PREMERA HMO

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY / MEDICAL POLICY – 5.01.629

Pharmacologic Treatment of Psoriasis

Effective Date:	**July 1, 2025***
Last Revised:	Apr. 8, 2025
Replaces:	N/A

*Click here to view the current policy.

RELATED MEDICAL POLICIES:

5.01.550 Pharmacotherapy of Arthropathies

11.01.523 Site of Service: Infusion Drugs and Biologic Agents

The Site of Service Medical Necessity criteria within this policy DOES NOT apply to Alaska fully-insured members; refer to the infusion drug Medical Necessity criteria only.

Site of Service *and* the infusion drug Medical Necessity criteria apply to all other plan members.

Please contact Customer Service for more information.

Select a hyperlink below to be directed to that section.

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

Introduction

Psoriasis is a skin condition caused by inflammation. It causes a red, scaly rash that can occur anywhere on the body. The patches of rash are called plaques, and the condition can be described as plaque psoriasis. Another less common type of psoriasis is known as pustular psoriasis, which can appear suddenly and may also cause a fever and fatigue. The treatment of psoriasis often starts with medications that are applied to the skin. If these don't help clear the skin, or if psoriasis affects a large part of the body, light therapy and drugs that are taken by mouth may be used. The newest type of therapy includes medications called "biologics." This policy discusses when each type of therapy may be considered medically necessary for psoriasis.

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

Site of Service Medical Necessity criteria does NOT apply to Alaska fully-insured members; refer to the infusion drug Medical Necessity criteria only. Please contact Customer Service for more information.

We will review specific intravenous (IV) and injectable drugs for medical necessity for all ages.

For those age 13 and older, we also will review the site of service for medical necessity. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home. Click **here** to be directed to the site of service review criteria.

Drugs subject to site of service review addressed in this policy are:

- Avsola (infliximab-axxq)
- Inflectra (infliximab-dyyb)
- Infliximab (Janssen – unbranded)
- Remicade (infliximab)
- Renflexis (infliximab-abda)
- Spevigo (spesolimab-sbzo)

Site of Service Administration	Medical Necessity
Medically necessary sites of service • **Physician's office** • **Infusion center** • **Home infusion**	**IV infusion therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost-effective site:** • These are the preferred **medically necessary** sites of service for specified drugs.
Hospital-based outpatient setting • **Outpatient hospital IV infusion department** • **Hospital-based outpatient clinical level of care**	**IV infusion therapy of various medical or biologic agents will be covered in the most appropriate, safe and cost-effective site.** **This site is considered medically necessary for the first 90 days for the following:** • The initial course of infusion of a pharmacologic or biologic agent **OR** • Re-initiation of an agent after 6 months or longer following discontinuation of therapy* ***Note:** This does not include when standard dosing between infusions is 6 months or longer **This site is considered medically necessary when there is no outpatient infusion center within 50 miles of the individual's home and there is no contracted home infusion agency that will travel to their home, or a hospital is the only place that offers infusions of this drug.** **This site is considered medically necessary only when the individual has a clinical condition which puts him or her at increased risk of complications for infusions, including any ONE of the following:** • Known cardiac condition (e.g., symptomatic cardiac arrhythmia) or pulmonary condition (e.g., significant respiratory disease, serious obstructive airway disease, %FVC less than or equal to 40%) that may increase the risk of an adverse reaction

Site of Service Administration	Medical Necessity

	• Unstable renal function which decreases the ability to respond to fluids
	• Difficult or unstable vascular access
	• Acute mental status changes or cognitive conditions that impact the safety of infusion therapy
	• A known history of severe adverse drug reactions and/or anaphylaxis to prior treatment with a related or similar drug
	
	This site is considered medically necessary when the individual has cytokine release syndrome (CRS) and all the following are met:
	• CRS is grade 3 or 4 as evidenced by ALL the following:
	  ○ Temperature greater than or equal to 38 °C
	  ○ Hypotension that requires one or more vasopressors
	  ○ Hypoxia that requires oxygen through a high-flow nasal cannula, face mask, non-rebreather mask, or Venturi mask OR positive pressure (continuous positive airway pressure [CPAP], bilevel positive airway pressure [BiPAP], intubation, or mechanical ventilation)
	AND
	• The individual will be admitted into an inpatient setting as soon as possible

Hospital-based outpatient setting • **Outpatient hospital IV infusion department** • **Hospital-based outpatient clinical level of care**	**These sites are considered not medically necessary for infusion and injectable therapy services of various medical and biologic agents when the site-of-service criteria in this policy are not met.**

Please note that claims billed for the drugs described in this policy that are administered via an intravenous route (IV) must be processed through a medical benefit only (not pharmacy).

Medications listed in this policy may also be subjected to quantity limits per the US Food and Drug Administration (FDA) labeled dosing.

Plaque Psoriasis Systemic Treatments – First Line					
IL-23 Inhibitors	**TNF-α Inhibitors**	**TYK2 Inhibitors**	**IL-17 Inhibitor**	**IL-12/23 Inhibitor**	**PDE-4 Inhibitor**
• Skyrizi (SC)	• Inflectra (IV) • Infliximab (Janssen • – unbranded) (IV) • Remicade (IV)	• Sotyktu (oral)	• Taltz (SC)	• Stelara (SC)	• Otezla (oral)
• Tremfya (SC)	• Enbrel (SC)				
	• Adalimumab-adaz (Hyrimoz unbranded) (SC) • Adalimumab-adbm (Cyltezo unbranded) (SC) • Adalimumab-ryvk (Simlandi unbranded) (SC) • Cyltezo (SC) • Simlandi (SC)				

Second Line		
IL-23 Inhibitors	**TNF-α Inhibitors**	**IL-17 Inhibitors**
• Ilumya (SC)	• Avsola (IV) • Renflexis (IV)	• Bimzelx (SC) • Cosentyx (SC)
	• Cimzia (SC)	
	• Abrilada (SC) • Adalimumab-aacf (Idacio unbranded (SC) • Adalimumab-fkjp (Hulio unbranded) (SC) • Amjevita (SC) • Hadlima (SC) • Hulio (SC) • Humira (SC) • Hyrimoz (SC) • Idacio (SC) • Yuflyma (SC) • Yusimry (SC)	• Siliq (SC)

Step therapy tiers are listed below; please refer to the Policy section for details.

Drug	Medical Necessity
TNF-α Antagonists – First Line	
Enbrel (etanercept) SC	**Enbrel (etanercept) may be considered medically necessary for the treatment of plaque psoriasis when:** • The individual is aged 4 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA) ○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement **OR** ▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist
• **Cyltezo (adalimumab-adbm) SC** • **Simlandi (adalimumab-ryvk) SC** • **Adalimumab-adaz (Hyrimoz unbranded) SC** • **Adalimumab-adbm (Cyltezo unbranded) SC** • **Adalimumab-ryvk (Simlandi unbranded) SC**	**Cyltezo (adalimumab-adbm), Simlandi (adalimumab-ryvk), adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded) and adalimumab-ryvk (Simlandi unbranded) may be considered medically necessary for the treatment of plaque psoriasis when:** • The individual is aged 18 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA) ○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement

