MEDICAL POLICY – 2.03.07

Cytoreductive Surgery and Perioperative Intraperitoneal Chemotherapy for Select Intra-Abdominal and Pelvic Malignancies

BCBSA Ref. Policy: 2.03.07

Effective Date: Oct. 1, 2018
Last Revised: Sept. 20, 2018
Replaces: N/A

RELATED MEDICAL POLICIES:
None

Select a hyperlink below to be directed to that section.

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

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Chemotherapy can be delivered directly into the abdominal cavity to treat certain types of cancer. However, chemotherapy has trouble penetrating large tumors. That’s why surgery is done to remove as much cancer as possible before chemotherapy is directly given into the abdomen. Removing or reducing the size of the tumor - also called debulking - provides the chemotherapy drug the best chance to kill the remaining cancer cells. There are several different types of cancer in which this treatment has been tried. This policy describes when debulking surgery followed by direct application of chemotherapy may be considered 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.
Note: This policy addresses “perioperative” intraperitoneal chemotherapy; that is intraperitoneal chemotherapy which occurs at the same operative session as the cytoreductive surgery. This policy does not address intraperitoneal chemotherapy which is delivered directly into the abdominal cavity through an indwelling catheter with an access port that was previously surgically placed, and given either in an inpatient or outpatient setting.

<table>
<thead>
<tr>
<th>Service</th>
<th>Medical Necessity</th>
</tr>
</thead>
</table>
| Cytoreductive surgery plus perioperative intraperitoneal chemotherapy | Cytoreductive surgery plus perioperative intraperitoneal chemotherapy may be considered medically necessary for the treatment of either of the following:  
  - Pseudomyxoma peritonei  
  - Diffuse malignant peritoneal mesothelioma |

<table>
<thead>
<tr>
<th>Service</th>
<th>Investigational</th>
</tr>
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</table>
| Cytoreductive surgery plus perioperative intraperitoneal chemotherapy | Cytoreductive surgery plus perioperative intraperitoneal chemotherapy is considered investigational for the treatment of ANY of the following:  
  - Peritoneal carcinomatosis from colorectal cancer, gastric cancer, or endometrial cancer  
  - Ovarian cancer  
  - All other indications, including goblet cell tumors of the appendix |

Documentation Requirements

The patient’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 relevant history and physical supporting diagnoses of:
  - Pseudomyxoma peritonei
  - OR
  - Diffuse malignant peritoneal mesothelioma

Coding
The coding for this overall procedure would likely involve codes for the surgery, the intraperitoneal chemotherapy, and the hyperthermia.

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>96446</td>
<td>Chemotherapy administration into the peritoneal cavity via indwelling port or catheter</td>
</tr>
<tr>
<td>96549</td>
<td>Unlisted chemotherapy procedure</td>
</tr>
</tbody>
</table>

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).

**Cytoreduction**

There is no specific CPT code for the surgical component of this complex procedure. It is likely that a series of CPT codes would be used describing exploratory laparotomies of various components of the abdominal cavity, in addition to specific codes for resection of visceral organs, depending on the extent of the carcinomatosis.

**Intraperitoneal Chemotherapy**

When performed using a temporary catheter or performed intraoperatively, the unlisted code 96549 (unlisted chemotherapy procedure) would be reported.

**Hyperthermia**

This procedure does not refer to external application of heat as described by CPT code 77605. There are no codes for the heating of the chemotherapy.

**Related Information**

N/A
Description

Cytoreductive surgery (CRS) comprises peritonectomy (ie, peritoneal stripping) procedures and multivisceral resections, depending on the extent of intra-abdominal tumor dissemination. CRS may be followed intraoperatively by infusion of intraperitoneal chemotherapy with or without heating, which is intended to improve the tissue penetration of the chemotherapy. When heated, this is referred to as hyperthermic intraperitoneal chemotherapy (HIPEC). CRS and HIPEC have been proposed for a number of intra-abdominal and pelvic malignancies such as pseudomyxoma peritonei and peritoneal carcinomatosis from colorectal, gastric, or endometrial cancer.

