 plus lenalidomide (25 mg) on Days 1 through 21 and dexamethasone (40 mg) on Days 1, 8, 15, and 22 of a 28-day cycle. Individuals with renal impairment received a starting dose of lenalidomide according to its prescribing information. Treatment continued until disease progression or unacceptable toxicities. The efficacy of Ninlaro was evaluated by progression-free survival (PFS) according to the 2011 International Myeloma Working Group (IMWG) Consensus Uniform Response Criteria as assessed by a blinded independent review committee (IRC) based on central lab results. Response was assessed every four weeks until disease progression.

The approval of Ninlaro was based upon a statistically significant improvement in PFS of the Ninlaro regimen compared to the placebo regimen. The median time to response was 1.1 months in the NINLARO regimen and 1.9 months in the placebo regimen. The median duration of response was 20.5 months in the Ninlaro regimen and 15 months in the placebo regimen for responders in the response evaluable population. A non-inferential PFS analysis was conducted at a median follow up of 23 months with 372 PFS events. Hazard ratio of PFS was 0.82 (95% confidence interval [0.67, 1.0]) for Ninlaro regimen versus placebo regimen, and estimated median PFS was 20 months in the Ninlaro regimen and 15.9 months in the placebo regimen. At the same time, a planned interim OS analysis was conducted with 35% of the required number of deaths for final OS analysis; there were 81 deaths in the Ninlaro regimen and 90 deaths in the placebo regimen. An OS benefit was not demonstrated.

Odomzo (sonidegib)

The safety of Odomzo was evaluated in Study 1, a randomized, double-blind, multiple cohort trial in which 229 individuals received Odomzo at either 200 mg (n=79) or 800 mg (n=150) daily. The frequency of common adverse reactions including muscle spasms, alopecia, dysgeusia, fatigue, nausea, decreased weight, decreased appetite, myalgia, pain, and vomiting was greater in individuals treated with Odomzo 800 mg as compared to 200 mg. The data described below reflect exposure to Odomzo 200 mg daily in 79 individuals with locally advanced BCC (laBCC; n=66) or metastatic BCC (mBCC; n=13) enrolled in Study 1. Individuals were followed for at least 18 months unless discontinued earlier. The median duration of treatment with Odomzo was 11.0 months (range 1.3 to 33.5 months). The study population characteristics were: median age of 67

years (range 25 to 92; 59% were ≥65 years), 61% male, and 90% white. The majority of individuals had prior surgery (75%), radiotherapy (24%), systemic chemotherapy (4%), or topical or photodynamic therapies (18%) for treatment of BCC. No individual had prior exposure to a hedgehog pathway inhibitor. Odomzo was permanently discontinued in 34% of individuals or temporarily interrupted in 20% of individuals for adverse reactions. Adverse reactions reported in at least two individuals that led to discontinuation of the drug were: muscle spasms and dysgeusia (each 5%), asthenia, increased lipase, and nausea (each 4%), fatigue, decreased appetite, alopecia, and decreased weight (each 3%). Serious adverse reactions occurred in 18% of individuals. The most common adverse reactions occurring in ≥10% of individuals treated with Odomzo 200 mg were muscle spasms, alopecia, dysgeusia, fatigue, nausea, musculoskeletal pain, diarrhea, decreased weight, decreased appetite, myalgia, abdominal pain, headache, pain, vomiting, and pruritus.

Ojjaara (momelotinib)

The approval is based on results from the Phase 3 MOMENTUM study (NCT04173494) and a subpopulation of adult individuals with myelofibrosis (MF) and anemia from the Phase 3 SIMPLIFY-1 trial (NCT01969838). MOMENTUM compared Ojjaara with danazol in 195 individuals with MF and anemia who had previously used a JAK inhibitor. The trial met all primary and key secondary endpoints, demonstrating statistically significant response in terms of symptoms, splenic improvement, and transfusion independence. In the SIMPLIFY-1 trial, which included 432 JAK inhibitor-naïve individuals with MF, a numerically lower percentage of individuals treated with Ojjaara (25%) achieved a Total Symptom Score reduction of 50% or more at Week 24 compared with Incyte's Jakafi (ruxolitinib) (36%).

Purixan (mercaptopurine)

Purixan (mercaptopurine) is an oral purine analog that undergoes intracellular transport and activation to form metabolites including thioguanine nucleotides. Incorporation of thioguanine nucleotides into DNA or RNA results in cell-cycle arrest and cell death. Thioguanine nucleotides and other mercaptopurine metabolites are also inhibitors of de novo purine synthesis and purine nucleotide interconversions. Mercaptopurine was cytotoxic to proliferating cancer cells in in vitro and had antitumor activity in mouse tumor models. It is not known which of the

biochemical effects of mercaptopurine and its metabolites are directly or predominantly responsible for cell death.

Retevmo (selpercatinib)

Retevmo was evaluated in individuals with advanced RET fusion-positive NSCLC enrolled in the LIBRETTO-001 study. The study enrolled individuals with advanced or metastatic RET fusion-positive NSCLC who had progressed on platinum-based chemotherapy. Outcome data showed an ORR of 64%, with 81% of these individuals maintaining their response for at least 6 months. In individuals who had received an anti-PD-1 or anti PD-L1 inhibitor in addition to platinum-based therapy, ORR was 66% and median DOR was 12.5 months. The MTC subgroup consisted of 143 individuals 12 harboring RET mutations. The study individuals were broken down into cohorts by those who had received Cabometyx (cabozantinib) or Caprelsa (vandetanib) and those that were Cabometyx-and Caprelsa-naïve. The ORR in the previously treated group was 69% with 76% of these responses lasting for at least 6 months. The ORR was 73% and 61% of these individuals maintained their response for at least 6 months. There were 27 individuals, adult and pediatric, with RET fusion-positive thyroid cancer in the study. The ORR in the previously treated subgroup was 79% with 87% of responders maintaining a response for at least 6 months. Common adverse events (AEs) with Retevmo included increased aspartate aminotransferase and alanine aminotransferase enzymes in the liver, increased blood sugar, decreased white blood cell count, decreased albumin in the blood, decreased calcium in the blood, dry mouth, diarrhea, increased creatinine, increased alkaline phosphatase, hypertension, fatigue, swelling in the body or limbs, low blood platelet count, increased cholesterol, rash, constipation, and decreased sodium in the blood. Serious adverse reactions occurred in 33% of individuals who received Retevmo. The most frequent serious adverse reaction (in ≥2% of individuals) was pneumonia.

Revuforj (revumenib)

Approval was based on results from the Phase 1/2 AUGMENT-101 trial, which included 104 individuals with relapsed/refractory acute leukemia (acute myeloid leukemia, acute lymphoblastic leukemia, or mixed phenotype acute leukemia) with a KMT2A translocation. Revuforj met the trial's primary endpoint, demonstrating a 21.2% rate of complete remission

(CR) plus CR with partial hematological recovery (CRh) (95% CI: 13.8, 30.3). The median duration of CR plus CRh was 6.4 months (95% CI: 2.7, not estimable), and the median time to CR or CRh was 1.9 months. Dose reduction or discontinuation due to treatment-emergent adverse events (TEAEs) occurred in 9.6% and 12.8% of individuals, respectively. TEAEs that led to discontinuation included septic shock (2%), respiratory failure (2%), and in 1% (intracranial hemorrhage, sudden death, AML, cardiac failure, febrile neutropenia, myocardial ischemia, pneumonia, nausea, and vomiting). TEAEs (except for nausea and vomiting) generally were unresponsive to dose modification. No individuals discontinued Revuforj due to QTc prolongation or differentiation syndrome.

Romvimza (vimseltinib)

Approval of Romvimza was supported by results from the Phase 3 MOTION trial (NCT05059262), which enrolled 123 individuals with TGCT that was not amenable to surgery and who had no prior anti-CSF1/CSF1R therapy. Individuals were randomly assigned (2:1) to receive either Romvimza 30 mg twice weekly or placebo for 24 weeks (Part 1). At Week 25 , the major efficacy outcome, overall response rate (ORR), was 40% in the Romvimza arm and 0% (no responses) in the placebo arm. The median duration of response (DOR) was not reached in the Romvimza arm. After an additional 6 months of follow-up, 85% of responders (28 individuals) had a DOR of 6 months or longer, and 58% had a DOR of 9 months or longer. The primary endpoint was supported by statistically significant improvements in active range of motion, individual-reported physical functioning, and individual-reported pain observed in the Romvimza arm compared to the placebo arm at Week 25. The most common adverse reactions (≥20%), including laboratory abnormalities, were increased aspartate aminotransferase, periorbital edema, fatigue, rash, increased cholesterol, peripheral edema, face edema, decreased neutrophils, decreased leukocytes, pruritus, and increased alanine aminotransferase.

Rozlytrek (entrectinib)

Rozlytrek (entrectinib) is an oral inhibitor of the tyrosine kinases TRKA, TRKB, TRKC, ROS1, and ALK. Pooled analyses of ALKA-372-001, STARTRK-1, and STARTRK-2 demonstrated that entrectinib was efficacious in adult individuals with neurotrophic tropomyosin receptor kinase (NTRK) fusion-positive tumors and adult individuals with ROS1-positive non-small cell lung

cancer (NSCLC). The overall response rate (ORR) of 77.4% in the latter, however, was more compelling than the ORR in the former. The 57.4% ORR rate in individuals with NTRK fusion-positive tumors, along with uncertainty about which cancer types would benefit in a larger individual sample, results in less certainty regarding the efficacy of entrectinib in this individual population. Although overall response rates (ORR) were similar in individuals with and without central nervous system (CNS) disease at baseline, which support findings of the ability of entrectinib to cross the blood-brain barrier (BBB), the median duration of response (DOR) and progression-free survival (PFS) were shorter for individuals with CNS disease. In the STARTRK-NG study of primarily pediatric individuals, entrectinib demonstrated efficacy in individuals with NTRK and ROS1 fusion-positive tumors. These findings further demonstrate its efficacy in individuals with NTRK and ROS1 gene fusions, especially in those with high-grade CNS tumors and extracranial tumors. Among individuals with neuroblastoma (n=15), however, only one individual (ALK fusion-positive) achieved complete response (CR).

Rubraca (rucaparib)

Rubraca (rucaparib) is an inhibitor of poly (ADP-ribose) polymerase (PARP) enzymes, including PARP-1, PARP-2, and PARP-3, which play a role in DNA repair. In vitro studies have shown that rucaparib-induced cytotoxicity may involve inhibition of PARP enzymatic activity and increased formation of PARP-DNA complexes resulting in DNA damage, apoptosis, and cell death. Increased rucaparib-induced cytotoxicity was observed in tumor cell lines with deficiencies in BRCA1/2 and other DNA repair genes. Rucaparib has been shown to decrease tumor growth in mouse xenograft models of human cancer with or without deficiencies in BRCA.

Rubraca (rucaparib) 600mg twice daily as monotherapy has been studied in 377 individuals with ovarian cancer treated in two open label, single arm trials. In these individuals, the median age was 62 years (range 31 to 86), 100% had an Eastern Cooperative Oncology Group (ECOG) performance status of 0 or 1, 38% had BRCA-mutated ovarian cancer, 45% had received 3 or more prior lines of chemotherapy, and the median time since ovarian cancer diagnosis was 43 months (range 6 to 197). Adverse reactions led to dose reduction or interruption in 62% of individuals, most frequently from anemia (27%), and fatigue/asthenia (22%). Adverse reactions led to dose discontinuation in 10% of individuals, most frequently from fatigue/asthenia (2%). The median duration of treatment was 5.5 months (range 0.1 to 28.0).

Rubraca (rucaparib) was approved for an expanded indication enabling its use prior to chemotherapy for eligible individuals with metastatic castration-resistant prostate cancer (mCRPC). The TRITON3 study is a Phase III, multicenter, open-label, randomized trial of rucaparib in chemotherapy-naïve mCRPC individuals who had been previously treated with an androgen receptor directed therapy. The study enrolled 405 individuals with a mutation in BRCA or ATM who were randomized to rucaparib or the control group, which consisted of physician's choice of docetaxel, abiraterone acetate, or enzalutamide. Approximately 55% of the individuals in the control arm received docetaxel. The primary endpoint was radiographic progression-free survival (rPFS) by independent radiology review (IRR), in individuals with mutations in BRCA1, BRCA2 or ATM. TRITON3 demonstrated a statistically significant improvement in IRR-assessed rPFS for RUBRACA compared to ARPI or docetaxel in individuals with BRCAm and in the overall population. The median duration of imaging-based progression-free survival was 11.2 months (95% confidence interval [CI], 9.2 to 13.8) in the rucaparib group and 6.4 months (95% CI, 5.4 to 8.3) in the control group (hazard ratio, 0.50; 95% CI, 0.36 to 0.69; $P < 0.001$ by long-rank test). In an exploratory analysis in the subgroup of BRCA mutations, the median duration of imaging-based progression-free survival was longer with rucaparib than with docetaxel (11.2 months vs. 8.3 months; hazard ratio, 0.53; 95% CI, 0.37 to 0.77).

Rydapt (midostaurin)

Rydapt (midostaurin) is approved for the first-line treatment of adults with FMS-like tyrosine kinase 3 mutation-positive (FLT3+) acute myeloid leukemia (AML) as detected by an FDA-approved test, in combination with chemotherapy. It is also approved to treat adults with aggressive systemic mastocytosis (ASM), systemic mastocytosis with associated hematological neoplasm (SM-AHN) or mast cell leukemia (MCL). The recommended dose for AML is 50mg twice daily with food. For ASM, SM-AHN and MCL, the recommended dose is 100mg twice daily with food. It will be available through open distribution.

This is the first significant advance in treatment of a subset of AML individuals. AML is difficult to treat, with one year survival rates less than 50%.

The safety and efficacy of Rydapt for individuals with AML were studied in a randomized trial of 717 individuals who had not been treated previously for AML. In the trial, individuals who received Rydapt in combination with chemotherapy lived longer than individuals who received chemotherapy alone, although a specific median survival rate could not be reliably estimated. In

addition, individuals who received Rydapt in combination with chemotherapy in the trial went longer (median 8.2 months) without certain complications (failure to achieve complete remission within 60 days of starting treatment, progression of leukemia or death) than individuals who received chemotherapy alone (median three months).

Common side effects of Rydapt in individuals with AML include low levels of white blood cells with fever (febrile neutropenia), nausea, inflammation of the mucous membranes (mucositis), vomiting, headache, spots on the skin due to bleeding (petechiae), musculoskeletal pain, nosebleeds (epistaxis), device-related infection, high blood sugar (hyperglycemia) and upper respiratory tract infection. Rydapt should not be used in individuals with hypersensitivity to midostaurin or other ingredients in Rydapt. Women who are pregnant or breastfeeding should not take Rydapt because it may cause harm to a developing fetus or a newborn baby. Individuals who experience signs or symptoms of lung damage (pulmonary toxicity) should stop using Rydapt.