Drug	Medical Necessity
	OR ▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist **Note:** This medical necessity criteria does not apply to one Open formulary (Formulary ID: 6062; Rx Plan F1) and one Incentive formulary (Formulary ID: 6064; Rx Plan G3). The criteria for members with these custom Open and Incentive formulary plans can be found in policy **5.01.647 Medical Necessity Criteria for Custom Incentive and Open Formularies**. Please check the member Plan booklet or member ID card to determine whether this policy criteria applies.
• **Inflectra (infliximab-dyyb) IV** • **Infliximab (Janssen – unbranded) IV** • **Remicade (infliximab) IV**	**Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) are subject to review for site of service administration.** **Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:** • The individual is aged 18 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA) ○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement **OR** ▪ There is pustular involvement of the hands and feet

Drug	Medical Necessity
	OR ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist **Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), and Remicade (infliximab) may be considered medically necessary as emergent treatment for severe pustular, exfoliative or inflammatory psoriasis without prior use or failure/intolerance of a first-line drug, in contrast to stable plaque psoriasis.**
IL-17 Inhibitors – First Line	
Taltz (ixekizumab) SC	**Taltz (ixekizumab) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:** • The individual is aged 6 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA) ○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement **OR** ▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g.,

Drug	Medical Necessity
	methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist
IL-12/23 Inhibitors – First Line	
Stelara (ustekinumab) SC	**Stelara (ustekinumab) SC may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:** • The individual is aged 6 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA) ○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement **OR** ▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist
IL-23 Inhibitors – First Line	
Skyrizi (risankizumab-rzaa) SC	**Skyrizi (risankizumab-rzaa) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:** • The individual is aged 18 years or older **AND**

Drug	Medical Necessity

	• Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA)
	  ○ **Exception**: This may be granted when **ANY** of the following are true:
	  ▪ There is extensive recalcitrant facial involvement
	  OR
	  ▪ There is pustular involvement of the hands and feet
	  OR
	  ▪ There is genital involvement which interferes with normal sexual function
	AND
	• Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated
	AND
	• Medication is being prescribed by or in consultation with a dermatologist

Tremfya (guselkumab) SC	**Tremfya (guselkumab) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:**
	• The individual is aged 18 years or older
	AND
	• Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA)
	  ○ **Exception**: This may be granted when **ANY** of the following are true:
	  ▪ There is extensive recalcitrant facial involvement
	  OR
	  ▪ There is pustular involvement of the hands and feet
	  OR
	  ▪ There is genital involvement which interferes with normal sexual function
	AND
	• Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g.,

Drug	Medical Necessity
	methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist
PDE4 Inhibitor – First Line	
Otezla (apremilast) oral	**Otezla (apremilast) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:** • The individual is aged 6 years or older **AND** • Weighs at least 20 kg **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA) ○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement **OR** ▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist
Tyrosine Kinase 2 (TYK2) Inhibitors – First Line	
Sotyktu (deucravacitinib) oral	**Sotyktu (deucravacitinib) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:** • The individual is aged 18 years or older **AND**

Drug	Medical Necessity

	• Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA)
	  ○ **Exception**: This may be granted when **ANY** of the following are true:
	  ▪ There is extensive recalcitrant facial involvement
	  OR
	  ▪ There is pustular involvement of the hands and feet
	  OR
	  ▪ There is genital involvement which interferes with normal sexual function
	AND
	• Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated
	AND
	• Medication is being prescribed by or in consultation with a dermatologist

IL-17 Inhibitors – Second Line	

Bimzelx (bimekizumab-bkzx) SC	**Bimzelx (bimekizumab-bkzx) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:**
	• The individual is aged 18 years or older
	AND
	• Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA)
	  ○ **Exception**: This may be granted when **ANY** of the following are true:
	  ▪ There is extensive recalcitrant facial involvement
	  OR
	  ▪ There is pustular involvement of the hands and feet
	  OR
	  ▪ There is genital involvement which interferes with normal sexual function
	AND
	• Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g.,

Drug	Medical Necessity

	methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated
	AND
	• Has had an inadequate response or is intolerant to one of the following agents:
	  ○ Enbrel (etanercept)
	  ○ Adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) **OR** Cyltezo (adalimumab-adbm) **OR** Simlandi (adalimumab-ryvk)
	  ○ Otezla (apremilast)
	  ○ Skyrizi (risankizumab-rzaa) SC
	  ○ Sotyktu (deucravacitinib)
	  ○ Stelara (ustekinumab) SC
	  ○ Taltz (ixekizumab)
	  ○ Tremfya (guselkumab)
	AND
	• Medication is being prescribed by or in consultation with a dermatologist

Siliq (brodalumab) SC	**Siliq (brodalumab) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:**
	• The individual is aged 18 years or older
	AND
	• Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA)
	  ○ **Exception**: This may be granted when **ANY** of the following are true:
	  ▪ There is extensive recalcitrant facial involvement
	  OR
	  ▪ There is pustular involvement of the hands and feet
	  OR
	  ▪ There is genital involvement which interferes with normal sexual function
	AND
	• Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g.,

Drug	Medical Necessity

	methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated
	AND
	• Has had an inadequate response or is intolerant to two of the following agents:
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-ryvk (Simlandi unbranded)
	  ○ Otezla (apremilast)
	  ○ Skyrizi (risankizumab-rzaa) SC
	  ○ Sotyktu (deucravacitinib)
	  ○ Stelara (ustekinumab) SC
	  ○ Taltz (ixekizumab)
	  ○ Tremfya (guselkumab)
	AND
	• Medication is being prescribed by or in consultation with a dermatologist

Cosentyx (secukinumab) SC	**Cosentyx (secukinumab) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:**
	• The individual is aged 6 years or older
	AND
	• Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA)
	  ○ **Exception**: This may be granted when **ANY** of the following are true:
	  ▪ There is extensive recalcitrant facial involvement
	  OR
	  ▪ There is pustular involvement of the hands and feet
	  OR
	  ▪ There is genital involvement which interferes with normal sexual function
	AND
	• Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g.,

Drug	Medical Necessity

	methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated
	AND
	• Has had an inadequate response or intolerance to two of the following agents:
	  ○ Enbrel (etanercept)
	  ○ Cyltezo (adalimumab-adbm) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-ryvk (Simlandi unbranded)
	  ○ Otezla (apremilast)
	  ○ Skyrizi (risankizumab-rzaa) SC
	  ○ Sotyktu (deucravacitinib)
	  ○ Stelara (ustekinumab) SC
	  ○ Taltz (ixekizumab)
	  ○ Tremfya (guselkumab)
	AND
	• Medication is being prescribed by or in consultation with a dermatologist

TNF-α Antagonists – Second Line	

• **Abrilada (adalimumab-afzb) SC**
• **Adalimumab-aacf (Idacio unbranded)**
• **Adalimumab-aaty (Yuflyma unbranded) SC**
• **Adalimumab-fkjp (Hulio unbranded) SC**
• **Amjevita (adalimumab-atto) SC**
• **Hadlima (adalimumab-bwwd) SC**
• **Hulio (adalimumab-fkjp) SC**
• **Humira (adalimumab) SC**
• **Hyrimoz (adalimumab-adaz) SC**
	Abrilada (adalimumab-afzb), adalimumab-aacf (Idacio unbranded), adalimumab-aaty (Yuflyma unbranded), adalimumab-fkjp (Hulio unbranded), Amjevita (adalimumab-atto), Hadlima (adalimumab-bwwd), Hulio (adalimumab-fkjp), Humira (adalimumab), Hyrimoz (adalimumab-adaz), Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of plaque psoriasis when:
	• The individual is aged 18 years or older
	AND
	• Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA)
	  ○ **Exception**: This may be granted when **ANY** of the following are true:
	  ▪ There is extensive recalcitrant facial involvement
	  OR