Background

**Cytoreductive Surgery Plus Hyperthermic Intraperitoneal Chemotherapy**

Cytoreductive surgery (CRS) comprises peritonectomy (ie, peritoneal stripping) procedures and multivisceral resections, depending on the extent of intra-abdominal tumor dissemination.\(^1\) CRS may be followed intraoperatively by the infusion of intraperitoneal chemotherapy, most commonly mitomycin C. The intraperitoneal chemotherapy may be heated, which is intended to improve the tissue penetration, and this is referred to as hyperthermic intraperitoneal chemotherapy (HIPEC). Inflow and outflow catheters are placed in the abdominal cavity, along with probes to monitor temperature. The skin is then temporarily closed during the chemotherapy perfusion, which typically runs for 1 to 2 hours.

**Pseudomyxoma Peritonei**

Pseudomyxoma peritonei is a clinicopathologic entity characterized by the production of mucinous ascites and mostly originates from epithelial neoplasms of the appendix. Appendix cancer is diagnosed in fewer than 1000 Americans each year; less than half are epithelial neoplasms.\(^2\) As mucin-producing cells of the tumor proliferate, the narrow lumen of the appendix becomes obstructed and subsequently leads to appendiceal perforation. Neoplastic
cells progressively colonize the peritoneal cavity and produce copious mucin, which collects in the peritoneal cavity. Pseudomyxoma peritonei ranges from benign (disseminated peritoneal adenomucinosis) to malignant (peritoneal mucinous carcinomatosis), with some intermediate pathologic grades. Clinically, this syndrome ranges from early pseudomyxoma peritonei, discovered on imaging or during a laparotomy performed for another reason, to advanced cases with a distended abdomen, bowel obstruction, and starvation. The conventional treatment of pseudomyxoma peritonei is surgical debulking repeated as necessary to alleviate pressure effects. However, repeated debulking surgeries become ever more difficult due to progressively thickened intra-abdominal adhesions, and this treatment is palliative, leaving visible or occult disease in the peritoneal cavity.\(^3\) Five-year overall survival depends on tumor histology and ranges from 6% for high-grade tumors to 75% for low-grade tumors.\(^4,5\)

**Gastrointestinal Cancers (Colorectal, Gastric) and Peritoneal Carcinomatosis**

Peritoneal dissemination develops in approximately 10% to 15% of patients with colon cancer and, despite the use of increasingly effective regimens of chemotherapy and biologic agents to treat advanced disease, peritoneal metastases are associated with a median survival of 6 to 7 months.

Peritoneal carcinomatosis is detected in more than 30% of patients with advanced gastric cancer and is a poor prognostic indicator. Median survival is 3 months, and 5-year survival is less than 1%.\(^6\) Sixty percent of deaths from gastric cancer are attributed to peritoneal carcinomatosis.\(^7\) Current chemotherapy regimens are nonstandard, and peritoneal seeding is considered unresectable for cure.\(^8\)

**Peritoneal Mesothelioma**

Malignant mesothelioma is a relatively uncommon malignancy that may arise from the mesothelial cells lining the pleura, peritoneum, pericardium, and tunica vaginalis testis. In the United States, 200 to 400 new cases of diffuse malignant peritoneal mesothelioma (DMPM) are registered every year, accounting for 10% to 30% of all-type mesothelioma.\(^9\) DMPM has traditionally been considered as a rapidly lethal malignancy with limited and ineffective therapeutic options.\(^9\) The disease is usually diagnosed at an advanced stage and is characterized by multiple variably sized nodules throughout the abdominal cavity. As the disease progresses, the nodules become confluent to form plaques, masses, or uniformly cover peritoneal surfaces.
In most patients, death eventually occurs as a result of locoregional progression within the abdominal cavity. In historical case series, treatment by palliative surgery, systemic or intraperitoneal chemotherapy, and abdominal irradiation resulted in a median survival of approximately 12 months.9

Surgical cytoreduction (resection of visible disease) in conjunction with HIPEC is designed to remove visible tumor deposits and residual microscopic disease. By delivering chemotherapy intraperitoneally, drug exposure to the peritoneal surface is increased some 20-fold compared with systemic exposure. In addition, previous animal and in vitro studies have suggested that the cytotoxicity of mitomycin C is enhanced at temperatures greater than 39°C (102.2°F).