Rydapt was also approved today for adults with certain types of rare blood disorders (aggressive systemic mastocytosis, systemic mastocytosis with associated hematological neoplasm or mast cell leukemia). Common side effects of Rydapt in these individuals include nausea, vomiting, diarrhea, swelling (edema), musculoskeletal pain, abdominal pain, fatigue, upper respiratory tract infection, constipation, fever, headache, and shortness of breath.

Rytelo (imetelstat)

The IMerge clinical trial (NCT02598661) is a Phase 2/3, multicenter study of Rytelo that consists of two parts:

- Part 1 was an open-label, single-arm design to assess the efficacy and safety of Rytelo. A total of 57 participants were enrolled in Part 1, including the expansion cohort.
- Part 2 is a double-blind, randomized design to compare the efficacy of Rytelo with placebo. In the main study in Part 2, 178 participants were enrolled and randomized 2:1 to receive either Rytelo or placebo, respectively.

In a separate ventricular repolarization substudy of Part 2, approximately 45 participants will be enrolled and randomized 2:1 to receive either Rytelo or placebo. If, after a minimum of two treatment cycles in the ventricular repolarization substudy, a participant has no significant

change to packed red blood cell (pRBC) transfusion burden or evidence of clinical benefit per investigator, after discussion with the sponsor, the participant may be unblinded. If the participant was on placebo treatment, he/she may be permitted to start treatment with Rytelo. The extension phase will begin after the end of the main study (24 months after the last participant was randomized in the main study of Part 2) and continue until participants who entered Part 2 of the main study participate in the study for up to 5 years from the first dose of Rytelo (including treatment and follow-up), or 3 years of post-treatment follow-up from the last dose of study treatment, whichever occurs later, or until death, withdrawal of consent, study termination, or until a subject is lost to follow-up. Participants ongoing on Rytelo and considered to be benefitting from treatment per investigator in Part 2 of the study will have the option to continue receiving Rytelo in the extension phase. Participants in the follow-up phase for Part 2 of the study will have the option to continue the follow-up in the extension phase. Part 1 and Part 2 of the study consist of three phases:

- A screening phase (up to 28 days)
- Treatment phase 3
- Post-treatment follow-up phase, which will continue until death, lost to follow-up, withdrawal of consent, or the end of the study (whichever occurs first)

The extension phase of the study will consist of an extended treatment phase and an extended follow-up phase, which will continue until death, lost to follow-up, withdrawal of consent, or the end of the study (whichever occurs first). Of the participants who received Rytelo, 39.8% and 28.0% achieved RBC transfusion independence (RBC-TI) for at least 8 and 24 consecutive weeks versus 15.0% and 3.3% of participants who received placebo, respectively. In IMerge, Grade 3 or 4 thrombocytopenia and neutropenia occurred. Among participants treated with Rytelo, 65% experienced Grade 3 or 4 decreased platelets, with a median time to onset of first occurrence of 6 weeks. Among participants treated with Rytelo, 72% experienced Grade 3 or 4 decreased neutrophils, with a median onset time of first occurrence of 4.6 weeks. The other most common adverse reactions (incidence ≥10% with a difference between arms of >5% compared to placebo) were decreased WBCs, increased AST, increased ALP, increased ALT, fatigue, prolonged partial thromboplastin time, arthralgia/myalgia, COVID-19 infections, and headache.

Talzenna (talazoparib)

Talzenna is a poly (ADP-ribose) polymerase (PARP) enzyme inhibitor, including PARP1 and PARP3, which play a role in DNR repair.

The safety and efficacy of Talzenna (talazoparib) was evaluated in Embraca study where 431 individuals with deleterious or suspected deleterious germline BRCA-mutated HER2-negative Locally Advanced or Metastatic Breast Cancer were randomized 2:1 to receive Talzenna 1 mg or healthcare provider's choice of chemotherapy (capecitabine, eribulin, gemcitabine or vinorelbine) until the disease progression or unacceptable toxicity.

The efficacy endpoint was progression-free survival (PFS) evaluated based on Response Evaluation Criteria in Solid Tumors (RECIST) version 1.1. There was a statistically significant improvement in the PFS as there was 65% disease progression or death in the Talzenna group compared to 58% in the chemotherapy group, with p-value < 0.0001.

The efficacy of Talzenna in combination with combination with Xtandi was evaluated in TALAPRO-2 trial, which was randomized, double-blind, placebo-controlled, multi-cohort trial. In this trial 399 individuals with HRR gene mutated (HRRm) mCRPC were randomized 1:1 to receive either enzalutamide 160 mg daily plus either Talzenna 0.5 mg or placebo daily until individual experiences unacceptable toxicity or progression. All the individuals received a GnRH analog or had prior bilateral orchiectomy and they were progressed on prior androgen deprivation therapy. Mutation in HRR gene was determined using either circulating tumor DNA based next generation sequencing assays or solid tumor tissue. The primary efficacy outcome was to evaluate radiographic progression-free survival (rPFS) and another efficacy outcome measure was overall survival. The number of rPFS events were in 33% individual in the treatment group versus 52% in the placebo group with p-value < 0.0001.

Tazverik (tazemetostat)

Tazemetostat is an inhibitor of the methyltransferase, enhancer of zeste homolog 2 (EZH2), and some EZH2 gain-of-function mutations including Y646X and A687V. EZH2 is a methyltransferase associated with inhibition of apoptosis and increased cellular proliferation that is mutated or overexpressed in a variety of solid and hematological cancers. Epithelioid sarcoma (ES) is a rare type (≤1%) of soft tissue sarcoma (STS), a solid malignancy arising from connective tissue that comprises approximately 1% of all cancers. Two subtypes of ES, classic (distal type) which

typically affects the distal upper extremity of adolescents and young adults and the less common and more aggressive proximal variant that affects young to middle-aged adults. The efficacy of tazemetostat was evaluated in an open-label, single-arm cohort (Cohort 5) of a multi-center study (Study EZH-202) in individuals with histologically confirmed, metastatic or locally advanced epithelioid sarcoma. Individuals were required to have INI1 loss, detected using local tests, and an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0-2. Individuals received tazemetostat 800 mg orally twice daily until disease progression or unacceptable toxicity. Tumor response assessments were performed every 8 weeks. The major efficacy outcome measures were confirmed overall response rate (ORR) according to Response Evaluation Criteria in Solid Tumors (RECIST) v1.1 as assessed by blinded independent central review (BICR) and duration of response (DOR). Median duration of follow-up was 14 months (range 0.4 to 31). In study EZH-202 the overall response rate (95% CI) for tazemetostat was 15% (7%, 26%).

Tecelra (afamitresgene autoleucel)

The approval of Tecelra was based on data from Cohort 1 of the Phase 2 SPEARHEAD-1 trial (NCT04044768), which included an efficacy analysis population of 44 individuals with previously treated inoperable or metastatic synovial sarcoma. Tecelra demonstrated a 43.2% overall response rate (ORR), a 4.5% complete response (CR) rate, and a median duration of response (DOR) of 6 months. Common side effects with Tecelra include nausea, vomiting, fatigue, and infections. Serious risks, such as cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS), necessitate careful monitoring. In the SPEARHEAD-1 trial, CRS occurred in 75% of individuals who received Tecelra, 2% of whom had Grade ≥3 CRS. Following treatment with Tecelra, individuals must be monitored at the healthcare facility for at least 7 days for CRS and ICANS.

Temodar (temozolomide)

Temodar (temozolamide) is an alkylating drug indication for the treatment of adult individuals with either newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment, or for refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine. Temozolomide goes

through rapid nonenzymatic conversion at physiologic pH to the reactive compound 5- (3-methyltriazen-1-yl)-imidazole-4-carboxamide (MTIC).

The efficacy and safety of Temodar in the individuals with newly diagnosed glioblastoma was evaluated in a randomized, multicenter, and open-label trial. In this trial, 573 individuals were randomized to receive either radiation therapy alone (n = 286) or Temodar along with the radiation (n = 287) for total of 42 days. The primary efficacy endpoint was the overall survival. The treatment group (Temodar plus radiotherapy) achieved statistically significant improvement in the overall survival compared to the placebo group (radiotherapy alone), with p-value < 0.0001. Also, the median survival increased by 2.5 months in the treatment group.

The efficacy and safety of Temodar in individuals with refractory anaplastic astrocytoma was studied in a single-arm, multicenter trial. In this trial, 54 individuals with anaplastic astrocytoma and Karnofsky performance status (KPS) of 70 or greater were included. These individuals had previously received radiation therapy and may also have previously received nitrosourea with or without other chemotherapy. The primary efficacy endpoints were overall response rate and median duration of response. Other efficacy endpoints also evaluated the progression free survival at 6 months and 12 months. The overall response rate in Temodar group was 22%, where 9% individuals had complete response. The median duration of response was 50 weeks. The progression-free survival at 6 months was 45% and at 12 months was 29%.

The most common adverse reactions are alopecia, nausea, vomiting, fatigue, headache, constipation, anorexia, and convulsions. Some individuals with anaplastic astrocytoma ($\geq$10% incidence) experienced Grade 3 to 4 hematologic laboratory abnormalities including reduced level of lymphocytes, platelets, neutrophils, and leukocytes.

Tibsovo (ivosidenib)

Tibsovo (ivosidenib) is the first approved oral therapy that targets mutant IDH1 in AML IDH1 is one of three known driver mutations with poor prognosis in AML. The efficacy of ivosidenib was evaluated in a Phase I, multicenter, open-label, dose-escalation and expansion clinical study of orally administered AG-120 in subjects with advanced hematologic malignancies with an IDH1 mutation. The first portion of the study is a dose-escalation to find the highest tolerable dose of the combination of ivosidenib that can be given to individuals with relapsed or refractory AML

with IDH1 mutation. The second part of the study or dose expansion found the highest tolerable dose of ivosidenib that can help to control the disease.

In the dose-escalation and expansion clinical trial of ivosidenib, the primary outcome was an objective response rate (ORR) of 41.6%. Ivosidenib induced a complete response (CR) or a CR with a partial hematologic recovery (CPh) in 30.4% of the study population. The secondary outcome was a median duration of response of 9.3 months for individuals who achieved a CR, 8.2 months for those who achieved a CR/CRh, and 6.5 months for all responders. The median time to first response was 1.9 months, median time to CR was 2.8 months, and the median time to CR/CRh was 2.7 months.

The safety of ivosidenib was evaluated in the Phase I dose-escalation and dose expansion study mentioned above. The most common adverse events were diarrhea (33.3%), elevated levels of white blood cells (30.2%), nausea (29.5%), fatigue (28.7%), and febrile neutropenia (25.2%); 10 (8%) of 125 individuals had grade 3 QT prolongation. Ivosidenib was reduced in one individual and held in five individuals (for any grade of QT prolongation), and no cases were Grade 4 or fatal. The prevalence of differentiation syndrome (DS) was observed in 11.2% of individuals, but no instances of DS leading to permanent treatment discontinuation or death.

Unituxin (dinutuximab)

Unituxin (dinutuximab) is a glycolipid GD2-binding monoclonal antibody. Glycolipid GD2 is expressed on neuroblastoma cells and on the normal cells of neuroectodermal origin, including the central nervous system and peripheral nerves. Dinutuximab works by biding to cell surface GD2 and inducing the cell lysis of GD2-expressing cells through antibody-dependent cell-mediated cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC).

The safety and efficacy of Unituxin was evaluated in a randomized, open-label, multicenter trial where 226 pediatric individuals with high-risk neuroblastoma were randomized to receive Unituxin treatment (n = 113) or RA treatment (n = 113). All individuals had previously received therapies including induction combination chemotherapy, maximum feasible surgical resection, myeloablative consolidation chemotherapy followed by autologous stem cell transplant, and radiation therapy to residual soft tissue disease. Individuals needed to have at least a partial response prior to autologous stem cell transplantation and have no evidence of disease

progression following completion of front-line multimodality therapy, and individuals have adequate pulmonary, hepatic, cardiac and renal functions.

Individuals in the Unituxin group received up to 5 cycles of Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF) or interleukin-2 (IL-2) plus 13-cis-retinoic acid (RA), followed by 1 cycle of RA alone. Meanwhile, individuals in the RA group received 6 cycles of RA. The individuals received Unituxin at a dose of 17.5 mg/m^2/day on 4 consecutive days. Individuals in both arms received 6 cycles of RA at a dose of 160 mg/m^2/day (individual's weight > 12kg) or 5.33 mg/kg/day (individual's weight $\leq$ 12 kg) in divided doses for 14 consecutive days.

The primary efficacy endpoint was investigator-assessed event-free survival (EFS), which is defined as the time from randomization to the first occurrence of relapse, progressive disease, secondary malignancy, or death. The efficacy outcome also evaluated the overall survival.

At the end of the study, the EFS was 29% in Unituxin/RA group compared to 44% in the RA group, with p- value of 0.01. Similarly the OS was 27% in Unituxin/RA arm compared to 42% in the RA arm, with hazard ratio of 0.58 (0.37, 0.91).

Verzenio (abemaciclib)

Verzenio (abemaciclib) selectively inhibits cyclin-dependent kinases (CDK) 4 and 6 (CDK 4/6). It blocks retinoblastoma tumor suppressor protein phosphorylation and prevents progression through the cell cycle, resulting in arrest at the G1 phase.

The efficacy of Verzenio (abemaciclib) in combination with Faslodex (fulvestrant) was evaluated in the Monarch 2 trial. Monarch 2 was a randomized, placebo-controlled, multicenter study in 669 women with HR-positive, HER2-negative metastatic breast cancer in individuals with disease progression on endocrine therapy. The primary endpoint was progression-free survival. The median extended progression free survival duration for abemaciclib plus fulvestrant vs. fulvestrant alone was 16.4 months vs. 9.3 months. The efficacy of Verzenio as monotherapy was evaluated in the Monarch 1 trial. Monarch 1 was a single-arm, open-label, multicenter study in 132 women with measurable HR-positive, HER2-negative metastatic breast cancer whose disease progressed during endocrine therapy, had received taxane in any setting, and who received 1 or 2 prior chemotherapy regimens in the metastatic setting. The primary objective of Monarch 1 was investigator-assessed objective response rate. Other endpoints were clinical

benefit rate, progression-free survival, and overall survival. At the 12-month final analysis, the confirmed objective response rate was 19.7%, median progression-free survival was 6 months and median overall survival was 17.7 months.

Vistogard (uridine triacetate)

Vistogard is a pyrimidine analog. Uridine triacetate is an acetylated pro-drug of uridine. Once the uridine triacetate is deacetylated in the body via nonspecific esterases, the end product uridine is yielded in the circulation. The uridine competitively inhibits the cell damage and cell death caused by fluorouracil.

The efficacy and safety of Vistogard was evaluated in two open-label trials, where 135 individuals with either fluorouracil or capecitabine overdose, or individuals with severe or life-threatening toxicities within 96 hours following the end of fluorouracil or capecitabine administration. The Vistogard was administered at dose of 10 grams orally every 6 hours for total of 20 doses or 6.2 grams/m^2/dose for total of 20 doses for individuals between the age of 1 to 7 years old.