Drug	Medical Necessity
• **Idacio (adalimumab-aacf) SC** • **Yuflyma (adalimumab-aaty) SC** • **Yusimry (adalimumab-aqvh) SC**	▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Has had an inadequate response or is intolerant to ALL the following agents: ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded) ○ Adalimumab-adaz (Hyrimoz unbranded) ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded) **AND** • Medication is being prescribed by or in consultation with a dermatologist **Note:** This medical necessity criteria does not apply to one Open formulary (Formulary ID: 6062; Rx Plan F1) and one Incentive formulary (Formulary ID: 6064; Rx Plan G3). The criteria for members with these custom Open and Incentive formulary plans can be found in policy **5.01.647 Medical Necessity Criteria for Custom Incentive and Open Formularies.** Please check the member Plan booklet or member ID card to determine whether this policy criteria applies.
Cimzia (certolizumab pegol) SC	**Cimzia (certolizumab pegol) may be considered medically necessary for the treatment of plaque psoriasis when:** • The individual is aged 18 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA) ○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement **OR**

Drug	Medical Necessity
	▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Has had an inadequate response or is intolerant to two of the following agents: ○ Enbrel (etanercept) ○ Cyltezo (adalimumab-adbm) **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** adalimumab-ryvk (Simlandi unbranded) ○ Otezla (apremilast) ○ Skyrizi (risankizumab-rzaa) SC ○ Sotyktu (deucravacitinib) ○ Stelara (ustekinumab) SC ○ Taltz (ixekizumab) ○ Tremfya (guselkumab) **AND** • Medication is being prescribed by or in consultation with a dermatologist
• **Avsola (infliximab-axxq) IV,** • **Renflexis (infliximab-abda) IV**	**Avsola (infliximab-axxq) and Renflexis (infliximab-abda) are subject to review for site of service administration.** **Avsola (infliximab-axxq) and Renflexis (infliximab-abda) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:** • The individual is aged 18 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA)

Drug	Medical Necessity
	○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement **OR** ▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Has had a documented trial and treatment failure with Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), or Remicade (infliximab) **AND** • Medication is being prescribed by or in consultation with a dermatologist **Avsola (infliximab-axxq) and Renflexis (infliximab-abda) may be considered medically necessary as emergent treatment for severe pustular, exfoliative or inflammatory psoriasis without prior use or failure/intolerance of a first-line agent, in contrast to stable plaque psoriasis.**
IL-23 Inhibitors – Second Line	
Ilumya (tildrakizumab-asmn) SC	**Ilumya (tildrakizumab-asmn) may be considered medically necessary for the treatment of moderate to severe plaque psoriasis when:** • The individual is aged 18 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 10% of his or her body surface area (BSA) ○ **Exception**: This may be granted when **ANY** of the following are true: ▪ There is extensive recalcitrant facial involvement

Drug	Medical Necessity
	OR ▪ There is pustular involvement of the hands and feet **OR** ▪ There is genital involvement which interferes with normal sexual function **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 approved systemic therapy (e.g., methotrexate, cyclosporine, acitretin or psoralen plus ultraviolet A light [PUVA]) unless contraindicated or not tolerated **AND** • Has had an inadequate response or is intolerant to two of the following agents: o Enbrel (etanercept) o Cyltezo (adalimumab-adbm) **OR** adalimumab-adaz (Hyrimoz unbranded) **OR** adalimumab-adbm (Cyltezo unbranded) **OR** Simlandi (adalimumab-ryvk) **OR** adalimumab-ryvk (Simlandi unbranded) o Otezla (apremilast) o Skyrizi (risankizumab-rzaa) SC o Sotyktu (deucravacitinib) o Stelara (ustekinumab) SC o Taltz (ixekizumab) o Tremfya (guselkumab) **AND** • Medication is being prescribed by or in consultation with a dermatologist

Plaque Psoriasis Topical Treatments – Second Line			
Aryl Hydrocarbon Receptor Agonist	**PDE-4 Inhibitor**	**Steroid Combinations**	**Vitamin D Analogs**
• Vtama (topical cream)	• Zoryve (topical cream)	• Duobrii (topical lotion)	• Brand calcipotriene (topical foam)
		• Enstilar (topical foam)	• Dovonex (topical cream)
		• Taclonex (topical ointment, suspension)	• Sorilux (topical foam)

		• Wynzora (topical cream)	• Vectical (topical ointment)

Drug	Medical Necessity
Plaque Psoriasis Topical Treatments – Second Line	
Aryl Hydrocarbon Receptor Agonist (Topical)	
Vtama (tapinarof) cream	**Vtama (tapinarof) may be considered medically necessary for the treatment of plaque psoriasis when:** • The individual is aged 18 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 3% of his or her body surface area (BSA) **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 topical corticosteroid (e.g., betamethasone, clobetasol, mometasone) unless contraindicated or not tolerated **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 vitamin D analogue (e.g., calcipotriene or calcitriol) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist
PDE-4 Inhibitor (Topical)	
Zoryve (roflumilast) 0.3% cream	**Zoryve (roflumilast) 0.3% cream may be considered medically necessary for the treatment of plaque psoriasis when:** • The individual is aged 6 years or older **AND** • Has a diagnosis of chronic plaque psoriasis involving greater than or equal to 2% of his or her body surface area (BSA) **AND** • Has a history of an adequate trial and treatment failure with greater than or equal to 1 topical corticosteroid (e.g., betamethasone, clobetasol, mometasone) unless contraindicated or not tolerated

Drug	Medical Necessity
Plaque Psoriasis Topical Treatments – Second Line	
	AND • Has a history of an adequate trial and treatment failure with greater than or equal to 1 vitamin D analogue (e.g., calcipotriene or calcitriol) unless contraindicated or not tolerated **AND** • Medication is being prescribed by or in consultation with a dermatologist
Steroid Combinations (Topical)	
Duobrii (halobetasol and tazarotene) lotion	**Duobrii (halobetasol and tazarotene) may be considered medically necessary for the treatment of plaque psoriasis when the following criteria are met:** • The individual has tried and failed or had intolerance to using concurrent generic topical halobetasol and generic topical tazarotene
• **Enstilar (betamethasone and calcipotriene) foam** • **Taclonex (betamethasone and calcipotriene) ointment, suspension** • **Wynzora (betamethasone and calcipotriene) cream**	**Enstilar (betamethasone and calcipotriene), Taclonex (betamethasone and calcipotriene), and Wynzora (betamethasone and calcipotriene) may be considered medically necessary for the treatment of plaque psoriasis when the following criteria are met:** • The individual has tried and failed or had intolerance to using concurrent generic topical betamethasone and generic topical calcipotriene
Vitamin D Analogs (Topical)	
• **Brand calcipotriene foam** • **Dovonex (calcipotriene) cream** • **Sorilux (calcipotriene) foam**	**Brand calcipotriene foam, Dovonex (calcipotriene), and Sorilux (calcipotriene) may be considered medically necessary for the treatment of plaque psoriasis when:** • The individual has tried and failed or had intolerance to generic topical calcipotriene
Vectical (calcitriol) ointment	**Vectical (calcitriol) may be considered medically necessary for the treatment of plaque psoriasis when:** • The individual has tried and failed or had intolerance to generic topical calcitriol

Retinoids - Psoriasis – Systemic Treatment – Second Line
• Soriatane (oral)

Drug	Medical Necessity
Retinoids - Psoriasis – Systemic Treatment – Second Line	
Soriatane (acitretin) oral	**Soriatane (acitretin) may be considered medically necessary for the treatment of psoriasis when:** • The individual has had a trial and treatment failure or intolerance to generic oral acitretin