**Ovarian Cancer**

Several different types of malignancies can arise in the ovary; epithelial carcinoma is the most common type, accounting for 90% of malignant ovarian tumors. Epithelial ovarian cancer is the fifth most common cause of cancer death in women in the United States. New cases and deaths from ovarian cancer in 2014 are estimated at 21,980 and 14,270, respectively.10 Most ovarian cancer patients (>70%) present with widespread disease, and annual mortality is approximately 65% of the incidence rate.

Current management of advanced epithelial ovarian cancer is CRS followed by combination chemotherapy. Treatment guidelines recommend intraperitoneal chemotherapy for patients with optimally debulked (<1 cm) stage 2 disease (pelvic extension of tumor) or stage 3 disease (peritoneal extension of tumor).10 Estimated median OS is 66 months with and 37 to 49 months without intraperitoneal chemotherapy, respectively.11,12 However, tumor recurrences are common, and prognosis for recurrent disease is poor.

CRS plus HIPEC in combination with systemic chemotherapy is being studied for primary and recurrent disease. Because HIPEC is administered at the time of surgery, treatment-related morbidity may be reduced compared with intraperitoneal chemotherapy administered postoperatively.

**Summary of Evidence**

For individuals who have pseudomyxoma peritonei who receive cytoreductive surgery (CRS) plus perioperative intraperitoneal chemotherapy, the evidence includes cohort studies and a systematic review. Relevant outcomes are overall survival (OS), disease-specific survival, quality
of life, and treatment-related mortality and morbidity. Uncontrolled studies of primary treatment of pseudomyxoma peritonei with CRS plus hyperthermic intraperitoneal chemotherapy (HIPEC) have reported a median and a 5-year OS ranging from 47 to 156 months and 41% to 96%, respectively. One retrospective study of 26 patients, who underwent CRS plus HIPEC for recurrence, indicated 5-year OS rate of 34%. Procedure-related morbidity and mortality have decreased over time. Controlled studies are needed to draw conclusions about the efficacy and safety of CRS plus HIPEC compared with standard treatment (CRS alone). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peritoneal carcinomatosis of colorectal origin who receive CRS plus perioperative intraperitoneal chemotherapy, the evidence includes a randomized controlled trial (RCT), systematic reviews, and a large number of observational studies. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. A 2016 meta-analysis identified 76 studies, 15 of which were controlled. A meta-analysis of controlled studies found that CRS plus HIPEC, compared with traditional therapy without HIPEC, was associated with significantly higher survival rates, and was not associated with significantly higher rates of treatment-related morbidity. The RCT, in which patients with peritoneal carcinomatosis due to colorectal cancer were followed for at least 6 years, demonstrated improved survival in patients who received CRS plus HIPEC and systemic chemotherapy compared with patients who received systemic chemotherapy alone. However, procedure-related morbidity and mortality were relatively high, and systemic chemotherapy regimens did not use currently available biologic agents. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peritoneal carcinomatosis of gastric origin who receive CRS plus perioperative intraperitoneal chemotherapy, the evidence includes 2 small RCTs, observational studies, and a systematic review. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. A 2017 meta-analysis identified 2 RCTs and 12 controlled nonrandomized studies comparing surgery plus HIPEC with standard surgical management in patients who had peritoneal carcinomatosis due to gastric cancer. A meta-analysis found significantly better survival in the surgery plus HIPEC group at 1 year but not at 2 or 3 years. One RCT found better survival in patients who received CRS plus HIPEC compared with an alternative treatment. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peritoneal carcinomatosis of endometrial origin who receive CRS plus perioperative intraperitoneal chemotherapy, the evidence includes cohort studies. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Only uncontrolled studies were available and they had small sample sizes (<25
patients). Randomized trials that compare CRS plus HIPEC with standard treatment (eg, CRS alone or systemic chemotherapy alone) are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have peritoneal mesothelioma who receive CRS plus perioperative intraperitoneal chemotherapy, the evidence includes retrospective cohort studies and systematic reviews. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Uncontrolled studies have shown median and 5-year OS ranging from 30 to 92 months and 33% to 68%, respectively, for patients with peritoneal mesothelioma who are treated with CRS plus HIPEC. Reported procedure-related morbidity and mortality were approximately 35% and 5%, respectively. Controlled studies are needed to draw conclusions about the efficacy and safety of CRS plus HIPEC compared with standard treatment (CRS alone).