The primary efficacy endpoint was individual's survival at 30 days or until the resumption of chemotherapy if prior to 30 days. Overall, out of 135 individuals, 96% (n = 130) achieved the primary endpoint of either survival at 30 days or the resumption of chemotherapy if prior to 30 days. Death occurred in 5 individuals with fluorouracil or capecitabine overdose.

The most common adverse reactions in individuals who received Vistogard included vomiting, nausea, and diarrhea.

Xpovio (selinexor)

Xpovio (selinexor) is a first-in-class, oral selective inhibitor of nuclear export (SINE) protein XPO1. This leads to accumulation of tumor suppressor proteins in the cell nucleus and selective induction of apoptosis in cancer cells. Selinexor has been granted Orphan Drug designation in multiple myeloma (MM) and Fast Tract approval in combination with dexamethasone (DEX) for the treatment of individuals with relapsed/refractory (R/R) MM who have received ≥4 prior therapies and whose disease is triple therapeutic class refractory (i.e., preteosome inhibitor,

immunomodulatory agent, and anti-CD38 monoclonal antibody), based upon the STORM study. A pivotal, randomized, open-label, Phase III trial (BOSTON) of selinexor in combination with bortezomib (VELCADE) and DEX in individuals with R/R MM is ongoing. The FDA extended the review period for selinexor from April to July 2019 in order to also review data from the BOSTON trial.

Zejula (niraparib)

Zejula (niraparib) offers a significant increase in PFS in individuals with platinum sensitive recurrent epithelial ovarian cancer. This is also the first PARPi to demonstrate efficacy in this population irrespective of BRCA mutation status. This is useful in that the individual will not be required to undergo expensive genetic testing prior to therapy.

The evidence supporting Zejula's efficacy is sufficient and was demonstrated in the multi-center, randomized, double-blind, placebo-controlled ENGOT-OV16/NOVA trial that included 553 individuals. The once-daily dosing and oral dosage form are also aspects which increase ease of use. Zejula has an extremely diverse adverse effect profile including an increased risk in MDS/AML and a warning for fetal toxicity. Post-marketing surveillance and individual reporting will be critical.

Voranigo (vorasidenib)

Voranigo is an oral, selective, brain-penetrant inhibitor of mutant IDH1 and IDH2 enzymes. Voranigo has been studied in individuals with astrocytoma or oligodendroglioma with susceptible IDH1 or IDH2 mutation in the Phase 1 AG881-C-002 trial (NCT02481154), the Phase 1 AG120-881-C-001 trial (NCT03343197), and the Phase 3 INDIGO trial (NCT04164901). The efficacy of Voranigo was evaluated in the INDIGO trial (NCT04164901, also referred to as Study AG881-C-004 in the prescribing information), a randomized, multicenter, double-blind, placebo-controlled study that included 331 individuals with residual or recurrent grade 2 nonenhancing glioma (astrocytoma or oligodendroglioma per WHO 2016 criteria) and an IDH1 or IDH2 mutation who had previously only undergone surgery. This individual population represents those who are 1–5 years post surgery and have not yet received any systemic anticancer therapy. The INDIGO trial met the primary endpoint of progression-free survival (PFS) as evaluated by a blinded independent review committee (BIRC) and the key secondary endpoint

of time to next intervention (TTNI) at the prespecified second interim analysis. The median PFS was 27.7 months in the Voranigo arm compared to 11.1 months in the placebo arm (hazard ratio [HR], 0.39; 95% CI, 0.27 to 0.56; 1-sided *P* <0.001). TTNI was found to be statistically significant (HR, 0.26; 95% CI, 0.15 to 0.43; 1-sided *P* <0.001). The median TTNI was not reached for Voranigo and was 17.8 months for placebo. The subgroup analyses for PFS and OS favored Voranigo over placebo in most subgroups. In clinical trials, frequently reported adverse reactions with Voranigo were fatigue (37%), COVID-19 (33%), musculoskeletal pain (26%), diarrhea (25%), and seizure (16%). Grade 3 or higher adverse events were reported in 22.8% of individuals in the Voranigo arm compared with 13.5% of individuals in the placebo arm; the most commonly reported grade 3 or higher adverse event was increased ALT, which occurred in 9.6% of individuals who received Voranigo and in zero individuals who received placebo. Dosage interruptions due to an adverse event occurred in 30% of individuals in the Voranigo arm, and the adverse events requiring dosage interruption included increased ALT (14%), COVID-19 (9%), and increased AST (6%). Dose reductions due to an adverse reaction occurred in 11% of individuals in the Voranigo arm, primarily due to increased ALT (8%).

Vyloy (zolbetuximab-clzb)

The approval was based on data from two Phase 3 randomized, double-blind, multicenter trials, SPOTLIGHT and GLOW, which enrolled individuals with CLDN18.2-positive, advanced unresectable or metastatic HER2-negative G/GEJ adenocarcinoma. Both trials met the primary endpoint of progression-free survival (PFS) and the key secondary endpoint of median overall survival (OS). In SPOTLIGHT, Vyloy plus folinic acid, fluorouracil, and oxaliplatin (mFOLFOX6) chemotherapy was compared with placebo plus mFOLFOX6 in a total of 565 individuals. Median PFS was 10.6 months in the Vyloy/mFOLFOX6 arm versus 8.7 months in the placebo/mFOLFOX6 arm. Median OS was 18.2 months for the Vyloy treatment arm versus 15.5 months for the placebo arm. In GLOW, Vyloy plus capecitabine and oxaliplatin (CAPOX) chemotherapy was compared with placebo plus CAPOX in a total of 507 individuals. Median PFS was 8.2 months in the Vyloy/CAPOX arm and 6.8 months in the placebo/CAPOX arm. Median OS was 14.4 months in the treatment arm versus 12.2 months in the placebo arm.

2013 Update

Policy was updated to reflect new NCCN guidelines which recommend abiraterone as an initial therapy for metastatic castrate-resistant prostate cancer.

2014 Update

A literature search from 7/1/12 to 10/31/14 found no new evidence requiring changes to this policy.

2015 Update

A literature search from 1/1/14 to 3/31/15 found no new evidence requiring changes to the Erivedge (vismodegib) policy. Added criteria for two recently approved drugs: Opdivo (nivolumab) and Lynparza (olaparib). Added criteria for recently approved drug: Ibrance (palbociclib).

2016 Update

A literature search and review were conducted focusing on recently FDA-approved indications for use of Opdivo (nivolumab) and Keytruda (pembrolizumab) in non-small cell lung cancer, and for nivolumab in renal cell carcinoma. We also reviewed this evidence for combined use of nivolumab and ipilimumab in unresectable or metastatic melanoma. Medical necessity language was updated per new product labels.

Reasonable evidence exists to support the use of ipilimumab, nivolumab, the combination of ipilimumab + nivolumab and Keytruda (pembrolizumab) in the treatment of advanced and metastatic melanoma. Median survival benefits seem to fall in the range of 3-4 months, with the combination PD-1/CTLA-4 inhibition yielding slightly longer survival. To date the evidence is spotty and lacking in head-to-head comparisons. NCCN guidelines do not rate one option over others. Given the number of different molecular targets now available (PD-1, CTLA-4, BRAF V600, MEK) it is impossible to say at this point which is the best treatment sequence to follow.

Tecentriq's label criteria was added to the policy, along with description and rationale sections for this drug. Keytruda recently got a new recommendation for use in NSCLC as a first-line agent. Added criteria (along with description and rationale) for recently approved drugs: Lonsurf, Ninlaro, and Lartruvo. Tecentriq's recent approval in the setting of NSCLC was also added to the policy.

Added criteria per label for Rubraca (rucaparib), along with the drug description and clinical trials rationale.

2017 Update

Added two new indications for Opdivo (nivolumab). Added four new indications for Keytruda (pembrolizumab) and included their references.

2018 Update

Added Paloma-2 study for Ibrance (palbociclib) and Rydapt (midostaurin) safety and efficacy study in drug description.

2019 Update

Reviewed prescribing information for all drugs and updated Tibsovo (ivosidenib) coverage criteria. No new evidence was identified that would require changes to other drugs listed in this policy. Added coverage criteria for the new drug Balversa (erdafitinib).

2021 Update

Reviewed prescribing information for all drugs in policy and no new evidence was identified from prescribing information that would require changes to the drugs listed in this policy. Added trial and failure with Ibrance (palbociclib) or Verzenio (abemaciclib) requirement to Kisqali (ribociclib) and Kisqali Femara Co-Pack (letrozole-ribociclib).

2022 Update

Reviewed prescribing information for all drugs in policy. Removed Aliqopa (copanlisib) as coverage criteria for Aliqopa are captured under Policy 5.01.592. Added to Darzalex (daratumumab) coverage for use in combination with carfilzomib and dexamethasone in individuals with relapsed or refractory multiple myeloma who have received one to three prior lines of therapy. Added a new indication to Tibsovo (ivosidenib) for use in combination with azacitidine or as monotherapy for the treatment of newly diagnosed acute myeloid leukemia. Added coverage for Leukine (sargramostim) as second-line therapy for the treated of individuals taking myelosuppressive anti-cancer regimens, at risk of severe febrile neutropenia.

2023 Update

Reviewed prescribing information for all drugs in policy. Updated Zejula criteria to indicate coverage for the maintenance treatment of adult individuals is limited to those with deleterious or suspected deleterious germline *BRCA*-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Updated Verzenio criteria to indicate coverage in combination with endocrine therapy for the adjuvant treatment of adult individuals with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence without requiring a Ki-67 score of 20 or greater. Added coverage criteria for Xgeva (denosumab). Added coverage criteria for Unituxin (dinutuximab). Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Added coverage criteria for Epkinly (epcoritamab-bysp) for the treatment of adult individuals with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy. Added coverage criteria for Lynparza (olaparib) for the treatment of adult individuals with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC) when used in combination with abiraterone and prednisone or prednisolone. Added coverage criteria for Talzenna, when used in combination with enzalutamide, for the treatment of adult individuals with HRR gene- mutated metastatic castration-resistant prostate cancer (mCRPC).

Added generic bortezomib to the criteria of Velcade (bortezomib). Added coverage criteria for Vistogard for the emergency treatment of fluorouracil or capecitabine overdose, or severe or life-threatening toxicity within 96 hours following the end of fluorouracil or capecitabine administration. Removed Gavreto's indication of adult and pediatric individuals 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy per FDA label changes. Added coverage for Leukine for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Added Brand paclitaxel protein- bound particles (american regent-unbranded) IV to Abraxane criteria. Added criteria for Lysodren (mitotane) for the treatment of adrenal cortical carcinoma when the tumor is inoperable. Added criteria for Matulane (procarbazine hydrochloride) for the treatment of stage III and IV Hodgkin's disease when used in combination with other anticancer drugs. Added coverage criteria for Temodar (temozolomide) and generic temozolomide for the treatment of adult individuals with newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment, or for refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine. 90 days notification is required for Temodar IV and Unituxin IV. Removed generic temozolomide IV criteria and added generic temozolomide oral criteria. Added Talvey and Elrexfio for the treatment of adult individuals with relapsed or refractory multiple myeloma where individual has tried at least four lines of prior therapies. Added coverage criteria for Purixan (mercaptopurine) for the treatment of acute lymphoblastic leukemia as part of a combination chemotherapy maintenance regimen.

2024 Update

Reviewed prescribing information for all drugs in policy. Added coverage criteria for Lonsurf (trifluridine and tipiracil) for the treatment of certain adult individuals with metastatic colorectal cancer in combination with bevacizumab. Added coverage criteria for Hepzato Kit (melphalan hepatic delivery system) for the treatment of certain adult individuals with unresectable or metastatic uveal melanoma. Added coverage criteria for Ogsiveo (nirogacestat) for the treatment of certain adult individuals with progressing desmoid tumors. Added coverage criteria for Tabloid (thioguanine) for the treatment of certain individuals with acute myeloid leukemia. Added coverage criteria for Iwilfin (eflornithine) for the treatment of certain individuals with high-risk neuroblastoma. Added coverage criteria for oral Temodar (temozolomide) and oral generic temozolomide for the treatment of certain adult individuals with glioblastoma or

anaplastic astrocytoma. Updated coverage criteria for IV Temodar (temozolomide) to include the treatment of certain adult individuals with newly diagnosed anaplastic astrocytoma. Updated coverage criteria for Tibsovo (ivosidenib) to include the treatment of certain adult individuals with myelodysplastic syndromes. Updated coverage criteria for Welireg (belzutifan) to include the treatment of certain adult individuals with renal cell carcinoma. Removed Truseltiq (infigratinib) coverage criteria as the product has been withdrawn from the market. Updated coverage criteria for Balversa (erdafitinib) to remove coverage criteria for the treatment of locally advanced or metastatic urothelial carcinoma with susceptible FGFR2 genetic alterations and broaden step therapy requirement from prior platinum-containing chemotherapy to prior systemic therapy. Added coverage criteria for Ojjaara (momelotinib) for the treatment of certain adults with myelofibrosis. Added coverage criteria for Thalomid (thalidomide). Added coverage criteria for Aphexda (motixafortide). Updated Onivyde (irinotecan) to include coverage criteria for the first-line treatment of certain adults with metastatic pancreatic adenocarcinoma. Updated Onivyde (irinotecan) to clarify that all coverage criteria is limited to adults. Updated Ogsiveo (nirogacestat) coverage criteria to include a requirement to try generic sorafenib first. Added coverage criteria for Amtagvi (lifileucel) for the treatment of certain individuals with unresectable or metastatic melanoma. Added coverage criteria for brand paclitaxel protein-bound particles (Teva – unbranded). Updated Gazyva (obinutuzumab) coverage criteria to include treatment of certain adults with follicular lymphoma in combination with zanubrutinib. Added coverage criteria for Imdelltra (tarlatamab-dlle) for the treatment of certain individuals with extensive-stage small cell lung cancer (ES-SCLC). Added coverage criteria for Dacogen (decitabine) and generic decitabine for the treatment of certain individuals with myelodysplastic syndrome. Added coverage criteria for Elitek (rasburicase) for the treatment of certain individuals with leukemia, lymphoma, or solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis. Added coverage criteria for Casodex (bicalutamide), Eulexin (flutamide), Nilandron (nilutamide), and generic nilutamide for the treatment of certain adults with prostate cancer. Updated Darzalex Faspro (daratumumab-hyaluronidase-fihj) coverage criteria to include treatment of certain adults with multiple myeloma in combination with bortezomib, lenalidomide, and dexamethasone. Added coverage criteria for Voranigo (vorasidenib) for the treatment of certain individuals with Grade 2 astrocytoma or oligodendroglioma. Added coverage criteria for Boruzu (bortezomib) for the treatment of certain individuals with mantle cell lymphoma and multiple myeloma. Updated Abraxane (paclitaxel protein-bound particles), brand paclitaxel protein-bound particles (American Regent – unbranded), and brand paclitaxel protein-bound particles (Teva – unbranded) coverage criteria to include treatment of certain adults who have tried paclitaxel. Updated Ibrance (palbociclib)

coverage criteria to include a requirement to have an inadequate response or intolerance to Verzenio (abemaciclib), Kisqali (ribociclib) or Kisqali Femara Co-Pack (letrozole-ribociclib). Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information.