IL-36 Receptor Antagonist – First Line
• Spevigo (SC/IV)

Drug	Medical Necessity
IL-36 Receptor Antagonist – First Line	
Spevigo (spesolimab-sbzo) SC/IV	**Spevigo (spesolimab-sbzo) IV is subject to review for site of service administration.** **Spevigo (spesolimab-sbzo) may be considered medically necessary for the treatment of generalized pustular psoriasis (GPP) when:** • The individual is aged 12 years or older **AND** • Is experiencing a GPP flare **AND** • Has documentation of a Generalized Pustular Psoriasis Physician Global Assessment (GPPPGA) total score of at least 3 (moderate) [the total GPPPGA score ranges from 0 (clear) to 4 (severe)] **AND** • The dose prescribed is 900 mg given as an IV infusion (an additional 900 mg dose may be administered one week after the initial dose) OR 600 mg given as a SC loading dose followed by 300 mg every 4 weeks

Drug	Medical Necessity
	AND • Medication is being prescribed by or in consultation with a dermatologist

Drug	Not Medically Necessary
As listed	**All other uses of the drugs for approved conditions listed in this policy are considered not medically necessary.**

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 above-named agents when used in combination with each other or for conditions not outlined in this policy, policy 5.01.550, policy 5.01.563, or policy 5.01.564 are considered investigational.**

Length of Approval	
Approval	**Criteria**
Initial authorization	**Non-formulary exception reviews for all drugs listed in the policy may be approved up to 12 months.** **All other reviews for all drugs listed in the policy EXCEPT Spevigo (spesolimab-sbzo) may be approved up to 12 months.** **All other reviews for Spevigo (spesolimab-sbzo) may be approved for one month.**
Re-authorization criteria	**Non-formulary exception reviews and all other reviews for 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	
J0135	Injection, adalimumab (Humira), 20 mg (code terminated 01/01/25)
J0139	Injection, adalimumab, 1 mg (new code effective 01/01/25)
J0717	Injection, certolizumab pegol (Cimzia), 1 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J1438	Injection, etanercept (Enbrel), 25 mg (code may be used for Medicare when drug administered under the direct supervision of a physician, not for use when drug is self-administered)
J1628	Injection, guselkumab (Tremfya), 1 mg
J1745	Injection, infliximab, excludes biosimilar (Remicade or Janssen unbranded), 10 mg
J1747	Injection, spesolimab-sbzo, (Spevigo), 1 mg
J3245	Injection, tildrakizumab (Ilumya), 1 mg
J3357	Injection, ustekinumab (Stelara), 1 mg
J3590	Unclassified biologics (use only to report Amjevita, Cosentyx, Siliq, Skyrizi, Spevigo, Taltz, Cyltezo, Hyrimoz HCF, Adalimumab-adaz HCF (Sandoz – unbranded), Abrilada, Hadlima, Hulio, Hyrimoz LCF, Yuflyma, Yusimry and Bimzelx)
Q5103	Injection, infliximab-dyyb, biosimilar, (Inflectra), 10 mg
Q5104	Injection, infliximab-abda, biosimilar, (Renflexis), 10 mg
Q5121	Injection, infliximab-axxq, biosimilar, (Avsola), 10 mg
Q5140	Injection, adalimumab-fkjp, biosimilar, 1 mg (new code effective 01/01/25)
Q5141	Injection, adalimumab-aaty, biosimilar, 1 mg (new code effective 01/01/25)

Code	Description
Q5142	Injection, adalimumab-ryvk biosimilar, 1 mg (new code effective 01/01/25)
Q5143	Injection, adalimumab-adbm, biosimilar, 1 mg (new code effective 01/01/25)
Q5144	Injection, adalimumab-aacf (idacio), biosimilar, 1 mg (new code effective 01/01/25)
Q5145	Injection, adalimumab-afzb (abrilada), biosimilar, 1 mg (new code effective 01/01/25)

Note: 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 FDA-approved indications, where applicable.

For site of service for medical necessity the age described in this policy is 13 years of age or older. Site of service is defined as the location where the drug is administered, such as a hospital-based outpatient setting, an infusion center, a physician's office, or at home. The age criterion for site of service for medical necessity is based on the following: Pediatric individuals are not small adults. Pediatric individuals differ physiologically, developmentally, cognitively, and emotionally from adult individuals, and vary by age groups from infancy to teen. Children often require smaller doses than adults, lower infusion rates, appropriately sized equipment, the right venipuncture site determined by therapy and age, and behavioral management during administration of care. Specialty infusion training is therefore necessary for pediatric IV insertions and therapy. Due to pediatrics unique physiology and psychology, site of service review is limited to individuals above the age of 13.

Benefit Application

Pharmacy Benefit

Bimzelx (bimekizumab-bkzx), brand calcipotriene foam, Dovonex (calcipotriene), Duobrii (halobetasol and tazarotene) Enstilar (betamethasone and calcipotriene), Otezla (apremilast), Soriatane (acitretin), Sorilux (calcipotriene), Sotyktu (deucravacitinib), Taclonex (betamethasone

and calcipotriene), Vectical (calcitriol), Vtama (tapinarof), Wynzora (betamethasone and calcipotriene), and Zoryve (roflumilast) cream are managed through the pharmacy benefit.

Medical Benefit

Avsola (infliximab-axxq), Inflectra (infliximab-dyyb), Infliximab (Janssen – unbranded), Spevigo (spesolimab-sbzo), Remicade (infliximab), and Renflexis (infliximab-abda) are managed through the medical benefit.

Medical / Pharmacy Benefit

Amjevita (adalimumab-atto), Cimzia (certolizumab pegol), Cosentyx (secukinumab), Enbrel (etanercept), Humira (adalimumab), Ilumya (tildrakizumab-asmn), Siliq (brodalumab), Skyrizi (risankizumab-rzaa), Stelara (ustekinumab), Taltz (ixekizumab), and Tremfya (guselkumab), Cyltezo (adalimumab-adbm), Hyrimoz (adalimumab-adaz), Abrilada (adalimumab-afzb), Hulio (adalimumab-fkjp), Yusimry (adalimumab-aqvh), Hadlima (adalimumab-bwwd), Yuflyma (adalimumab-aaty), adalimumab-adbm (Cyltezo unbranded), adalimumab-aacf (Idacio unbranded), and adalimumab-adaz (Hyrimoz unbranded) are managed through both the pharmacy and medical benefit.

Evidence Review

Psoriasis

Psoriasis is a chronic, multifactorial, noncontagious skin disorder that affects about 2.1% of the US population and 1-3% of persons worldwide. About 4.5 million, or 1 in 65, Americans have psoriasis. Onset is typically between the ages of 15 and 35 and prevalence is slightly greater in women. It is also more common in some ethnic groups (Caucasians) than others (African American or Asians). A genetic component has also been identified. There are several forms of psoriasis, but plaque psoriasis (or psoriasis vulgaris) is the most common form of the disease, affecting about 80% of psoriatic individuals.

About 20-30% of people with psoriasis have cases that are considered moderate to severe (covering more than 3% of their body). Although not typically life-threatening, psoriasis can have a large impact on quality of life. Seventy-five percent of people with moderate to severe

psoriasis report their disease has a moderate to large impact on their everyday lives. Individuals with palmar-plantar disease may have less than 3% involvement, but often have debilitating and recalcitrant disease. Further, approximately 7% of psoriatic individuals have concurrent arthritis (which may be particularly relevant to one's choice of therapy).