For individuals who have ovarian cancer who receive CRS plus perioperative intraperitoneal chemotherapy, the evidence includes an RCT, systematic reviews, and uncontrolled studies. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Results from an RCT with methodologic flaws, case-control studies, and cohort studies are inconsistent; the RCT and case-control studies showed improved survival with CRS plus HIPEC in the second-line setting compared with CRS without HIPEC, but retrospective cohort studies have not shown a clear survival advantage compared with current treatment in the first- or the second-line setting. Results of at least some of these studies were confounded by prognostic factors (completeness of cytoreduction, extent of peritoneal carcinomatosis, chemosensitivity to platinum). Well-designed, RCTs are needed to control for potential covariates and to demonstrate improvements in the net health outcome compared with current treatment approaches (ie, CRS plus systemic chemotherapy). The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have appendiceal goblet cell tumors who receive CRS plus perioperative intraperitoneal chemotherapy, the evidence includes a case series. Relevant outcomes are OS, disease-specific survival, quality of life, and treatment-related mortality and morbidity. One retrospective series was identified. Additional studies—preferably controlled and ideally RCTs—are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 1.
Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT</th>
<th>Title</th>
<th>Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colorectal and appendiceal cancer</strong></td>
<td>ICARuS Post-operative Intraperitoneal Chemotherapy (EPIC) and Hyperthermic Intraperitoneal Chemotherapy (HIPEC) After Optimal Cytoreductive Surgery (CRS) for Neoplasms of the Appendix, Colon or Rectum With Isolated Peritoneal Metastasis</td>
<td>220</td>
<td>Mar 2018</td>
</tr>
<tr>
<td>NCT02179489</td>
<td>Trial Evaluating Surgery With Hyperthermic Intraperitoneal Chemotherapy (HIPEC) in Treating Patients With a High Risk of Developing Colorectal Peritoneal Carcinomatosis</td>
<td>300</td>
<td>Oct 2023</td>
</tr>
<tr>
<td><strong>Gastric cancer</strong></td>
<td>Efficacy of HIPEC in the Treatment of Patients With Locally Advanced Gastric Cancer</td>
<td>582</td>
<td>July 2019</td>
</tr>
<tr>
<td>NCT02158988</td>
<td>Cytoreductive Surgery (CRS) With/Without HIPEC in Gastric Cancer With Peritoneal Carcinomatosis (GASTRIPEC)</td>
<td>180</td>
<td>Sep 2020</td>
</tr>
<tr>
<td><strong>Ovarian cancer</strong></td>
<td>Secondary Debulking Surgery +/- Hyperthermic Intraperitoneal Chemotherapy in Stage III Ovarian Cancer</td>
<td>280</td>
<td>Dec 2016 (ongoing)</td>
</tr>
<tr>
<td>NCT01628380</td>
<td>Outcomes After Secondary Cytoreductive Surgery With or Without Carboplatin Hyperthermic Intraperitoneal Chemotherapy (HIPEC) Followed by Systemic Combination Chemotherapy for Recurrent Platinum-Sensitive Ovarian, Fallopian Tube, or Primary Peritoneal Cancer</td>
<td>98</td>
<td>Jan 2018</td>
</tr>
<tr>
<td>NCT01539785</td>
<td>Hyperthermic Intra-peritoneal Chemotherapy (HIPEC) in Ovarian Cancer Recurrence (HORSE)</td>
<td>158</td>
<td>Sep 2018</td>
</tr>
<tr>
<td>NCT02124421</td>
<td>Outcomes in CRS/HIPEC as Initial Treatment of Ovarian, Fallopian Tube and Primary Peritoneal Cancer</td>
<td>48</td>
<td>Apr 2020</td>
</tr>
<tr>
<td>NCT01376752</td>
<td>Hyperthermic Intra-Peritoneal Chemotherapy (HIPEC) in Relapse Ovarian Cancer Treatment (CHIPOR)</td>
<td>444</td>
<td>Dec 2020</td>
</tr>
</tbody>
</table>