2025 Update

Reviewed prescribing information for all drugs in policy. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Added coverage criteria for Xeloda (capecitabine) for certain adults with cancer. Added coverage criteria for Rytelo (Imetelstat) for certain adults with myelodysplastic syndromes. Updated Retevmo (selpercatinib) coverage criteria from adult individuals with metastatic *rearranged during transfection (RET)* fusion-positive non-small cell lung cancer (NSCLC) to adult individuals with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a *RET* gene fusion. Updated Retevmo (selpercatinib) medullary thyroid cancer and advanced or metastatic thyroid cancer age requirement from 12 years and older to 2 years and older. Updated Retevmo (selpercatinib) solid tumors age requirement from 18 years and older to 2 years and older. Updated Blincyto (blinatumomab) coverage criteria to include an age requirement of one month and older, clarify that the disease should be CD19-positive and include treatment of certain individuals with Philadelphia chromosome-negative acute lymphoblastic leukemia (ALL). Updated Krazati (adagrasib) coverage criteria to include treatment of certain adults with colorectal cancer. Added coverage criteria for Tepylute (thiotepa). Added coverage criteria for Tecelra (afamitresgene autoleucel). Added coverage criteria for Vyloy (zolbetuximab-clzb). Updated Sarclisa (isatuximab-irfc) coverage criteria to include treatment of certain individuals with newly diagnosed multiple myeloma. Updated Kisqali (ribociclib) and Kisqali Femara Co-Pack (ribociclib-letrozole) coverage criteria to include treatment of certain adults with stage II or III early breast cancer. Updated Voranigo (vorasidenib) coverage criteria by adding a prescriber requirement and quantity limit. Updated Ibrance (palbociclib) coverage criteria to include treatment of certain adults with breast cancer in combination with Itovebi (inavolisib). Updated Lumakras (sotorasib) coverage criteria to include treatment of certain adults with colorectal cancer. Moved Blincyto (blinatumomab), Elrexfio (elranatamab-bcmm), Epkinly (epcoritamab-bysp), Imdelltra (tarlatamab-dlle), Talvey (talquetamab-tgvs), and Tecvayli (teclistamab-cqyv) from policy 5.01.540 Miscellaneous Oncology Drugs to policy 5.01.650 Bispecific Antibodies. Added coverage criteria for Beizray (docetaxel). Added coverage criteria for Revuforj

(revumenib). Added coverage criteria for Romvimza (vimseltinib). Updated Dacogen (decitabine) and generic decitabine coverage criteria to include treatment of acute myeloid leukemia. Updated Tabloid (thioguanine) coverage criteria to include treatment of acute lymphoblastic leukemia. Updated Jakafi (ruxolitinib) coverage criteria to limit dose to 50 mg daily and two tablets daily. Added Zusduri (mitomycin) coverage criteria for the treatment of certain individuals with bladder cancer. Updated Welireg (belzutifan) coverage criteria to include treatment of certain individuals with pheochromocytoma or paraganglioma. Added IVRA (melphalan) coverage criteria for the treatment of certain individuals with multiple myeloma. Updated Welireg (belzutifan) coverage criteria to clarify that use for advanced renal cell carcinoma (RCC) is intended for individuals with advanced RCC with a clear cell component. Updated Zejula (niraparib) coverage criteria to indicate that maintenance treatment of adults with advanced ovarian cancer in the first-line setting is limited to those with HRD-positive tumors only. Updated Zejula (niraparib) coverage criteria to include a quantity limit. Updated Darzalex Faspro (daratumumab and hyaluronidase-fihj) and Darzalex (daratumumab) coverage criteria to include treatment of certain individuals with smoldering multiple myeloma. Updated brand bendamustine, Belrapzo (bendamustine), Bendeka (bendamustine), and Vivimusta (bendamustine) coverage criteria to clarify that treatment for follicular lymphoma in combination with rituximab is not limited to first-line use. Moved Xgeva (denosumab) from policy 5.01.540 Miscellaneous Oncology Drugs to 5.01.658 Denosumab Products. Added coverage criteria for Inlexzo (gemcitabine intravesical system), Modeyso (dordaviprone), Ixempra (ixabepilone), generic clofarabine and Clolar (clofarabine).

2026 Update

Reviewed prescribing information for all drugs in policy. Updated coverage criteria for Rozlytrek (entrectinib) for the treatment of solid tumors age requirement from 12 years to 1 month and older. Updated coverage criteria for Matulane (procarbazine hydrochloride) removing the requirement for trial of generic procarbazine hydrochloride. Updated coverage criteria for Rubraca (rucaparib) removing requirement for prior therapy with a taxane-based chemotherapy for treatment of mCRPC. Added coverage criteria for Komzifti (ziftomenib) for the treatment of adult individuals with relapsed or refractory acute myeloid leukemia (AML) with a susceptible nucleophosmin 1 (NPM1) mutation. Updated coverage criteria for Lumakras (sotorasib) and Ojjaara (momelotinib) adding a quantity limit per 30 days. Updated coverage criteria of Pemazyre (pemigatinib) adding a quantity limit per 28 days. Updated coverage criteria for

Kyprolis (carfilzomib) to include isatuximab and dexamethasone in list of treatments for relapsed or refractory multiple myeloma. Updated coverage criteria of Darzalex (daratumumab), Hepzato Kit, Ibrance (palbociclib), Romvimza (vimseltinib), Tecelra (afamitresgene autoleucel), and Vyloy (zolbetuximab-clzb) removing ECOG requirement. Updated coverage criteria for Romvimza (vimseltinib) quantity limit to 2 capsules weekly. Removed coverage criteria for Temodar (temozolomide) oral as product has been discontinued. Updated coverage criteria for Darzalex Faspro removing ECOG requirement, and adding new indication in combination with bortezomib, lenalidomide, and dexamethasone in newly diagnosed individuals who are ineligible for autologous stem cell transplant. Updated coverage criteria for generic temozolomide oral and Temodar (temozolomide) IV for treatment of glioblastoma removing requirement individual is newly diagnosed.

References

1. Danila DC, Morris MJ, de Bono JS, et al. Phase II multicenter study of abiraterone acetate plus prednisone therapy in patients with docetaxel-treated castration resistant prostate cancer. J Clin Oncol 2010; 28(9): 1496-1501.
2. Bianchini D. Durable disease control, safety, and tolerability of abiraterone acetate (AA) in advanced castration-resistant prostate cancer (CRPC). J Clin Oncol 2010;28(15_suppl): 4672.
3. Attard G, Reid AH, A'Hern R, Parker C, Oommen NB, et al. Selective inhibition of CYP17 with abiraterone acetate is highly active in the treatment of castration-resistant prostate cancer. J Clin Oncol 2009; 27(23): 3742-3748.
4. Ryan CJ, Smith MR, Logothetis CJ, et al. Median time to progression in chemotherapy (chemo)-naïve patients with castration-resistant prostate cancer (CRPC) treated with abiraterone acetate and low-dose prednisone (Pred). J Clin Oncol 2010;28(15 suppl):Abstract 4671.
5. Ryan CJ, Efstathiou E, Smith M, et al. Phase II multicenter study of chemotherapy (chemo)-naïve castration-resistant prostate cancer (CRPC) not exposed to ketoconazole (keto), treated with abiraterone acetate (AA) plus prednisone. J Clin Oncol 2009;27(15 suppl):Abstract 5046.
6. Ryan CJ, Efstathiou E, Smith M, et al. Phase II multicenter study of chemotherapy (chemo)-naïve castration-resistant prostate cancer (CRPC) not exposed to ketoconazole (keto), treated with abiraterone acetate (AA) plus prednisone. J Clin Oncol 2009;27(15 suppl):Abstract 5046.
7. Kaufman B, Shapira-Frommer R, Schmutzler RK, et al. Olaparib Monotherapy in Patients With Advanced Cancer and a Germline BRCA1/2 Mutation. J Clin Oncol. Jan 20 2015;33(3):244-250. PMID 25366685
8. Ledermann J, Harter P, Gourley C, et al. Olaparib maintenance therapy in platinum-sensitive relapsed ovarian cancer. N Engl J Med. Apr 12 2012;366(15):1382-1392.
9. Ledermann J, Harter P, Gourley C, et al. Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a preplanned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial. Lancet Oncol. May 29 2014.

10. Jelovac D, Armstrong DK. Recent progress in the diagnosis and treatment of ovarian cancer. CA Cancer J Clin. May-Jun 2011;61(3):183-203.
11. Pruthi S, Gostout BS, Lindor NM. Identification and Management of Women With BRCA Mutations or Hereditary Predisposition for Breast and Ovarian Cancer. Mayo Clin Proc. Dec 2010;85(12):1111-1120.
12. Roett MA, Evans P. Ovarian cancer: an overview. Am Fam Physician. Sep 15 2009;80(6):609-616.
13. National Cancer Institute. Surveillance Epidemiology and End Results. SEER Stat Fact Sheets: Ovary Cancer. Available at: **http://seer.cancer.gov/statfacts/html/ovary.html** Accessed January 27, 2026.
14. Russo A, Calo V, Bruno L, Rizzo S, Bazan V, Di Fede G. Hereditary ovarian cancer. Crit Rev Oncol Hematol. Jan 2009;69(1):28-44.
15. Goff BA, Mandel LS, Drescher CW, et al. Development of an ovarian cancer symptom index: possibilities for earlier detection. Cancer. Jan 15 2007;109(2):221-227.
16. Griffiths RW, Zee YK, Evans S, et al. Outcomes after multiple lines of chemotherapy for platinum-resistant epithelial cancers of the ovary, peritoneum, and fallopian tube. Int J Gynecol Cancer. Jan 2011;21(1):58-65.
17. Del Conte G, Sessa C, von Moos R, et al. Phase I study of olaparib in combination with liposomal doxorubicin in patients with advanced solid tumours. Br J Cancer. Aug 12 2014;111(4):651-659.
18. Ledermann J, Harter P, Gourley C, et al. Olaparib maintenance therapy in patients with platinum-sensitive relapsed serous ovarian cancer: a preplanned retrospective analysis of outcomes by BRCA status in a randomised phase 2 trial. Lancet Oncol. Jul 2014;15(8):852-861.
19. Dent RA, Lindeman GJ, Clemons M, et al. Phase I trial of the oral PARP inhibitor olaparib in combination with paclitaxel for first- or second-line treatment of patients with metastatic triple-negative breast cancer. Breast Cancer Res. 2013;15(5):R88.
20. Benedet JL, Bender H, Jones H, 3rd, Ngan HY, Pecorelli S. FIGO staging classifications and clinical practice guidelines in the management of gynecologic cancers. FIGO Committee on Gynecologic Oncology. Int J Gynaecol Obstet. Aug 2000;70(2):209-262.
21. Ibrance (palbociclib) [package insert]. New York, NY; Pfizer Labs; Revised June 2026.
22. Gazyva (obinutuzumab) [package insert]. South San Francisco, CA; Genetech, Inc. Revised December 2025.
23. Lonsurf (trifluridine and tipiracil) [prescribing information]. Taiho Oncology. Princeton, New Jersey. Revised August 2023.
24. Ninlaro (ixazomib) [prescribing information]. Takeda Pharmaceutical Company Ltd. Lexington, MA. Revised July 2024.
25. Rubraca (rucaparib) [prescribing information]. pharmaand GMbH; Wien, Austria. Revised December 2025.
26. Odomzo (sonidegib) [prescribing information]. Novartis Pharmaceuticals Corporation. East Hanover, New Jersey. Revised August 2023.
27. Idhifa (enasidenib) [package insert]. Cambridge, MA; Celgene Corporation and Agios Pharmaceuticals; Revised January 2025.
28. Kisqali (ribociclib) [prescribing information]. East Hanover, NJ; Novartis Pharmaceuticals Corporation. Revised September 2025.
29. Verzenio (abemaciclib). Prescribing Information. Indianapolis, IN: Eli Lilly and Company; Revised September 2026.
30. Balversa (erdafitinib) [prescribing information]. Horsham, PA: Janssen Products, LP; Revised October 2025.
31. Asparlas (calaspargase pegol-mknl) [prescribing information]. Boston, MA: Servier Pharmaceuticals LLC; Revised December 2023.
32. Intron A (inteferon alfa-2b) [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; Revised March 2023.

33. Sylatron (peginteferon alfa-2b) [prescribing information]. Whitehouse Station, NJ: Merck Sharp & Dohme Corp; Revised January 2019.

34. Popovici-Muller, Janeta. Discovery of AG-120 (Ivosidenib): A First-in-Class Mutant IDH1 Inhibitor for the Treatment of IDH1 Mutant Cancers. ACS Medicinal Chemistry Letters 2018 9 (4), 300-305.

35. DiNardo, Courtney et al. "Ivosidenib (AG-120) In Mutant IDH1 AML And Advanced Hematologic Malignancies: Results Of A Phase 1 Dose Escalation And Expansion Study". Blood Journal, 2018, Available at: **https://ashpublications.org/blood/article/130/Supplement%201/725/83443/Ivosidenib-AG-120-in-Mutant-IDH1-AML-and-Advanced?searchresult=1** Accessed January 27, 2026.

36. "New Data From Ivosidenib Phase 1 Dose-Escalation And Expansion Trial Demonstrate Durable Responses In Patients With Idh1m Relapsed Or Refractory AML | Agios Pharmaceuticals, Inc.". Agios Pharmaceuticals, Inc., 2017, **http://investor.agios.com/news-releases/news-release-details/new-data-ivosidenib-phase-1-dose-escalation-and-expansion-trial** Accessed January 27, 2026.

37. Fizazi K, et al. Rucaparib or Physician's Choice in Metastatic Prostate Cancer. N Engl J Med 2023;388:719-32. DOI: 10.1056/NEJMoa2214676.

38. Wang ES, et al. Ziftomenib in Relapsed or Refractory NPM1-Mutated AML. J Clin Oncol. 2025 Nov;43(31):3381-3390. doi: 10.1200/JCO-25-01694. Epub 2025 Sep 25.

39. Metzger O, Mandrekar S, Goel S, et al. Palbociclib for Hormone-Receptor-Positive, HER2-Positive Advanced Breast Cancer. N Engl J Med 2026;394:451-462. DOI: 10.1056/NEJMoa2511218.

40. Landgren O, Jultcrantz M, Diamond B, et al. Safety and Effectiveness of Weekly Carfilzomib, Lenalidomide, Dexamethasone, and Daratumumab Combination Therapy for Patients with Newly Diagnosed Multiple Myeloma: The MANHATTAN Nonrandmized Clinical Trial. JAMA Oncol 2021;7:862-868.

41. Olawaiye AB, et al. Relacorilant and nab-paclitaxel in patients with platinum-resistant ovarian cancer (ROSELLA): an open-label, randomised, controlled, Phase 3 trial. Lancet. 2025;405(10496):2205-2216.

42. Tian H, Wang R, Cong D, et al. Evolution of conditioning regimens prior to autologous stem cell transplantation in lymphoma patients. Translational Oncology. 202663:102594.