Psoriasis is a chronic immune-mediated inflammatory disease characterized by T-cell activation and accumulation in the epidermis and dermis, leading to abnormal differentiation and hyperproliferation of keratinocytes. Recent advances in the understanding of the cellular mechanisms underlying psoriasis have given rise to a generation of highly targeted biotechnologies for this indication.

As the severity of psoriasis ranges from mild to severe, with or without concurrent arthritis, available treatments lie along a spectrum from minimally invasive with a low risk of systemic side effects, to systemic therapy with a risk of potentially severe side effects. Non-invasive, topical treatments may also have significant side effects; for example, topical corticosteroids applied to large areas of skin may result in significant levels of systemic absorption. Many treatments have a cumulative toxicity potential, but the benefit of prolonged remissions makes the use of the more potent treatments relatively attractive.

Topical therapy, usually corticosteroids, is recommended as first-line treatment in psoriasis because these products are easy to administer, inexpensive, and safe. However, application to large areas of involvement can be time-consuming, expensive, and messy. Most individuals with moderate to severe disease will not achieve clearance or long-term remission. Tachyphylaxis may also develop with long-term use of topical corticosteroids. In individuals whose moderate to severe psoriasis fails topical therapy, the therapeutic options that remain are systemic agents, phototherapy and biologics.

Approved systemic agents (methotrexate, cyclosporine, and acitretin) are highly effective in the treatment of psoriasis; however, these therapies have limitations due to serious toxicities that require monitoring. Methotrexate can cause hepatotoxicity. Methotrexate is also associated with bone marrow toxicity, severe pulmonary toxicity, and serious drug-drug interactions (e.g., trimethoprim-sulfamethoxazole). Cyclosporine is nephrotoxic and can cause interstitial fibrosis and renal tubular atrophy in individuals treated for more than two years. Hypertension, laboratory abnormalities (electrolytes, liver function tests, lipids), and numerous drug-drug interactions are also among the problems associated with cyclosporine. Because methotrexate and cyclosporine are potent immunosuppressive drugs, individuals are at increased risk of infections and malignancies, including skin cancers and lymphoproliferative disorders. Like all retinoids, acitretin is highly teratogenic, posing a long-lasting risk (up to three years) in women of childbearing potential. Elevation in liver function tests, hyperlipidemia, and mucocutaneous reactions are additional adverse events associated with acitretin. Systemic corticosteroids are

generally avoided as they may be associated with severe exacerbations, both during and after treatment.

Phototherapy (e.g., UVB, narrowband UVB, PUVA) is used for individuals who fail topicals or those with disease too extensive for topical therapy. Phototherapy can be effective for many individuals, but may be inconvenient and time-consuming, if frequent office or clinic visits are required and the availability of specialized phototherapy clinics may be limited. Individuals with a durable medical equipment (DME) benefit may purchase a home unit for easier access. Cumulative exposure to PUVA is associated with an increased risk of squamous cell carcinoma and malignant melanoma.

Various other strategies using traditional therapies have also been used to maintain remission and decrease the risk of cumulative end-organ toxicities. Rotational therapy involves the use of a therapy for some time and then switching to another form of therapy. Combination therapy uses low-dosages of different treatments concurrently to minimize toxicity and enhance efficacy. Traditionally, these strategies usually involve topicals, phototherapy, and systemics in various combinations.

Biologic agents have been shown effective for many individuals in randomized, double-blind, placebo-controlled clinical trials, but few head-to-head clinical trials comparing these agents with traditional therapies exist. NBUVB continues to appear a very effective therapy in terms of achievement of greater than or equal to 75% response, global assessment ("clear or almost clear"), and length of remission. While the long-term risks of PUVA, methotrexate, and cyclosporine use in psoriatic individuals have become more clearly identified, these data are not available for the biologics in this population. The new biologic agents are clearly more widely available and convenient than the mainstay of psoriasis therapy, NBUVB, which may require anywhere from 30-100 outpatient visits to specialized facilities per year, unless a home system is purchased. On the other hand, biologics are all administered by injection, making them less convenient than systemic oral therapy.

Remicade (infliximab) is approved for the treatment of adults with chronic severe plaque psoriasis who are candidates for systemic therapies and clinical trial results for Humira (adalimumab), Remicade, and Enbrel (etanercept) have been published. Of these, three Humira studies added enough new information to warrant off-label use consideration. In the first multicenter, randomized, double-blind, placebo-controlled study, 147 individuals received Humira 80 mg at week 0, then 40 mg every other week beginning week 1, Humira 80 mg at week 0 and 1, then 40 mg every week beginning at week 1, or placebo for 12 weeks, after which placebo individuals were crossed over to Humira 40 mg every other week in a 48-week open label extension trial. At week 12, 53% of individuals taking Humira every other week, 80% of individuals taking Humira weekly, and 4% of individuals taking placebo achieved 75%

improvement in Psoriasis Area and Severity Index score (Pless than 0 .001). Responses were sustained for 60 weeks. Humira was safe and well tolerated in this population.

In the Phase III REVEAL study (Randomized Controlled Evaluation of adalimumab Every Other Week Dosing in Moderate to Severe Psoriasis TriAL), 1,212 individuals with moderate to severe chronic plaque psoriasis were randomized to treatment with Humira 80 mg at week 0, then 40 mg every other week beginning at week 1 or placebo. The trial was comprised of 3 periods, a 16-week, double-blind period for assessment of initial response; a 17-week open-label sustained response period, in which responders to either treatment (those achieving a PASI-75) received Humira 40 mg every other week; and a final 19-week, double-blind loss of response period, in which individuals receiving Humira throughout the previous 2 study periods were re-randomized to either Humira every other week or placebo. In the initial response phase, more Humira-treated individuals achieved a PASI-75 compared to those receiving placebo beginning at week 4 and at every visit throughout the 16-week evaluation period. At week 16, 71% of Humira- and 6.5% of placebo-treated individuals achieved a PASI-75 (Pless than 0.001). In Humira responders, mean PASI scores were maintained throughout the subsequent maintenance of response period (weeks 16-33) of the study. In the last period of the study examining loss of response, 28.4% of individuals re-randomized to placebo lost response by week 52 compared to 4.9% of individuals maintaining Humira (Pless than 0.001). Humira was generally well tolerated, and no unexpected adverse events were observed over the 52 weeks of the trial.

In a second Phase III trial, CHAMPION (Comparative Study of Humira vs. Methotrexate vs. Placebo In PsOriasis Patients), 271 individuals were randomized to treatment with Humira 80 mg at week 0, then 40 mg every other week beginning at week 1 (n=108), methotrexate 7.5 mg x 2 weeks, 10 mg x 2 weeks, then 15 mg orally (n=110), or placebo (n=53) for a total of 16 weeks. At week 16, more Humira-treated individuals achieved a PASI-75 response (80%) than individuals receiving either methotrexate (36%, Pless than 0.001) or placebo (19%, Pless than 0.001). Similar results were observed for PASI-90 response and PGA "clear" or "minimal" response. Humira was generally well-tolerated, with a safety profile similar to that known for an arthritis population.

In September 2009, the FDA approved the use of ustekinumab to treat plaque psoriasis. Ustekinumab is a human IgG1κ monoclonal antibody that binds to the shared p40 subunit of interleukins 12 and 23, blocking signaling of their cognate receptors. It is known that IL-12 and IL-23 plays important roles in the pathogenesis of psoriasis. IL-12 causes differentiation of CD4+ T cells to interferon-gamma (IFN-gamma)-producing T helper 1 (Th1) cells, while IL-23 induces differentiation to IL-17-producing pathogenic Th17 cells. In in vitro models, ustekinumab was shown to disrupt IL-12 and IL-23 mediated signaling and cytokine cascades by disrupting the interaction of these cytokines with a shared cell-surface receptor chain, IL-12 β1.