NCT: National Clinical Trial
Practice Guidelines and Position Statements

**National Comprehensive Cancer Network**

National Comprehensive Cancer Network (NCCN) guidelines in oncology include the following relevant recommendations for colon cancer (v.2.2017) and rectal cancer (v.3.2017): “The panel currently believes that complete cytoreductive surgery and/or intraperitoneal chemotherapy can be considered in experienced centers for selected patients with limited peritoneal metastases for whom R0 resection can be achieved. The panel recognizes the need for randomized clinical trials that will address the risks and benefits associated with each of these modalities.”

NCCN guidelines for gastric cancer (v.1.2017) and for uterine neoplasms (v.2.2017) do not include cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC).

NCCN guidelines for ovarian cancer (v.1.2017) include recommendations for intraperitoneal chemotherapy in patients with optimally debulked (<1 cm) stage II or III (category 1 recommendation) disease. Use of hyperthermic chemotherapy is not specified.

**American Society of Colon and Rectal Surgeons**

A 2012 practice parameter on the management of colon cancer by the American Society of Colon and Rectal Surgeons has stated that treatment of patients with peritoneal carcinomatosis may include CRS. The role of HIPEC was “insufficiently defined.”

**Society of Surgical Oncology**

In 2007, the Society of Surgical Oncology issued a consensus statement on CRS and HIPEC in the management of peritoneal surface malignancies of colonic origin. The Society recommended that patients with peritoneal carcinomatosis without distant disease, in whom complete cytoreduction is possible, undergo HIPEC before systemic therapy. As of June 2016, an updated consensus statement has not been published.

**Canadian HIPEC Collaborative Group**

Consensus guidelines published in 2015 specified patient selection criteria for CRS plus HIPEC to treat selected indications.
For patients with peritoneal surface malignancy of colorectal origin, eligibility criteria with the highest (A) level of consensus include Eastern Cooperative Oncology Group Performance Status score of 0, patient age of 65 years or younger, body mass index of 35 kg/m² or less, classical I or II histologic grade, 6-month or more interval from primary tumor to peritoneal carcinomatosis, extraperitoneal disease absent, Peritoneal Carcinomatosis Index score of 20 or less, and predicted score for completeness of cytoreduction of 0.

For patients with peritoneal surface malignancy of appendiceal origin, eligibility criteria with the highest (A) level of consent include Eastern Cooperative Oncology Group Performance Status score of 0 or 1, patient age of 65 years or younger, body mass index of 35 kg/m² or less, classical I or II histologic grade, any time interval from primary tumor to peritoneal carcinomatosis, extraperitoneal disease absent, any Peritoneal Carcinomatosis Index, and predicted score for completeness of cytoreduction of 0 or 1.

**Medicare National Coverage**

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**Regulatory Status**

Mitomycin, carboplatin, and other drugs used for HIPEC have not been approved by the U.S. Food and Drug Administration (FDA) for this indication. Cyclophosphamide and nitrogen mustard are FDA-approved for intraperitoneal administration, but neither drug is regularly used for this purpose.¹³

Several peritoneal lavage systems (FDA product code: LGZ) have been cleared for marketing by FDA through the 510(k) process to provide “warmed, physiologically compatible sterile solution” (eg, Performer® HT perfusion system; RanD Srl, Medolla, Italy¹⁴). None have received marketing approval or clearance to administer chemotherapy. FDA has issued warnings to manufacturers of devices that are FDA-cleared for peritoneal lavage using sterile saline solutions when these devices are marketed for off-label use in HIPEC (eg, ThermaSolutions, Minneapolis, MN¹⁵; Belmont Instrument, Billerica, MA¹⁶).