43. Decnupaz (pivekimab sunirine-pvzy). Prescribing Information. AbbVie Inc.; North Chicago, IL. Revised May 2026.

44. Rozlytrek (entrectinib) [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; Revised January 2024.

45. Xpovio (selinexor). Prescribing information. Newton, MA: Karyopharm Therapeutics Inc.; Revised April 2026.

46. Tazverik (tazemetostat) [prescribing information]. Cambridge, MA: Epizyme Inc.; Revised August 2024.

47. Cosela (trilaciclib) [prescribing information]. Durham, NC: G1 Therapeutics, Inc.; Revised August 2025.

48. Onivyde (irinotecan liposome injection) [prescribing information]. Cambridge, MA; Merrimack Pharmaceuticals, Inc. Revised December 2024.

49. Elzonris (tagraxofusp-erzs) [prescribing information]. New York, NY; Stemline Therapeutics, Inc. Revised July 2023.

50. Zejula (niraparib) [prescribing information]. Durham, NC; GlaxoSmithKline. Revised June 2025.

51. Pemazyre (pemigatinib) [prescribing information]. Wilmington, DE; Incyte Corporation. Revised June 2023.

52. Rezlidhia (olutasidenib) [prescribing information]. Greenville, NC; Forma Therapeutics, Inc. Revised April 2024.

53. Yoo C, Kim, K, Jeong, J, et al. Liposomal irinotecan plus fluorouracil and leucovorin versus fluorouracil and leucovorin for metastatic biliary tract cancer after progression on gemcitabine plus cisplatin (NIFTY): a multicentre, open-label, randomized, phase 2b study. Lancet Oncol 2021;22:1560-72. Doi: https://doi.org/10.1016/ S1470-2045(21)00486-1

54. Unituxin (dinutuximab) [prescribing information]. Research Triangle Park, NC; United Therapeutics Corp. Revised October 2025.
55. Lynparza (olaparib). [prescribing information]. Wilmington, DE; AstraZeneca Pharmaceuticals LP. Revised July 2025.
56. Talzenna (talazoparib). [prescribing information]. New York, NY; Pfizer Labs. Revised June 2025.
57. Vistogard (uridine triacetate) [prescribing information]. Rockville, MD; Wellstat Therapeutics Corporation. Revised October 2023.
58. Lysodren (mitotane) [prescribing information]. Farmingdale, NJ; Direct Success Inc. Revised January 2024.
59. Matulane (procrbazine hydrochloride) [prescribing information]. Wilmington, NC; Alcami Corporation. Revised November 2023.
60. Dunsmore KP, Winter SS, Devidas M, et al. Children's Oncology Group AALL0434: A Phase III Randomized Clinical Trial Testing Nelarabine in Newly Diagnosed T-Cell Acute Lymphoblastic Leukemia. J Clin Oncol 2020;38(28):3282.
61. Hayashi RJ, Winter SS, Dunsmore KP, et al. Successful Outcomes of Newly Diagnosed T Lymphoblastic Lymphoma: Results From Children's Oncology Group AALL0434. J Clin Oncol 2020 Sep 10;38(26):3062-3070.
62. Purixan (mercaptopurine) [prescribing information]. Franklin, TN; Rare Disease Therapeutics, Inc. Revised October 2024.
63. Hepzato Kit (melphalan hepatic delivery system) [prescribing information]. New York, NY; Delcath. Revised August 2023.
64. Ogsiveo (nirogacestat) [prescribing information]. Stamford, CT; SpringWorks Therapeutics, Inc. Revised April 2024.
65. Tabloid (thioguanine) [prescribing information]. Wixom, MI; Woodward Pharma Services LLC. Revised January 2025.
66. Iwilfin (eflornithine) [prescribing information]. Louisville, KY; USWM, LLC. Revised November 2024.
67. Tibsovo (ivosidenib) [prescribing information]. Boston, MA; Servier Pharmaceuticals LLC. Revised October 2023.
68. Welireg (belzutifan) [prescribing information]. Rahway, NJ; Merck Sharp & Dohme LLC. Revised June 2026.
69. Ojjaara (momelotinib) [prescribing information]. Durham, NC; GlaxoSmithKline. Revised April 2025.
70. Thalomid (thalidomide) [prescribing information]. Princeton, NJ; Bristol Myers Squibb. Revised March 2023.
71. Aphexda (motixafortide) [prescribing information]. Waltham, MA; BioLineRx. Revised September 2023.
72. Amtagvi (lifileucel) [prescribing information]. Philadelphia, PA; Iovance Biotherapeutics, Inc. Revised September 2025.
73. Dacogen (decitabine) [prescribing information]. Dublin, CA; Otsuka America Pharmaceutical, Inc. Revised June 2020.
74. Elitek (rasburicase) [prescribing information]. Bridgewater, NJ; Sanofi-Aventis US LLC. Revised December 2022.
75. Casodex (bicalutamide) [prescribing information]. Baudette, MN; ANI Pharmaceuticals, Inc. Revised December 2023.
76. Eulexin (flutamide) [prescribing information]. Wixom, MI; Waylis Therapeutics LLC. Revised January 2022.
77. Nilandron (nilutamide) [prescribing information]. Dublin, Ireland; Concordia Pharmaceuticals Inc. Revised December 2024.
78. Voranigo (vorasidenib) [prescribing information]. Boston, MA; Servier Pharmaceuticals. Revised April 2024.
79. Xeloda (capecitabine) [prescribing information]. South San Francisco, CA; Genentech. Revised October 2025.
80. Rytelo (Imetelstat) [prescribing information]. Foster City, CA; Geron Corporation. Revised June 2024.
81. Retevmo (selpercatinib) [prescribing information]. Indianapolis, IN; Eli Lilly and Company. Revised November 2025.
82. Krazati (adagrasib) [prescribing information]. Princeton, NJ; Bristol-Myers Squibb. Revised August 2026.
83. Tepylute (thiotepa) [prescribing information]. Cambridge, MA; Shorla Oncology. Revised July 2025.
84. Tecelra (afamitresgene autoleucel) [prescribing information]. Philadelphia, PA; Adaptimmune LLC. Revised June 2026.

85. Vyloy (zolbbetuximab-clzb) [prescribing information]. Northbrook, IL; Astellas Pharma US, Inc. Revised June 2025.
86. Greenberg PL, Tuechler H, Schanz J, et al. Revised International Prognostic Scoring System (IPSS-R) for myelodysplastic syndromes. Blood 2012.
87. Beizray (docetaxel) [prescribing information]. Guangdong, China; Zhuhai Beihai Biotech Co., Ltd. Revised October 2024.
88. Revuforj (revumenib) [prescribing information]. Waltham, MA; Syndax Pharmaceuticals, Inc. Revised October 2025.
89. Romvimza (vimseltinib) [prescribing information]. Waltham, MA; Deciphera Pharmaceuticals, LLC. Revised February 2025.
90. Zusduri (mitomycin) [prescribing information]. Princeton, NJ; UroGen Pharma. Revised June 2025.
91. IVRA (melphalan) [prescribing information]. Toronto, Ontario; Apotex Corp. Revised July 2024.
92. Grafapex (treosulfan) [prescribing information]. Chicago, IL; Medexus Pharma, Inc. Revised February 2025.
93. Inlexzo (gemcitabine) [prescribing information]. Horsham, PA; Janssen Biotech, Inc. Revised September 2025.
94. Modeyso (dordaviprone) [prescribing information]. Palo Alto, CA; Chimerix. Revised August 2025.
95. Ixempra Kit (ixabepilone) [prescribing information]. Princeton, NJ; R-Pharm US. Revised January 2023.
96. Komzifti (ziftomenib) [prescribing information]. San Diego, CA; Kura Oncology, Inc. Revised November 2025.
97. Erivedge (vismodegib) [prescribing information]. Mississauga, Canada; Patheon, Inc. Revised March 2023.
98. Daurismo (glasdegib) [prescribing information]. New York, NY; Pfizer. Revised March 2023.
99. Vitrakvi (Larotrectinib) [prescribing information]. Whippany, NJ; Bayer HealthCare Pharmaceuticals Inc. Revised April 2025.
100. Gleostine (lomustine) [prescribing information]. Miami, FL; Corden Pharma Latina S.p.A. Revised January 2016.
101. Jakafi (ruxolitinib) [prescribing information]. Wilmington, DE; Incyte Corporation. Revised January 2023.
102. Vonjo (pacritinib) [prescribing information]. Waltham, MA; Sobi, Inc. Revised October 2025.
103. Gavreto (pralsetinib) [prescribing information]. South San Francisco, CA; Rigel Pharmaceuticals, Inc. Revised December 2025.
104. Onureg (azacitidine) [prescribing information]. Summit, NJ; Celgene Corporation. Revised May 2021.
105. Inqovi (decitabine and cedazuridine) [prescribing information]. Princeton, NJ; Otsuka Pharmaceutical Co., Ltd. Revised May 2026.
106. Inrebic (fedratinib) [prescribing information]. Princeton, NJ; Bristal-Myers Squibb Company. Revised May 2025.
107. Lumakras (sotorasib) [prescribing information]. Thousand Oaks, CA; Amgen Inc. Revised January 2025.
108. Lytgobi (futibatinib) [prescribing information]. Princeton, NJ; Taiho Pharmaceutical Co., Ltd. Revised October 2025.
109. Rydapt (midostaurin) [prescribing information]. East Hanover, NJ; Novartis Pharmaceuticals Corporation. Revised May 2023.
110. Abraxane (paclitaxel protein-bound particles) [prescribing information]. Summit, NJ; Celgene Corporation. Revised August 2020.
111. Arranon (nelarabine) [prescribing information]. Princeton, NJ. Fareva Unterach GmbH. Revised March 2025.
112. Blenrep (belantamab mafodotin-blmf) [prescribing information]. Durham, NC; GlaxoSmithKline LLC. Revised October 2025.
113. Danyelza (naxitamab-gqgk) [prescribing information]. Princeton, NJ; Y-mAbs Therapeutics, Inc. Revised August 2025.
114. Darzalex (daratumumab) [prescribing information]. Horsham, PA; Janssen Biotech, Inc. Revised April 2025.
115. Darzalex Faspro (daratumumab and hyaluronidase-fihj) [prescribing information]. Horsham, PA; Janssen Biotech, Inc. Revised January 2026.

116. Halaven (eribulin mesylate) [prescribing information]. Nutley, NJ; Eisai R&D Management Co., Ltd. Revised September 2022.
117. Jelmyto (mitomycin) [prescribing information]. Princeton, NJ. UroGen Pharma, Inc. Revised October 2024.
118. Kepivance (palifermin) [prescribing information]. Stockholm, Sweden; Swedish Orphan Biovitrum AB. Revised December 2019.
119. Khapzory (levoleucovorin) [prescribing information]. East Windsor, NJ; Acrotech Biopharma LLC. Revised March 2020.
120. Kimmtrak (tebentafusp-tebn) [prescribing information]. Conshohocken, PA; Immunocore Commercial LLC. Revised June 2024.
121. Kyprolis (carfilzomib) [prescribing information]. Thousand Oaks, CA; Onyx Pharmaceuticals, Inc. Revised May 2025.
122. Leukine (sargramostim) [prescribing information]. Lexington, MA; Partner Therapeutics, Inc. Revised May 2022.
123. Oncaspar (pegaspargase) [prescribing information]. Boston, MA; Servier Pharmaceuticals LLC. Revised March 2024.
124. Rylaze (asparaginase Erwinia chrysanthemi (recombinant)-rywn) [prescribing information]. Dublin, Ireland; Jazz Pharmaceuticals Ireland Limited. Revised April 2024.
125. Sarclisa (isatuximab-irfc) [prescribing information]. Bridewater, NJ; Sanofi-Aventis U.S. LLC. Revised October 2024.
126. Sarclisa Esena (isatuximab-irfc) [prescribing information]. Bridewater, NJ; Sanofi-Aventis U.S. LLC. Revised July 2026.
127. Trodelvy (sacituzumab govitecan-hziy) [prescribing information]. Foster City, CA; Gilead Sciences, Inc. Revised June 2026.
128. Velcade (bortezomib) [prescribing information]. Takeda Pharmaceuticals America, Inc.; Lexington, MA. Revised November 2021.
129. Vyxeos (daunorubicin and cytarabine liposome) [prescribing information]. Jazz Pharmaceuticals, Inc.; Palo Alto, CA. Revised September 2022.
130. Zepzelca (lurbinectedin) [prescribing information]. Jazz Pharmaceuticals, Inc.; Palo Alto, CA. Revised September 2026.
131. Yondelis (trabectedin) [prescribing information]. Janssen Products, LP; Horsham, PA. Revised December 2025.
132. Lifyorli (relacorilant). Prescribing Information. Corcept Therapeutics Incorporated; Redwood City, CA. Revised March 2026.
133. Evdi (trabectedin). Prescribing Information. Apotex Corp.; Weston, FL. Revised May 2026.

Appendix

Biomarker Testing For Lynparza Individual Selection

Indication	Biomarker	Sample type		
		Tumor	Blood	Plasma (ctDNA)
Germline or somatic HRR gene-mutated metastatic	ATMm, BRCA1m, BRCA2m, BARD1m, BRIP1m, CDK12m, CHEK1m, CHEK2m, FANCLm, PALB2m,	X		

castration-resistant prostate cancer	RAD51Bm, RAD51Cm, RAD51Dm, RAD54Lm			
	gBRCA1m, gBRCA2m		X	
	ATMm, BRCA1m, BRCA2m			X
BRCA-mutated metastatic castration-resistant prostate cancer in combination with abiraterone and prednisone or prednisolone	BRCA1m, BRCA2m	X	X	X

Homologous recombination repair (HRR) Gene mutation

HRR gene mutations can be found in 23% of metastatic castration-resistant prostate cancer. The most frequent gene mutations are found on breast cancer susceptibility gene (BRCA)2, ataxia-telangiectasia mutated (ATM), checkpoint kinase 2 (CHECK2), and BRCA1 genes.

Select individuals for the treatment of HRR gene-mutated mCRPC with Talzenna based on the following HRR gene mutations: ATM, ATR, BRCA1, BRCA2, CDK12, CHEK2, FANCA, MLH1, MRE11A, NBN, PALB2, or RAD51C.

The FDA approved test to detect HRR gene mutation for use with Talzenna is not available currently.

History

Date	Comments
06/12/12	New policy, add to Prescription Drug section. Reviewed by Pharmacy & Therapeutics Committee, June 2012.