The evidence of efficacy consists mainly of two pivotal trials (PHOENIX I and PHOENIX II) submitted for FDA approval. Both studies showed robust clinical results against placebo. The primary endpoint for both studies was the proportion of individuals achieving a PASI 75 in the 12-week placebo-controlled trial. Both the 45mg and 90 mg groups achieved statistically significantly higher PASI 75 rate compared to placebo (67.1%, 66.4%, 3.1%, respectively; each pless than 0.0001 vs. placebo). Both studies also showed favorable secondary endpoint results for PGA score and DLQI vs. placebo. Ustekinumab was found to be more efficacious compared to etanercept during a Phase III, multi-center, active controlled trial with 930 individuals (ACCEPT trial). For the primary efficacy endpoint of PASI 75 at week 12, a greater proportion of individuals treated with ustekinumab 45mg and 90mg achieved a PASI 75 compared to those receiving etanercept 50mg.

More recently, phosphodiesterase 4 inhibitor apremilast has been now approved for moderate to severe plaque psoriasis. Two multicenter, randomized, double-blind, placebo-controlled trials (PSOR-1 and PSOR-2) enrolled a total of 1257 subjects with moderate to severe plaque psoriasis. In both studies, subjects were randomized 2:1 to apremilast 30 mg BID or placebo for 16 weeks. Primary endpoints were the proportion of subjects who achieved PASI-75 at Week 16 and the proportion of subjects who achieved a sPGA score of clear (0) or almost clear (1) at Week 16. Approximately 30% of all subjects had received prior phototherapy and 54% had received prior conventional systemic and/or biologic therapy for the treatment of psoriasis with 37% receiving prior conventional systemic therapy and 30% receiving prior biologic therapy. A total of 18% of subjects had a history of psoriatic arthritis. Approximately 33% of individuals receiving apremilast in PSOR-1 achieved a PASI-75 (vs. 5% on placebo), and 29% of apremilast individuals in PSOR-2 (vs. 6% on placebo). In all groups, approximately two-thirds of individuals achieving PASI-75 also had sPGA scores of clear (0) or almost clear (1).

Tremfya (guselkumab): Evidence of efficacy comes from three phase 3 clinical trials: VOYAGE-1, VOYAGE-2, and NAVIGATE in which guselkumab yielded significantly increased symptomatic improvement for individuals with moderate to severe PsO symptoms vs adalimumab and among individuals who had an inadequate response to ustekinumab. In VOYAGE-1, symptom resolution occurred in significantly more guselkumab individuals vs adalimumab as assessed by achieving IGA 0/1 (85.1% vs 65.9%), PASI 90 (73.3% vs 49.7%), and PASI 75 (91.2% vs 73.1%) (Pless than 0.001 for each). In VOYAGE-2, guselkumab yielded higher rates of symptom resolution vs adalimumab as measured by the proportion of individuals achieving IGA 0/1 (84.1% vs 67.7%), PASI 90 (70.0% vs 46.8%), and PASI 75 (86.3% vs 68.5%) (Pless than 0.001 for each). In NAVIGATE, guselkumab yielded higher rates of symptom resolution vs ustekinumab at weeks 28 and 52 as measured by the proportion of individuals achieving IGA 0/1 (31.1% and 36.3% vs 14.3% and 17.3%), and PASI 90 (48.1% and 51.1% vs 22.6% and 24.1%) (Pless than or equal to 0.001 for each).

The approval of Bimzelx was supported by safety and efficacy data from three Phase 3, multicenter, randomized, placebo- and/or active comparator-controlled trials (BE VIVID, BE READY, and BE SURE) in 1480 adults with moderate to severe PsO. In total, 1480 individuals aged 18 years and older with moderate to severe plaque psoriasis who were eligible for systemic plaque psoriasis therapy and/or phototherapy were included in the trials. Individuals included in the trials had a BSA involvement of greater than or equal to 10%, an Investigator's Global Assessment (IGA) score of greater than or equal to 3 ("moderate") in the overall assessment of plaque psoriasis on a severity scale of 0 to 4, and a Psoriasis Area and Severity Index (PASI) score greater than or equal to 12 (the PASI ranges from 0 to 72, where 0–5 = "no to mild PsO," 6–10 = "moderate," and greater than or equal to 11 = "severe"; scores greater than 40 are considered rare). Bimzelx showed superior efficacy compared to placebo, Stelara, and Humira in trial results submitted to the FDA to support its approval. By Week 4, a greater proportion of individuals receiving Bimzelx achieved PASI 75 compared to placebo. The most common adverse reactions (greater than or equal to 1%) with Bimzelx are upper respiratory tract infections, oral candidiasis, headache, injection site reactions, tinea infections, gastroenteritis, herpes simplex infections, acne, folliculitis, other Candida infections, and fatigue.

Pustular psoriasis

Pustular psoriasis is characterized by neutrophil-filled pustules and is distinct from plaque psoriasis, though the two may occur concurrently. The ERASPEN defines three subtypes of pustular psoriasis.

1. Generalized pustular psoriasis: sterile, visible pustules on non-acral skin which may occur with or without systemic inflammation or psoriasis vulgaris.[8] Generalized pustular psoriasis is a rare, multisystem disease which can cause life-threatening systemic disease as well as chronic skin disease and symptoms.

2. Palmoplantar pustulosis: persistent disease (greater than 3 months) with sterile, visible pustules on the palms and soles.[8] There is some disagreement if PPP is a subtype of pustular psoriasis, closely related to GPP, or a distinct entity.

3. Acrodermatitis continua of Hallopeau: persistent symptoms (greater than 3 months) with sterile, visible pustules impacting the nails.

Pustular psoriasis makes up 1% of all psoriasis. The global prevalence of GPP is 1.76/million; the US prevalence is estimated at less than 1/10,000.7 Overall, GPP is more common in Asian populations than Caucasian.[10] While GPP can occur at any age, it is less common among children.

Generalized pustular psoriasis is characterized by disease flares which can be triggered by a variety of factors including withdrawal of systemic steroids, certain medications such as lithium, infections especially streptococcal, stress, hypocalcemia associated with hypoparathyroidism, and pregnancy. Gene mutations also play a role in pustular psoriasis, particularly GPP. Overall, GPP has a relapsing/remitting course which can include relapsing disease with recurrent flares, or persistent symptoms with intermittent flares. Symptoms of GPP include sudden appearance of extensive superficial pustules on the trunk and limbs, erythema, inflammation, and systemic symptoms.[10] Pustules seen with GPP often coalesce. Typically, individuals report less than or equal to 1 flare per year; however, almost one-third report two to three flares annually. Length of flares ranges from 2 weeks to 3 months.[7] During a flare, the skin loses its protective barrier functions and risk of bacterial infection is high. Time to resolution is 2-4 weeks for pustules and 1-3 months for erythema and scaling. Symptoms seen with persistent disease may include erythematous plaques and pustules. Systemic symptoms may include fever, chills, malaise, nausea, and pain. Extracutaneous symptoms such as sublingual pustules, fissured tongue, arthritis, uveitis, acute respiratory distress syndrome, cardiovascular shock, and neutrophilic cholangitis can also occur. Laboratory changes include elevated C-reactive protein, leukocytosis, neutrophilia, and abnormal liver function tests. Mortality rates due to flares range from 3%-25% of individuals, most commonly due to bacterial infection and/or cardiorespiratory failure.