<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>06/23/06</td>
<td>Update Scope and Disclaimer - No other changes.</td>
</tr>
<tr>
<td>07/10/07</td>
<td>Replace policy - Policy updated with literature review; references added. No change in policy statement.</td>
</tr>
<tr>
<td>10/9/07</td>
<td>Cross References Updated - No other changes.</td>
</tr>
<tr>
<td>07/08/08</td>
<td>Replace policy - Policy updated with literature search; no change to the policy statement. References added.</td>
</tr>
<tr>
<td>08/11/09</td>
<td>Replace policy - Policy updated with literature search; no change to the policy statement References added.</td>
</tr>
<tr>
<td>12/14/10</td>
<td>Replace policy - Policy updated with literature search; Rationale and Background sections revised extensively. Policy statement added that cytoreduction and hyperthermic intraperitoneal chemotherapy for the treatment of pseudomyxoma peritoneii may be considered medically necessary; investigational policy statement clarified to specify that the indication considered is peritoneal carcinomatosis from colorectal cancer. The term, “pseudomyxoma peritoneii” was added to the policy title. References 1-8, 10-12, and 17 added; reference 18 updated.</td>
</tr>
<tr>
<td>11/08/11</td>
<td>Replace policy – Policy updated with literature search. References 2, 4 and 20 added; references renumbered. Title changed to include peritoneal mesothelioma. Policy statement added that cytoreductive surgery and perioperative intraperitoneal chemotherapy for the treatment of peritoneal mesothelioma, previously not addressed, may be considered medically necessary. Use of the term “hyperthermic” changed to “perioperative” in the title and policy statements to include early postoperative intraperitoneal chemotherapy. Use of the term “cytoreduction” changed to “cytoreductive surgery” to be more specific. CPT codes added.</td>
</tr>
<tr>
<td>01/03/12</td>
<td>Deleted code 96445 removed.</td>
</tr>
<tr>
<td>12/19/12</td>
<td>Replace policy. Policy updated with literature search. No references added. No change to policy statements. ICD-10 codes are now effective 10/01/2014.</td>
</tr>
<tr>
<td>12/09/13</td>
<td>Replace policy. Policy updated with literature search through August 2013, references 18-22, 27, and 28 added; reference 26 updated. No change to policy statements.</td>
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<tr>
<td>03/11/14</td>
<td>Coding Update. Code 99.85 was removed per ICD-10 mapping project; this code is not utilized for adjudication of policy.</td>
</tr>
<tr>
<td>12/17/14</td>
<td>Annual Review. Policy updated with literature search; policy statements unchanged. ICD-9 diagnosis and ICD-10 diagnosis and procedure codes removed; these are not utilized in adjudication of the policy.</td>
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<td>03/10/15</td>
<td>Annual Review. Policy updated with literature review through January 2, 2015 references 4-8, 10-14, 18-19, 24, 26-35, 43, 51-61, 63-80, and 83-85 added; references 14 and 23-24 deleted. Investigational policy statement for ovarian cancer, peritoneal carcinomatosis due to gastric cancer or endometrial cancer, and for all other indications added. Medically necessary policy statement unchanged. Clarification note added to policy statement regarding perioperative Title changed to “Select Intra-</td>
</tr>
<tr>
<td>Date</td>
<td>Comments</td>
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<tr>
<td></td>
<td>Abdominal and Pelvic Malignancies™ to include the additional indications. Clinical trials note added to Benefit Application.</td>
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<tr>
<td>10/01/16</td>
<td>Annual Review, approved September 13, 2016. Policy updated with literature review through June 10, 2016; references 73 and 86 added. Policy statements unchanged.</td>
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</tbody>
</table>

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Email AppealsDepartmentInquiries@Premera.com

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U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)
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Ilokko (Ilocano):
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Premera Blue Cross.

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Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang paunawa na ito ay maaring malaman ng mga taga-paunawa ng Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring maaring maunawa o maunawa sa pagbibigay ng ganitong impormasyon para sa iyong kalusugan.

家庭 (Farsi):

این اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاуیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایای اطلاعیه مربوط به مالاتیاها و مزایا