Date	Comments
07/08/13	Minor Update – Clarification was added to the policy that it is managed through the member's pharmacy benefit; this is now listed in the header and within the coding section.
10/14/13	Replace policy. Policy updated to reflect new NCCN guidelines which recommend abiraterone as an initial therapy for metastatic castrate-resistant prostate cancer.
11/11/13	Replace policy. Policy section updated with the removal of *Zytiga (abiraterone)*; Rationale section updated in accordance with this change. (See policy 5.01.544 for coverage on Zytiga).
12/08/14	Annual Review. Policy updated with literature review; no change in policy statement.
05/27/15	Annual Review. Policy updated with literature review. Title changed to match the scope of the policy which is no longer limited to oral medications. New policy statements added: nivolumab and olaparib may be considered medically necessary; Opdivo for treatment metastatic squamous non-small cell lung cancer with progression on or after platinum-based chemotherapy may be considered medically necessary; all other uses of Erivedge, Lynparza or Opdivo are considered investigational. Rationale section updated in accordance with this change and new references added. The word "oral" removed from the title to match the scope of the policy.
07/14/15	Interim Update. Added new policy statements for newly approved drug palbociclib.
01/19/16	Coding update. New HCPCS codes J3380 and J9299 – effective 1/1/16 – added to policy.
01/29/16	Minor update. Removed code J3380.
04/01/16	Annual Review, approved March 8, 2016. Policy updated to reflect current labeling indications.
05/26/16	Coding update. J9271 added, effective 1/1/16.
10/01/16	Interim Review, approved September 13, 2016: inclusion of a new indication for Opdivo and Keytruda. Addition of length of approval as 3 months. Inclusion of Gazyva criteria, and rationale for Yervoy.
11/01/16	Interim Review, approved October 11, 2016. Tecentriq criteria and description added to the policy.
12/01/16	Interim Review, approved November 8, 2016. Keytruda's criteria was updated to reflect first-line use in NSCLC. Also, Lonsurf, Ninlaro, and Lartruvo criteria was added to the policy. Tecentriq's newest indication for NSCLC was also added to the policy.
01/01/17	Interim Review, approved December 13, 2016. Minor clarifications made to the criteria language. Also, Yervoy's criteria has been expanded based on NCCN guidelines.

Date	Comments
02/01/17	Annual Review, approved January 10, 2017. Added rupacarib's labeled criteria, as well as drug description and clinical trials rationale. References section has been updated accordingly.
03/01/17	Interim Review, approved February 14, 2017. Added two new indications for nivolumab (recurrent or metastatic squamous cell carcinoma of the head and neck; urothelial carcinoma).
04/01/17	Interim Review, approved March 14, 2017. Updated criteria for Lartruvo.
06/01/17	Interim Review, approved May 16, 2017. Updated an indication for Tecentriq. Updated criteria for Ibrance to include any aromatase inhibitor therapy. Fixed minor grammatical/formatting errors. Added coverage criteria for Odomzo (sonidegib).
07/01/17	Interim Review, approved June 13, 2017. Added coverage criteria for Kisqali, Zejula, Bavencio, Rydapt, and Imfinzi.
09/01/17	Minor update; updated title of related policy 5.01.543.
10/01/17	Interim Review, approved September 21, 2017. Added coverage criteria for Idhifa.
11/01/17	Interim Review, approved October 19, 2017. Added coverage criteria for Verzenio.
12/01/17	Interim Review, approved November 14, 2017. Added new indications for Keytruda and its new references. Added new indication for Lynparza.
01/01/18	Coding update, added HCPCS codes J9022, J9023, and J9285 (new codes effective 1/1/18).
02/01/18	Interim Review, approved January 16, 2018. Added coverage criteria for Aliqopa (copanlisib) and added new indication for Opdivo
03/01/18	Interim Review, approved February 27, 2018. Added new indication for Lynparza - deleterious or suspected deleterious germline BRCA-mutated (gBRCAm), human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer who have been previously treated with chemotherapy either in the neoadjuvant, adjuvant or metastatic setting. Updated Opdivo and Imfinzi criteria to include all FDA approved indications.
06/01/18	Interim Review, approved May 3, 2018. Updated criteria for combination therapy with Opdivo and Yervoy as well as Rubraca to include newly approved FDA labeled indications.
07/01/18	Annual Review, approved June 22, 2018. Added Paloma-2 study for Ibrance and safety and efficacy study for Rydapt. Updated Keytruda criteria for clarity. Added general reauthorization criteria and documentation requirements.
11/01/18	Interim Review, approved October 26, 2018. Added Tibsovo (ivosidenib). Updated indications for all agents per labels. Added criteria for Talzenna (talazoparib).

Date	Comments
	Organized by pharmacology. Moved immunotherapy drugs to new policy 5.01.591. Removed HCPCS codes J9022, J9228, J9271, and J9299.
01/01/19	Coding update, added new HCPCS code J9057 (new code effective 1/1/19).
02/01/19	Interim Review, approved January 8, 2019. Added coverage criteria for Daurismo (glasdegib) and Vitrakvi (larotrectinib) and added new indication for Lynparza (olaparib).
04/01/19	Interim Review, approved March 12, 2019. Updated criteria for Erivedge (vismodegib), Odomzo (sonidegib) and Lonsurf (trifluridine and tipiracil).
07/01/19	Interim Review, approved June 4, 2019. Updated criteria for Ibrance (palbociclib). Removed HCPCS code J3490.
08/01/19	Annual Review, approved July 9, 2019. Added coverage criteria for Balversa (erdafitinib). Updated criteria for Tibsovo (ivosidenib).
10/01/19	Interim Review, approved September 10, 2019, effective January 3, 2020. Bavencio (avelumab) moved to policy 5.01.591 Immune Checkpoint Inhibitors. Added coverage criteria for Asparlas (calaspargase pegol-mknl), Intron A (interferon alfa-2b), and Sylatron (peginterferon alfa-2b). Removed HCPCS code J9023, added HCPCS codes J9118 (new code effective 10/1/19) and J9213.
12/01/19	Interim Review, approved November 12, 2019. Added coverage criteria for Piqray (alpelisib), Rozlytrek (entrectinib), Vitrakvi (larotrectinib), Xpovio (selinexor), and Kisqali Femara co-pack (ribociclib – letrozole).
02/01/20	Interim Review, approved January 14, 2020. Added criteria for Inrebic per August 2019 P&T. Removed HCPCS code J9213, added HCPCS code J9214.
03/01/20	Interim Review, approved February 11, 2020. Updated coverage criteria for Lynparza (olaparib) and Zejula (niraparib) effective for dates of service on or after March 1, 2020. Added coverage criteria for Darzalex (daratumumab) (HCPCS code J9145) which becomes effective for dates of service on or after June 5, 2020.
04/01/20	Interim Review, approved March 10, 2020. Added Padcev (enfortumab vedotin-ejfv) to policy with coverage criteria for urothelial cancer, effective for dates of service on or after July 2, 2020, after provider notification. Added Tazverik (tazemetostat) to policy with coverage criteria for epithelioid sarcoma; these criteria become effective April 1, 2020.
07/01/20	Annual Review, approved June 9, 2020, effective July 1, 2020. Added a dose limit of 200 mg per day to Odomzo (sonidegib). Added a dose limit of 150 mg per day to Erivedge (vismodegib). Added new indication to Zejula (niraparib) for the treatment of advanced ovarian cancer. Added new indications to Lynparza (olaparib) for the treatment of ovarian cancer when used in combination with bevacizumab and for the treatment of prostate cancer. Added new indication to Rubraca (rucaparib) for the

Date	Comments
	treatment of prostate cancer. Added coverage criteria for Pemazyre (pemigatinib) for the treatment of cholangiocarcinoma. Added coverage criteria for Gleostine (lomustine) for the treatment of brain tumors and Hodgkin's lymphoma. Added coverage criteria for Sarclisa (isatuximab-irfc) for the treatment of multiple myeloma. Added coverage criteria for Trodelvy (sacituzumab govitecan-hziy) for the treatment of mTNBC. Removed Lartruvo (olaratumab) from policy as drug was withdrawn from the market on April 25, 2019. Changes to Kyprolis (carfilzomib) and Velcade (bortezomib) are effective for dates of service on or after October 2, 2020, following 90-day provider notification. Added coverage criteria for Velcade (bortezomib) for the treatment of multiple myeloma and mantle cell lymphoma. Added coverage criteria for Kyprolis (carfilzomib) for the treatment of multiple myeloma. Added J9177 effective 7/2/20. Added codes J9041 and J9047 effective 10/2/20. Removed code J9285 effective 7/1/20.
09/01/20	Interim Review, approved August 11, 2020, effective September 1, 2020. Added coverage criteria for Blenrep (belantamab mafodotin-blmf) for the treatment of multiple myeloma. Added coverage criteria for Darzalex Faspro (daratumumab and hyaluronidase-fihj) for the treatment of multiple myeloma. Added new indications to Tazverik (tazemetostat) for the treatment of follicular lymphoma. Added new indication to Xpovio (selinexor) for the treatment of diffuse large B-cell lymphoma. Added Blincyto (blinatumomab) to policy with coverage criteria for acute lymphoblastic leukemia (ALL) effective for dates of service on or after December 3, 2020, after provider notification. Added Leukine (sargramostim) to policy with coverage criteria for AML, progenitor cell mobilization, progenitor cell transplantation, BMT failure or engraftment delayed, and H-ARS effective for dates of service on or after December 3, 2020, after provider notification. Added HCPCS J2820 and J9039.
10/01/20	Coding update. Added HCPCS code J9227.
11/01/20	Interim Review, approved October 13, 2020. Added Jakafi (ruxolitinib) for the treatment of myelofibrosis, polycythemia vera, and acute GVHD. Added Zepzelca (lurbinectedin) for the treatment of metastatic SCLC. Added Inqovi (decitabine and cedazuridine) for the treatment of MDS. Added Retevmo (selpercatinib) for the treatment of NSCLC, MTC, and thyroid cancer. Added a dose limit to Pemazyre (pemigatinib). Added Zepzelca to J3590.
01/01/21	Interim Review, approved December 8, 2020. Updated Kyprolis (carfilzomib) criteria adding in combination with daratumumab plus dexamethasone for relapsed or refractory multiple myeloma. Added new HCPCS codes C9069, J9144, J9281, and J9317 - effective 1/1/21. Added HCPCS J9280 for Jelmyto. Added Jelmyto (mitomycin) to policy with coverage criteria for LG-UTUC effective for dates of service on or after April 7, 2021, after provider notification.

Date	Comments
02/01/21	Interim Review, approved January 12, 2021. Added Gavreto (pralsetinib) for the treatment of NSCLC, MTC, and thyroid cancer. Added Danyelza (naxitamab-gqgk) for the treatment of relapsed or refractory high-risk neuroblastoma in the bone or bone marrow. Updated Leukine (sargramostim) criteria to include in combination with Danyelza (naxitamab-gqgk) for the treatment of relapsed or refractory high-risk neuroblastoma in the bone or bone marrow. Added Onureg (azacitidine) for the treatment of AML. Added new indication to Xpovio (selinexor) for treatment of MM in combination with bortezomib and dexamethasone. Added drug name Danyelza to HCPC code J3590.
04/01/21	Coding update. Added term date to HCPC C9069 and added new HCPC code J9037.
04/07/21	Coding update. Added HCPC code J9280.
06/01/21	Interim Review, approved May 11, 2021. Added Pepaxto (melphalan flufenamide) for the treatment of MM. Added Cosela (trilaciclib) to decrease the incidence of chemotherapy-induced myelosuppression for extensive-stage SCLC. Added new indication to Sarclisa (isatuximab-irfc) for use in combination with Kyprolis (carfilzomib) and dexamethasone for MM. Added coverage for Darzalex Faspro (daratumumab and hyaluronidase-fihj) for use in combination with bortezomib, thalidomide, and dexamethasone as first-line therapy for MM. Added new indication to Darzalex Faspro for the treatment of light chain (AL) amyloidosis. Updated criteria for Trodelvy (sacituzumab govitecan-hziy) for treatment of TNBC to include unresectable locally advanced. Added new indication to Trodelvy (sacituzumab govitecan-hziy) for the treatment of urothelial cancer.
07/01/21	Annual Review, approved June 8, 2021. Added trial and failure with Ibrance (palbociclib) or Verzenio (abemaciclib) requirement to Kisqali (ribociclib) and Kisqali Femara Co-Pack (letrozole-ribociclib). Added HCPCS C9078, C9080 and J9348.
08/01/21	Interim Review, approved July 13, 2021. Added Empliciti (elotuzumab) for the treatment of multiple myeloma. Added Yondelis (trabectedin) for the treatment of unresectable or metastatic liposarcoma or leiomyosarcoma. Added Halaven (eribulin mesylate) for the treatment of metastatic breast cancer and unresectable or metastatic liposarcoma. Added Erwinaze (asparaginase *Erwinia chrysanthemi*) as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL. Added Abraxane (paclitaxel protein-bound particles) for the treatment of metastatic breast cancer, locally advanced or metastatic NSCLC, and metastatic adenocarcinoma of the pancreas. Added Arranon (nelarabine) for the treatment of T-ALL and T-LBL. Added Rylaze (asparaginase erwinia chrysanthemi (recombinant)-rywn) as a component of a multi-agent chemotherapeutic regimen for the treatment of ALL and LBL. Added Lumakras (sotorasib) for the treatment of KRAS G12C-mutated locally advanced or metastatic NSCLC. Added Truseltiq (infigratinib) for the treatment of unresectable locally advanced or metastatic cholangiocarcinoma. Policy updates for Abraxane,

Date	Comments
	Arranon, Empliciti, Erwinaze, Halaven, and Yondelis are effective for dates of service on or after November 5, 2021, after provider notification. Added HCPCS codes J9019, J9176, J9179, J9261, J9264 and J9352.
10/01/21	Interim Review, approved September 14, 2021. Added Welireg (belzutifan) for treatment of adult individuals with von Hippel-Lindau disease who require therapy for associated RCC, CNS hemangioblastomas, or pNET. Added a new indication to Padcev (enfortumab vedotin-ejfv) for the treatment of UC for individuals ineligible for cisplatin-containing chemotherapy who have previously received one or more prior lines of therapy. Added a new indication to Darzalex Faspro (daratumumab and hyaluronidase-fihj) for the treatment of multiple myeloma in combination with pomalidomide and dexamethasone. Added a new indication to Tibsovo (ivosidenib) for the treatment of cholangiocarcinoma with an IDH1 mutation. Updated Tibsovo criteria for newly diagnosed AML to require a susceptible IDH1 mutation. Removed effective date 10/1/2020 from HCPC code J9227. Added HCPC code J9281 for Jelmyto and removed HCPC code J9280. Added HCPCS J1448 and J9247.
01/01/22	Interim Review, approved December 14, 2021. Added a new indication to Jakafi (ruxolitinib) for the treatment of chronic graft-versus-host disease. Added a new indication to Verzenio (abemaciclib) for the treatment of early breast cancer at high risk of recurrence and a Ki-67 score ≥20%. Added a new indication to Darzalex Faspro (daratumumab and hyaluronidase-fihj) for the treatment of multiple myeloma in combination with Kyprolis (carfilzomib) and dexamethasone. Added a new indication to Kyprolis (carfilzomib) for the treatment of multiple myeloma in combination with Darzalex Faspro (daratumumab and hyaluronidase-fihj) and dexamethasone. Added generic nelarabine to policy with identical coverage criteria as brand Arranon (nelarabine). Removed Pepaxto (melphalan flufenamide) from policy as drug was withdrawn from the market on October 22, 2021. Moved Padcev (enfortumab vedotin-ejfv) from Policy 5.01.540 to Policy 5.01.582 with no changes to coverage criteria. Added HCPCS J9021. Removed HCPCS J9177.
06/01/22	Interim Review, approved May 10, 2022. Added Vonjo (pacritinib) for the treatment of adults with myelofibrosis . Added Kimmtrak (tebentafusp-tebn) for the treatment of adult individuals with unresectable or metastatic uveal melanoma. Added a new indication to Lynparza (olaparib) for the adjuvent treatment of adult individuals with high risk early breast cancer. Updated Lynparza indication for metastatic breast cancer to include PALB2 mutation and to require cancer is HER2-negative. Removed from Kisqali (ribociclib) and Kisqali Femara Co-Pack (ribociclib – letrozole) the requirement to have previously tried and failed Ibrance (palbociclib) or Verzenio (abemaciclib). Added a note to Inrebic (fedratinib) regarding documentation of intermediate-2 or high-risk MF. Removed HCPCS code C9069.
07/01/22	Annual Review, approved June 14, 2022. Added HCPCS code C9095. Removed HCPCS code J9057 and J9247. Removed Aliqopa (copanlisib) as coverage criteria for Aliqopa