Palmoplantar pustulosis differs from GPP in several ways. Palmoplantar pustulosis is characterized by pustules on the palms and soles, pain, and pruritus. Risk factors for PPP include tobacco smoke and oral infections. The clinical course is chronic and relapsing, often impacting QoL. Depression is common. The prevalence of PPP ranges from 0.01% to 0.05%, but has been reported to occur in 0.12% of the population in Japan. Mutations involving the IL-36 receptor are less common in individuals with PPP than GPP.

In individuals with GPP, excess inflammatory signaling recruits immune cells, leading to symptoms of GPP. Overexpression of IL-36 and loss-of-function mutations in IL-36 receptor antagonists have been reported in individuals with GPP. Interleukin-36 receptors are expressed in keratinocytes, fibroblasts, macrophages, dendritic cells, and certain T cell subsets. Activation of IL-36 leads to neutrophil chemotaxis and neutrophil inflammatory response. When cytokines bind to the IL-36 receptor, pro-inflammatory responses occur such as activation of transcription factors, secretion of IL-8 (a chemokine), and increased proinflammatory cytokines such as tumor necrosis factor-α (TNF-α), IL-1, IL-23, and T helper-17 (Th17). This increases inflammation and recruitment of neutrophils and macrophages, resulting in the symptoms of GPP.

Spesolimab has been studied in a Phase 2 trial in individuals with a current GPP flare and a Phase 2 trial in individuals with PPP.[1,2] Another Phase 2 trial is under way in individuals with a

history of GPP without a current flare. To date, the manufacturer is seeking a GPP flare indication only.

The EFFISAYIL 1 trial is a 12-week, multicenter, double-blind, placebo-controlled, Phase 2 trial in which 53 individuals with a current GPP flare were randomized to spesolimab 900 mg IV or placebo. Inclusion criteria were age 18-75 years, history of GPP according to European Rare and Severe Psoriasis Expert Net-work (ERASPEN) criteria, and a current moderate-to-severe flare defined as a GPPGA pustulation sub-score greater than or equal to 2 and greater than or equal to 5% body surface area (BSA) involvement. Individuals received study drug on Day 1. All individuals with persistent symptoms at the end of Week 1, defined as GPPGA total score greater than or equal to 2 and GPPGA pustulation subscore greater than or equal to 2, were eligible to receive an open-label dose of spesolimab 900 mg IV on Day 8. After this point, those with a reoccurrence of flare could receive a rescue dose of spesolimab. Flare recurrence was defined as GPPGA total score increase of greater than or equal to 2 points after a score of 0/1 had been achieved. Individuals could also receive escape treatment (physician's choice standard of care therapy) if immediate treatment was required during Week 1, or if the individual was not eligible for a rescue dose of spesolimab. Individuals receiving escape treatment were considered nonresponders. Baseline characteristics included median age 43 years, 60%-83% female, 46%-72% Asian, and generalized pustular psoriasis area and severity index (GPPASI) total score 29.0-27.4. Of note, baseline characteristics differed be-tween groups for the proportion of female and Asian individuals as well as GPPASI total score. Significantly more individuals on spesolimab than placebo were able to achieve the primary endpoint of GPPGA pustulation subscore 0 at the end of Week 1 (54% vs 6%, pless than 0.001). Additionally, the key secondary endpoint of the proportion of individuals with GPPGA total score 0/1 at the end of Week 1 also was significantly in-creased with spesolimab compared to placebo (43% vs 11%, p=0.002). However, 15 of 18 individuals randomized to placebo received an open-label dose of spesolimab on Day 8. Because of this, the planned hierarchical testing of secondary outcomes with endpoints occurring after Day 8 was not possible. Instead, these outcomes were reported descriptively. In individuals who received greater than or equal to 1 dose of spesolimab (n=50), GPPASI-75 occurred in 11.4% of individuals at Week 1 and 51.4% at Week 8. Pain visual analogue scores (VAS) decreased 21.3 and 53.4 points on a 100 point scale at Weeks 1 and 8. The change from baseline (BL) in psoriasis symptom scale (PSS), a 17 point scale, was -4.0 at Week 1 and -7.0 at Week 8. The change from BL in Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) increased by 7.0 at Week 1 and 22.0 at Week 8, indicating an improvement in quality of life (QoL). Lastly, the GPPGA pustulation subscore 0 outcome was assessed at Week 8 for each subgroup of individuals who received spesolimab. The proportion of individuals achieving a score of 0 at Week 8 was 71%, 78%, 58%, and 60% for those randomized to spesolimab (n=35), randomized to spesolimab who received a single dose (n=23), randomized to spesolimab who

received greater than 1 dose (n=12), and those randomized to placebo who received open-label spesolimab (n=15).

Individuals in the EFFISAYIL 1 trial were eligible for enrollment in a 5-year, open-label trial extension with spesolimab SC if the individual had a response to spesolimab and did not have an additional flare during the trial.1 No results are available to date.

The EFFISAYIL 2 trial is a 48-week, multicenter, randomized, double-blind, placebo-controlled Phase 2b trial in individuals 12-75 years of age with a history of GPP flares in the past who have clear/almost clear skin at the time of enrollment. Individuals are randomized to one of four arms including three spesolimab SC arms and placebo.[3] Study drug is administered once a month. The primary endpoint is time to first GPP flare. Study completion is expected in February 2023; no data is available to date.

Spesolimab has also been studied in individuals with PPP, a type of pustular psoriasis, in a 16-week, multi-center, double-blind, placebo-controlled, Phase 2a trial. The manufacturer is not currently seeking FDA approval for treatment of PPP. The trial included 59 individuals with PPP who were randomized to spesolimab 900 mg IV q4 weeks, spesolimab 300 mg IV q4 weeks, or placebo. Inclusion criteria were age 18-65 years, diagnosis of PPP with active pustules present, PPPASI greater than or equal to 12, and palmoplantar pustulosis physician's global assessment (PPPGA) greater than or equal to 3. Of note, the trial was considered exploratory and formal statistical analysis was not done. Also, there were differences in baseline characteristics between groups for time since diagnosis (6.7 years placebo vs 10.4 years spesolimab). No difference was found between spesolimab and placebo in the primary outcome of PPPASI-50 at Week 16 (23.8% placebo, 31.6% spesolimab 300 mg, and 31.6% spesolimab 900 mg, risk difference vs placebo 0.078). The secondary end-point of PPPASI-75 was achieved in 9.5%, 0%, and 21%, respectively, while the mean change in PPPASI from BL was -40%, -32.7%, and -45.8%, respectively.

In the GPP trial, Grade 3/4 AEs occurred in less than 10% of individuals on spesolimab; no further information was provided. Serious AEs with spesolimab occurred in 6% of individuals in Week 1 and 12% in Week 12.1 At Week 12, the most common SAE was DRESS (n=2 [4%]); all remaining SAEs occurred in single individuals (UTI, drug-induced hepatic injury, arthritis, worsening plaque psoriasis, influenza, and squamous cell skin carcinoma). Of the two individuals listed as DRESS, one had a RegiSCAR score of 1 (no DRESS) and the other had a score of 3 (possible DRESS). Symptoms resolved without drug treatment in both cases. Both individuals developed ADAs. No deaths occurred in the trial.