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	are captured under Policy 5.01.592. Moved Piqray (alpelisib) from Policy 5.01.540 to Policy 5.01.592 with no changes to coverage criteria. Added coverage for Leukine (sargramostim) as second-line therapy for the treated of individuals taking myelosuppressive anti-cancer regimens, at risk of severe febrile neutropenia. Added to Darzalex (daratumumab) coverage for use in combination with carfilzomib and dexamethasone in individuals with relapsed or refractory MM who have received one to three prior lines of therapy. Added a new indication to Tibsovo (ivosidenib) for use in combination with azacitidine or as monotherapy for the treatment of newly diagnosed AML.
10/01/22	Coding update. Added HCPCS code J9274.
11/01/22	Interim Review, approved October 11, 2022. Updated Pemazyre (pemigatinib) criteria to include coverage for relapsed or refractory myeloid/lymphoid neoplasms (MLNs) with FGFR1 rearrangement. Removed from Zejula (niraparib) coverage for the treatment of advanced homologous recombination deficiency (HRD) positive ovarian cancer after > 3 lines of chemotherapy, as GSK voluntarily withdrew indication. Added coverage for Elzonris (tagraxofusp-erzs) for the treatment of blastic plasmacytoid dendritic cell neoplasm (BPDCN). Added coverage for Onivyde (irinotecan liposome injection) for treatment of metastatic adenocarcinoma of the pancreas and metastatic cholangiocarcinoma. Added a new indication to Retevmo (selpercatinib) for the treatment of locally advanced or metastatic RET fusion-positive solid tumors. Added coverage for Lytgobi (futibatinib) for the treatment of intrahepatic cholangiocarcinoma. Policy updates for Onivyde and Elzonris are effective for dates of service on or after February 3, 2023, after provider notification. Added HCPCS codes J9205 and J9269.
01/01/23	Interim Review, approved December 13, 2022. Added coverage for Rezlidhia (olutasidenib) for the treatment of adult individuals with relapsed or refractory AML with a susceptible IDH1 mutation. Added coverage for Tecvayli (teclistamab -cqyv) for the treatment of adult individuals with relapsed or refractory multiple myeloma. Removed Blenrep (belantamab mafodotin-blmf) from policy as drug is being withdrawn from market by the manufacturer due to lack of efficacy in follow-up trials. Added new HCPC codes J9046, J9048, J9049. Added name Tecvayli to HCPC J3590. Removed HCPC code J9037. Removed termed codes C9078 and C9080. Removed new code date from J9021.
03/01/23	Interim Review, approved February 14, 2023. Added coverage for Krazati (adagrasib) for the treatment of KRAS G12C-mutated locally advanced or metastatic NSCLC. Updated Ibrance (palbociclib) criteria when used in combination with an aromatase inhibitor as initial endocrine-based therapy removing the requirement individual is postmenopausal. Added a new indication to Trodelvy (sacituzumab govitecan-hziy) for

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	the treatment of unresectable locally advanced or metastatic HR+, HER2-negative breast cancer. Removed new code effective date from HCPC code J9021.
04/01/23	Coding update. Added new HCPCS code C9148.
05/01/23	Annual Review, approved April 11, 2023. Changed the wording from "patient" to "individual" throughout the policy for standardization. Reviewed prescribing information for all drugs in policy. Updated Zejula criteria to indicate coverage for the maintenance treatment of adult individuals is limited to those with deleterious or suspected deleterious germline *BRCA*-mutated recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to platinum-based chemotherapy. Updated Verzenio criteria to indicate coverage in combination with endocrine therapy for the adjuvant treatment of adult individuals with HR-positive, HER2-negative, node-positive early breast cancer at high risk of recurrence without requiring a Ki-67 score of 20 or greater. Added coverage criteria for Xgeva (denosumab) effective for dates of service on or after August 4, 2023, following 90-day provider notification. Added HCPC code J0897 to report Xgeva.
07/01/23	Coding update. Termed HCPCS code C9148 and added new HCPCS code J9380.
09/01/23	Interim Review, approved August 8, 2023. Added coverage criteria for Epkinly (epcoritamab-bysp) for the treatment of adult individuals with relapsed or refractory diffuse large B-cell lymphoma (DLBCL), not otherwise specified, including DLBCL arising from indolent lymphoma, and high-grade B-cell lymphoma after two or more lines of systemic therapy. Added coverage criteria for Lynparza (olaparib) for the treatment of adult individuals with deleterious or suspected deleterious BRCA-mutated (BRCAm) metastatic castration-resistant prostate cancer (mCRPC) when used in combination with abiraterone and prednisone or prednisolone. Added coverage criteria for Talzenna, when used in combination with enzalutamide, for the treatment of adult individuals with HRR gene- mutated metastatic castration-resistant prostate cancer (mCRPC). Added generic bortezomib to the criteria of Velcade (bortezomib). Added coverage criteria for Vistogard for the emergency treatment of fluorouracil or capecitabine overdose, or severe or life-threatening toxicity within 96 hours following the end of fluorouracil or capecitabine administration. Removed Gavreto's indication of adult and pediatric individuals 12 years of age and older with advanced or metastatic RET-mutant medullary thyroid cancer (MTC) who require systemic therapy per FDA label changes. Added coverage for Leukine for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Added Brand paclitaxel protein-bound particles (american regent-unbranded) IV to Abraxane criteria. Added criteria for Lysodren (mitotane) for the treatment of adrenal cortical carcinoma when the tumor is inoperable. Added criteria for Matulane (procarbazine hydrochloride) for the treatment of stage III and IV Hodgkin's disease when used in combination with other anticancer drugs. Added coverage criteria for Temodar (temozolomide) IV and generic

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	temozolomide oral for the treatment of adult individuals with newly diagnosed glioblastoma concomitantly with radiotherapy and then as maintenance treatment, or for refractory anaplastic astrocytoma who have experienced disease progression on a drug regimen containing nitrosourea and procarbazine. Added coverage criteria for Unituxin (dinutuximab). Unituxin in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), interleukin-2 (IL-2), and 13-cis-retinoic acid (RA), for the treatment of pediatric individuals with high-risk neuroblastoma who achieve at least a partial response to prior first-line multiagent, multimodality therapy. Policy changes to Temodar IV and Unituxin IV are effective December 7, 2023. Added HCPCS codes C9399, J9259 and J9328.
10/01/23	Coding update. Added new HCPCS codes C9155 and J9051.
11/01/23	Interim Review, approved October 10, 2023. Added Talvey and Elrexfio for the treatment of adult individuals with relapsed or refractory multiple myeloma where individual has tried at least four lines of prior therapies. Updated coverage criteria for Arranon to be included as first-line treatment when added to the ABFM regimen in intermediate to high-risk individuals or ABFM regimen induction failures. Added brand bortezomib to policy with identical coverage criteria as generic bortezomib and Velcade (bortezomib).
01/01/24	Interim Review, approved December 12, 2023. Added coverage criteria for Purixan (mercaptopurine) for the treatment of acute lymphoblastic leukemia as part of a combination chemotherapy maintenance regimen. Removed HCPCS code C9155. Added new HCPCS codes C9163, C9165, J1246 and J9321.
02/01/24	Annual Review, approved January 9, 2024. Added coverage criteria for Lonsurf (trifluridine and tipiracil) for the treatment of certain adult individuals with metastatic colorectal cancer in combination with bevacizumab. Added coverage criteria for Hepzato Kit (melphalan hepatic delivery system) for the treatment of certain adult individuals with unresectable or metastatic uveal melanoma. Added coverage criteria for Ogsiveo (nirogacestat) for the treatment of certain adult individuals with progressing desmoid tumors. Added Hepzato to C9399 and added HCPC code J9999 for Hepzato.
03/01/24	Interim Review, approved February 13, 2024. Added coverage criteria for Tabloid (thioguanine) for the treatment of certain individuals with acute myeloid leukemia. Added coverage criteria for Iwilfin (eflornithine) for the treatment of certain individuals with high-risk neuroblastoma. Added coverage criteria for oral Temodar (temozolomide) and oral generic temozolomide for the treatment of certain adult individuals with glioblastoma or anaplastic astrocytoma. Updated coverage criteria for IV Temodar (temozolomide) to include the treatment of certain adult individuals with newly diagnosed anaplastic astrocytoma. Updated coverage criteria for Tibsovo (ivosidenib) to include the treatment of certain adult individuals with myelodysplastic

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	syndromes. Updated coverage criteria for Welireg (belzutifan) to include the treatment of certain adult individuals with renal cell carcinoma. Removed Truseltiq (infigratinib) coverage criteria as the product has been withdrawn from the market. Updated coverage criteria for Balversa (erdafitinib) to remove coverage criteria for the treatment of locally advanced or metastatic urothelial carcinoma with susceptible FGFR2 genetic alterations and broaden step therapy requirement from prior platinum-containing chemotherapy to prior systemic therapy. Added coverage criteria for Ojjaara (momelotinib) for the treatment of certain adults with myelofibrosis.
04/01/24	Coding update. Added new HCPCS codes J1323, J3055, J9248. Termed HCPCS codes C9163 and C9165.
05/01/24	Interim Review, approved April 9, 2024. Added coverage criteria for Thalomid (thalidomide). Added coverage criteria for Aphexda (motixafortide). Updated Onivyde (irinotecan) to include coverage criteria for the first-line treatment of certain adults with metastatic pancreatic adenocarcinoma. Updated Onivyde (irinotecan) to clarify that all coverage criteria is limited to adults. Updated Ogsiveo (nirogacestat) coverage criteria to include a requirement to try generic sorafenib first. Added HCPCS code J2277.
08/01/24	Interim Review, approved July 9, 2024. Added coverage criteria for Amtagvi (lifileucel) for the treatment of certain individuals with unresectable or metastatic melanoma. Added coverage criteria for brand paclitaxel protein-bound particles (Teva – unbranded). Updated Gazyva (obinutuzumab) coverage criteria to include treatment of certain adults with follicular lymphoma in combination with zanubrutinib. Added drug name Amtagvi to unlisted HCPCS code, J3590. Added new HCPCS code J9258.
09/01/24	Interim Review, approved August 13, 2024. Added coverage criteria for Imdelltra (tarlatamab-dlle) for the treatment of certain individuals with extensive-stage small cell lung cancer (ES-SCLC). Added coverage criteria for Dacogen (decitabine) and generic decitabine for the treatment of certain individuals with myelodysplastic syndrome. Added coverage criteria for Elitek (rasburicase) for the treatment of certain individuals with leukemia, lymphoma, or solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis. Added coverage criteria for Casodex (bicalutamide), Eulexin (flutamide), Nilandron (nilutamide), and generic nilutamide for the treatment of certain adults with prostate cancer. Added HCPCS codes J0894 & J2783.
10/01/24	Coding update. Added new HCPCS code C9170 effective 10/1/2024 for Imdelltra.
11/01/24	Interim Review, approved October 8, 2024. Updated Darzalex Faspro (daratumumab-hyaluronidase-fihj) coverage criteria to include treatment of certain adults with multiple myeloma in combination with bortezomib, lenalidomide, and dexamethasone.

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	Added coverage criteria for Voranigo (vorasidenib) for the treatment of certain individuals with Grade 2 astrocytoma or oligodendroglioma. Added coverage criteria for Boruzu (bortezomib) for the treatment of certain individuals with mantle cell lymphoma and multiple myeloma. Updated Abraxane (paclitaxel protein-bound particles), brand paclitaxel protein-bound particles (American Regent – unbranded), and brand paclitaxel protein-bound particles (Teva – unbranded) coverage criteria to include treatment of certain adults who have tried paclitaxel. Removed HCPCS code J1246 as this new code was never implemented by CMS. The following policy changes are effective February 7, 2025 following a 90-day provider notification. Added coverage criteria for Nipent (pentostatin) for the treatment of certain individuals with hairy cell leukemia. Added coverage criteria for Oncaspar (pegaspargase) for the treatment of certain individuals with acute lymphoblastic leukemia. Added brand bendamustine, Belrapzo (bendamustine), Bendeka (bendamustine), and Vivimusta (bendamustine) for the treatment of certain individuals with chronic lymphocytic leukemia (CLL) or non-Hodgkin lymphoma (NHL). Added Vyxeos (cyatarabine-daunorubicin) coverage criteria for the treatment of certain individuals with acute myeloid leukemia. Added HCPCS codes J9034, J9036, J9056, J9153, J9266, and J9268.
01/01/25	Interim Review, approved December 10, 2024. Updated Ibrance (palbociclib) coverage criteria to include a requirement to have an inadequate response or intolerance to Verzenio (abemaciclib), Kisqali (ribociclib) or Kisqali Femara Co-Pack (letrozole-ribociclib). Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Added new HCPCS code J9026.
03/01/25	Annual Review, approved February 11, 2025. Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Added coverage criteria for Xeloda (capecitabine) for certain adults with cancer. Added coverage criteria for Rytelo (Imetelstat) for certain adults with myelodysplastic syndromes. Updated Retevmo (selpercatinib) coverage criteria from adult individuals with metastatic *rearranged during transfection (RET)* fusion-positive non-small cell lung cancer (NSCLC) to adult individuals with locally advanced or metastatic non-small cell lung cancer (NSCLC) with a *RET* gene fusion. Updated Retevmo (selpercatinib) medullary thyroid cancer and advanced or metastatic thyroid cancer age requirement from 12 years and older to 2 years and older. Updated Retevmo (selpercatinib) solid tumors age requirement from 18 years and older to 2 years and older. Updated Blincyto (blinatumomab) coverage criteria to include an age requirement of one month and older, clarify that the disease should be CD19-positive and include treatment of certain individuals with Philadelphia chromosome-negative acute lymphoblastic leukemia (ALL). Updated Krazati (adagrasib) coverage criteria to include treatment of certain adults with colorectal cancer. Added coverage criteria for Tepylute (thiotepa). Added coverage criteria for Tecelra (afamitresgene autoleucel).

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	Added coverage criteria for Vyloy (zolbetuximab-clzb). Updated Sarclisa (isatuximab-irfc) coverage criteria to include treatment of certain individuals with newly diagnosed multiple myeloma. Updated Kisqali (ribociclib) and Kisqali Femara Co-Pack (ribociclib-letrozole) coverage criteria to include treatment of certain adults with stage II or III early breast cancer. Updated Voranigo (vorasidenib) coverage criteria by adding a prescriber requirement and quantity limit. Updated Ibrance (palbociclib) coverage criteria to include treatment of certain adults with breast cancer in combination with Itovebi (inavolisib). Updated Lumakras (sotorasib) coverage criteria to include treatment of certain adults with colorectal cancer. Added HCPCS code J0870 for Rytelo and J3490 for Tepylute. Vyloy and Tecelra were added to the parentheticals for J3590 and C9399.
03/18/25	Minor update. Added February 7, 2025 coding updates back to the coding table. Added HCPCS codes J9034, J9036, J9056, J9153, J9266, and J9268.
04/01/25	Coding update. Added new HCPCS codes C9303, J9054, Q2057.
05/01/25	Interim Review, approved April 8, 2025. Moved Blincyto (blinatumomab), Elrexfio (elranatamab-bcmm), Epkinly (epcoritamab-bysp), Imdelltra (tarlatamab-dlle), Talvey (talquetamab-tgvs), and Tecvayli (teclistamab-cqyv) from policy 5.01.540 Miscellaneous Oncology Drugs to policy 5.01.650 Bispecific Antibodies. Added coverage criteria for Beizray (docetaxel). Added coverage criteria for Revuforj (revumenib). Added coverage criteria for Romvimza (vimseltinib). Updated Dacogen (decitabine) and generic decitabine coverage criteria to include treatment of acute myeloid leukemia. Updated Tabloid (thioguanine) coverage criteria to include treatment of acute lymphoblastic leukemia. Removed HCPCS J9039, C9165, J1323, J9321, C9170, J9026, C9163, J3055, C9148, J9380. Added unlisted HCPCS J9999 for Revuforj.
07/01/25	Coding update. Added HCPCS codes J1326, J9341, J9174 due to quarterly coding updates.
08/01/25	Interim Review, approved July 8, 2025. Added two new indications to all bendamustine products for the treatment of mantle cell lymphoma and for the treatment of follicular lymphoma. Added generic eribulin mesylate to policy with the same coverage criteria as Halaven (eribulin mesylate). Added coverage criteria for Leukeran (chlorambucil). Updated Matulane (procarbazine hydrochloride) coverage criteria to require the individual has first tried generic procarbazine hydrochloride. Added HCPCS J9179 for eribulin mesylate to match criteria. HCPCS J0893 was added following a 90 day hold, effective August 1, 2025. The following policy changes are effective November 7, 2025 following a 90-day provider notification. Added coverage criteria for Treanda (bendamustine). Added coverage criteria for dactinomycin. Added coverage criteria for Docivyx (docetaxel). Added coverage criteria for Doxil (doxorubicin hydrochloride

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	liposome) and generic doxorubicin hydrochloride liposome. Added coverage criteria for Evomela (melphalan). Added coverage criteria for Kepivance (palifermin). Added coverge criteria for Khapzory (levoleucovorin). Added coverage criteria for floxuridine. Added coverage criteria for Portrazza (necitumumab). Added coverage criteria for Trisenox (arsenic trioxide). Added HCPCS codes J9120 (Dactinomycin), J9172 (Dacvyx), Q2050 (Doxil and doxorubicin hydrochloride liposome), J9246 (Melphalan), J2425 (Kepivance), J9200 (fluoxinidine), J9295 (Portrazza), J9017 (Trisenox) and J9033 (Treanda) due to criteria update following 90-day hold.
09/01/25	Interim Review, approved August 12, 2025. Updated Jakafi (ruxolitinib) coverage criteria to limit dose to 50 mg daily and two tablets daily. Added Zusduri (mitomycin) coverage criteria for the treatment of certain individuals with bladder cancer. Updated Welireg (belzutifan) coverage criteria to include treatment of certain individuals with pheochromocytoma or paraganglioma. Added IVRA (melphalan) coverage criteria for the treatment of certain individuals with multiple myeloma. Updated Welireg (belzutifan) coverage criteria to clarify that use for advanced renal cell carcinoma (RCC) is intended for individuals with advanced RCC with a clear cell component. Updated Zejula (niraparib) coverage criteria to indicate that maintenance treatment of adults with advanced ovarian cancer in the first-line setting is limited to those with HRD-positive tumors only. Updated Zejula (niraparib) coverage criteria to include a quantity limit. Updated Darzalex Faspro (daratumumab and hyaluronidase-fihj) and Darzalex (daratumumab) coverage criteria to include treatment of certain individuals with smoldering multiple myeloma. Updated brand bendamustine, Belrapzo (bendamustine), Bendeka (bendamustine), and Vivimusta (bendamustine) coverage criteria to clarify that treatment for follicular lymphoma in combination with rituximab is not limited to first-line use. Added HCPCS code J9249 for IVRA infusion.
11/01/25	Interim Review, approved October 14, 2025. Moved Xgeva (denosumab) from policy 5.01.540 Miscellaneous Oncology Drugs to 5.01.658 Denosumab Products. Added coverage criteria for Inlexzo (gemcitabine intravesical system) and Modeyso (dordaviprone). Removed HCPCS Codes J0897 and added HCPCS Codes J0614 (new code effective October 1. 2025), J8999 for Modeyso and also added Inlexzo and Modeyso to the parenthetical for HCPCS codes C9399 and J9999. The following policy change is effective February 6, 2026, following 90-day provider notification. Added coverage criteria for Ixempra (ixabepilone), generic clofarabine and Clolar (clofarabine). Added HCPCS codes J9027 and J9207.
12/01/25	Interim Review, approved November 11, 2025. Added a new indication to Zepzelca (lurbinectedin) for the treatment of extensive-stage small cell lung cancer (ES-SCLC). Added a new indication to Revuforj (revumenib) for the treatment of acute myeloid leukemia (AML). Added a new indication to Gazyva (obinutuzumab) for the treatment of adults with active lupus nephritis.

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01/01/26	Interim Review, approved December 9, 2025. Removed Kisqali Femara Co-Pack as drug was withdrawn from the market. Removed coverage criteria for Casodex (bicalutamide), Eulexin (flutamide), Nilandron (nilutamide), and generic nilutamide, and quantity limits moved to 5.01.656 Drug Quantity Management. Updated Inrebic (fedratinib), Lynparza (olaparib), Retevmo (selpercatinib) coverage criteria to include a quantity limit. Added coverage criteria for Blenrep (belantamab mafodotin-blmf) for the treatment of adult individuals with relapsed or refractory multiple myeloma who have received at least two prior lines of therapy, including a proteasome inhibitor and an immunomodulatory agent. Added Cosmegen (dactinomycin) to the criteria of dactinomycin. Indicated HCPCS code J9019 is termed effective January 1, 2026.
03/01/26	Annual Review, approved February 10, 2026. Updated coverage criteria for Rozlytrek (entrectinib) for the treatment of solid tumors age requirement from 12 years to 1 month and older. Updated coverage criteria for Matulane (procarbazine hydrochloride) removing the requirement for trial of generic procarbazine hydrochloride. Updated coverage criteria for Rubraca (rucaparib) removing requirement for prior therapy with a taxane-based chemotherapy for treatment of mCRPC. Added coverage criteria for Komzifti (ziftomenib) for the treatment of adult individuals with relapsed or refractory acute myeloid leukemia (AML) with a susceptible nucleophosmin 1 (NPM1) mutation. Updated coverage criteria for Lumakras (sotorasib) and Ojjaara (momelotinib) adding a quantity limit per 30 days. Updated coverage criteria of Pemazyre (pemigatinib) adding a quantity limit per 28 days. Updated coverage criteria for Kyprolis (carfilzomib) to include isatuximab and dexamethasone in list of treatments for relapsed or refractory multiple myeloma. Updated coverage criteria of Darzalex (daratumumab), Hepzato Kit, Ibrance (palbociclib), Romvimza (vimseltinib), Tecelra (afamitresgene autoleucel), and Vyloy (zolbetuximab-clzb) removing ECOG requirement. Updated coverage criteria for Romvimza (vimseltinib) quantity limit to 2 capsules weekly. Removed coverage criteria for Temodar (temozolomide) oral as product has been discontinued. Updated coverage criteria for Darzalex Faspro removing ECOG requirement, and adding new indication in combination with bortezomib, lenalidomide, and dexamethasone in newly diagnosed individuals who are ineligible for autologous stem cell transplant. Updated coverage criteria for generic temozolomide oral and Temodar (temozolomide) IV for treatment of glioblastoma removing requirement individual is newly diagnosed.
04/01/26	Coding update. Added new HCPCS code J9183, effective April 1, 2026.
05/01/26	Interim Review, approved April 14, 2026. Updated initial authorization for all other reviews for oral drugs listed in the policy from 3 months to 6 months. Updated criteria for Blenrep (belantamab) when used in combination with bortezomib and dexamethasone clarifying it is for the first 8 cycles, then continued as monotherapy. Added generic lomustine to the policy with the same criteria as Gleostine (lomustine).

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	Updated criteria for Beizray (docetaxel) and Docivyx (docetaxel) adding new indication in combination with carboplatin, trastuzumab with/without pertuzumab as neoadjuvant or adjuvant therapy for previously untreated, recurrent, or metastatic HER2-positive breast cancer. Updated criteria for Ibrance (palbociclib) adding new indication for the treatment of adults with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-positive metastatic breast cancer. Updated criteria for Kyprolis (carfilzomib) adding new indication as first line treatment for multiple myeloma when used in combination with daratumumab, lenalidomide, and dexamethasone. Updated criteria for Darzalex (daratumumab) adding new indication for multiple myeloma in combination with Kyprolis (carfilzomib), lenalidomide, and dexamethasone as first-line treatment. Updated criteria for Darzalex Faspro adding new indication in combination with Tecvayli (teclistamab-cqyv) in individuals with relapsed or refractory multiple myeloma who have received at least 1 prior line of therapy including a proteasome inhibitor (PI) (e.g., bortezomib, carfilzomib, ixazomib) and an immunomodulatory agent (e.g., thalidomide, pomalidomide, lenalidomide).
07/01/26	Interim Review, approved June 9, 2026. Added coverage criteria for Lifyorli (relacorilant) for the treatment of adult individuals with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received 1 to 3 prior systemic treatment regimens, which included a bevacizumab-containing regimen, and when used in combination with nab-paclitaxel. Updated Abraxane (paclitaxel protein bound particles) and brand paclitaxel protein-bound particles adding indication for the treatment of adult individuals with platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer who have received 1 to 3 prior systemic treatment regimens, which included a bevacizumab-containing regimen, and when used in combination with Lifyorli (relacorilant). Added Jakafi XR (ruxolitinib extended-release) to the policy with the same clinical criteria as Jakafi (ruxolitinib); clarified Jakafi XR dose is limited to 55 mg daily and the quantity is limited to 30 tablets per 30 days. Updated Inqovi (decitabine and cedazuridine) adding criteria when used in combination with venetoclax for the treatment of newly diagnosed acute myeloid leukemia (AML) in adult individuals aged 75 years or older, OR who have comorbidities that preclude use of intensive induction chemotherapy. Updated Voranigo (vorasidenib) and Ogsiveo (nirogacestat) adding a quantity limit per 30 days. Updated criteria for Evomela (melphalan) for use as a high-dose conditioning treatment prior to hematopoietic progenitor (stem) cell transplantation removing the requirement in individuals with multiple myeloma. Added Evdi (trabectedin) to the policy with same criteria as Yondelis (trabectedin). Updated Xpovio (selinexor) removing coverage criteria for treatment of relapsed or refractory diffuse large B-cell lymphoma. Removed reference to non-formulary exception reviews. Added HCPCS codes J9053 and J9282, effective July 1, 2026. Removed “new code effective 07/01/25” from table.

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09/01/26	Interim Review, approved August 11, 2026. Updated Ibrance (palbociclib) adding criteria when used in combination with trastuzumab, with or without pertuzumab, and endocrine therapy for the maintenance treatment of HR-positive, HER2-positive locally advanced or metastatic breast cancer following induction treatment. Added Sarclisa Escena (isatuximab-irfc) to the policy for the treatment of multiple myeloma. Updated criteria for Tecelra (afamitresgene autoleucel) age requirement from 18 years to 12 years or older. Updated Trodelvy (sacituzumab govitecan-hziy) adding criteria for the first-line treatment of mTNBC either as a single agent or in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph. Updated Welireg (belzutifan) adding criteria when used in combination with pembrolizumab or pembrolizumab and berahyaluronidase alfa-pmph, for the adjuvant treatment of adult individuals with ccRCC at intermediate-high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions. Removed termed codes C9303, J8999, J9019, J9259.
10/01/26	Coding update. HCPCS code J9352 termed September 30, 2026 and updated HCPCS J9033 code description. Added new HCPCS code J9362.
11/01/26	Interim Review, approved October 13, 2026. Updated criteria for temozolomide and Temodar (temozolomide) in anaplastic astrocytoma by replacing "newly diagnosed" with "used as first-line therapy" and removing the requirement for disease progression on nitrosourea and procarbazine regimens in refractory disease. Updated Gazyva (obinutuzumab) adding criteria when used in combination with venetoclax for CLL. Updated Krazati (adagrasib) removing coverage criteria for the treatment of KRAS G12 mutated locally advanced or metastatic CRC. Updated Verzenio (abemaciclib) adding criteria when used in combination with imlunestrant for the treatment of adults with estrogen receptor (ER)-positive, HER2-negative, estrogen receptor-1 (ESR1)-mutated advanced or metastatic breast cancer. Updated Zepzelca (lurbinectedin) removing the indication for metastatic SCLC. Removed coverage criteria for Tazverik (tazemetostat) as product has been withdrawn from the market. Removed quantity limits for Gavreto, Inrebic, Jakafi, Jakafi XR, Komzifti, Lifyorli, Lumakras, Lynparza, Modeyso, Ogsiveo, Ojjaar, Pemazyre, Revuforj, Romvimza, Voranigo, and Welireg as quantity limits are addressed in policy 5.01.656 Drug Quantity Management. Removed Tecelra from HCPCS code J3590. Removed Hepzato, Zusduri and Inlexzo from HCPCS code J9999. Removed HCPCS code J3490 for Tepylute . The following policy changes are effective February 5, 2027, following 90-day provider notification. Added coverage criteria for Decnupaz (pivekimab sunirine-pvzy) for the treatment of adult individuals with blastic plasmacytoid dendritic cell neoplasm. Updated criteria for Elzonris (tagraxofusp-erzs) adding medication will not be used in combination with Decnupaz, and added a specialist requirement. Added Decnupaz to HCPCS code J9999.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2026 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.