In the PPP trial, Grade 3/4 AEs occurred in 10.5% of individuals on spesolimab 900 mg and 300 mg compared to 9.5% on placebo. Drug-related Grade 3/4 AEs included syncope in the

spesolimab 900 mg group and worsening PPP in the placebo group. Serious AEs occurred in 4.8% of individuals on placebo, 5.3% on spesolimab 300 mg, and none on spesolimab 900 mg. Of these, one SAE was considered drug related (worsening PPP in the placebo group). No DRESS was reported. No deaths occurred.

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27. Spevigo (spesolimab-sbzo). Prescribing Information. Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, CT. Revised March 2024.
28. Sotyktu (deucravacitinib). Prescribing Information. Bristol-Myers Squibb. Princeton, NJ. Revised September 2022.

History

Date	Comments
11/01/22	New policy, approved October 11, 2022, effective for dates of service on or after November 1, 2022. For the treatment of plaque psoriasis moved Enbrel, Humira, Infliximab (Janssen – unbranded), Inflectra, Remicade, Taltz, Stelara SC, Skyrizi, Tremfya, Otezla, Siliq, Cosentyx, Cimzia, Renflexis, Avsola, and Ilumya from Policy 5.01.550 to Policy 5.01.629 with no changes to coverage criteria. Added coverage for the topical drugs Vtama (tapinarof) and Zoryve (roflumilast) for the treatment of plaque psoriasis. Added coverage for Spevigo (spesolimab-sbzo) for the treatment of generalized pustular psoriasis flares in adults.
12/01/22	Interim Review, approved November 8, 2022. Added coverage for Sotyktu (deucravacitinib) for the treatment of plaque psoriasis.

Date	Comments
02/01/23	Interim Review, approved January 10, 2023. Added coverage for the biosimilar Amjevita (adalimumab-atto) for the treatment of plaque psoriasis with the identical coverage criteria as Humira (adalimumab). Added Amjevita as a prerequisite medication, on par with Humira, for the treatment of plaque psoriasis to Siliq, Cosentyx, Cimzia, Ilumya, and Sotyktu. Added coverage for brand calcipotriene foam, Dovonex (calcipotriene), Duobrii (halobetasol and tazarotene), Enstilar (betamethasone and calcipotriene), Sorilux (calcipotriene), Taclonex (betamethasone and calcipotriene), Vectical (calcitriol), and Wynzora (betamethasone and calcipotriene) for the topical treatment of plaque psoriasis. Added coverage for Soriatane (acitretin) for the systemic treatment of psoriasis. Added Amjevita to HCPC code J3590.
04/01/23	Annual Review, approved March 14, 2023. Added clarification of coverage for the biosimilar Amjevita (adalimumab-atto) with NDCs starting with 55513 versus NDCs starting with 72511. Changed the wording from "patient" to "individual" throughout the policy for standardization. Added new HCPCS code J1747.
07/01/23	Interim Review, approved June 13, 2023. Minor update made to Sotyktu criteria. Instead of two, individuals need to try three of the following agents: Enbrel, Humira, Amjevita, Otezla, Skyrizi, Stelara, Taltz, Tremfya.
08/01/23	Interim Review, approved July 11, 2023. Added coverage for the biosimilars Hyrimoz LCF (adalimumab-adaz) SC, Abrilada (adalimumab-afzb) SC, Hulio ((adalimumab-fkjp) SC, Yusimry (adalimumab-aqvh) SC, Hadlima (adalimumab-bwwd) SC and Yuflyma (adalimumab-aaty) SC for the treatment of plaque psoriasis as non-preferred products and with the identical coverage criteria as Amjevita (adalimumab-atto) [NDCs starting with 72511]. Added coverage for Cyltezo LCF (adalimumab-adbm), Hyrimoz HCF (adalimumab-adaz) and Adalimumab-adaz HCF (Sandoz – unbranded) SC for the treatment of plaque psoriasis as preferred products and with the identical coverage criteria as Amjevita (adalimumab-atto) [NDCs starting with 55513]. Added Cyltezo, Hyrimoz HCF, Adalimumab-adaz HCF (Sandoz – unbranded), Abrilada, Hadlima, Hulio, Hyrimoz LCF, Yuflyma and Yusimry to code J3590.
08/01/23	Interim Review, approved July 24, 2023. Updated preferred Humira biosimilars (Cyltezo LCF, Hyrimoz HCF, Adalimumab-adaz HCF (Sandoz-unbranded)) along with Humira and Amjevita (NDC starting with 55513) in the list of agents to be tried and failed prior to using nonpreferred agents, such as Siliq, Cosentyx, Ilumya, Sotyktu.
09/01/23	Interim Review, approved August 8, 2023. The following policy changes are effective September 1, 2023: Added Humira biosimilars Adalimumab-fkjp (Biocon-unbranded) and Idacio (adalimumab-aacf) as non-preferred products with similar criteria as Amjevita (adalimumab-atto) [NDCs starting with 72511]. Updated Cosentyx coverage criteria for psoriasis to require two agents (instead of four) and removed requirements of trying agents from two or more different drug classes. The following policy changes are effective January 1, 2024 following a 90-day provider notification due to changes in the preferred medical benefit drugs: moved Avsola to 1st line (preferred); added Avsola to the list of preferred infliximab products to be tried and failed prior to non-preferred infliximab products; moved Inflectra to 2nd line (non-preferred) infliximab

Date	Comments
	products; removed Inflectra from the list of preferred infliximab products to be tried and failed prior to trying non-preferred infliximab products.
01/01/24	Interim Review, approved December 12, 2023. Updated Amjevita [NDCs starting with 55513] to a non-preferred product. Added Hyrimoz (Cordavis) [NDCs starting with 83457] as a non-preferred product. Added adalimumab-adbm (Cyltezo unbranded) as a preferred product. Updated Hyrimoz LCF (Sandoz) from a non-preferred to a preferred product.
02/01/24	Annual Review, approved January 9, 2024. Added coverage for Bimzelx (bimekizumab-bkzx) for the treatment of plaque psoriasis. Updated Zoryve (roflumilast) coverage criteria to treatment of individuals 6 years of age and older. Added Bimzelx to HCPC code J3590.
03/01/24	Interim Review, approved February 13, 2024. Removed Stelara (ustekinumab) subcutaneous (SC) injection site of service requirement.
04/01/24	Interim Review, approved March 12, 2024. Updated brand preferred product step therapy requirement for Sotyktu (deucravacitinib) from trial of three agents to one agent.
05/01/24	Interim Review, approved April 9, 2024. Added Humira (adalimumab) (Cordavis) [NDCs starting with 83457] as a non-preferred product. Added Spevigo (spesolimab-sbzo) SC injection coverage criteria. Updated age requirement for Spevigo (spesolimab-sbzo) coverage criteria to 12 years or older.
07/01/24	Interim Review, approved June 11, 2024. Added adalimumab-aaty (Yuflyma unbranded) as a non-preferred product. Added Simlandi (adalimumab-ryvk) and adalimumab-ryvk (Simlandi unbranded) as preferred products. Updated non-preferred adalimumab coverage criteria to require trial and treatment failure with all preferred adalimumab products. Updated Otezla (apremilast) age requirement from adults to individuals 6 years of age and older who weigh at least 20 kg. Added Simlandi to J3590.
08/01/24	Interim Review, approved July 22, 2024. Updated Sotyktu (deucravacitinib) from a non-preferred to a preferred product.
09/01/24	Interim Review, approved August 26, 2024. Updated Zoryve (roflumilast) to indicate coverage criteria is limited to the 0.3% cream. The following policy changes are effective December 5, 2024, following 90-day provider notification. Added Spevigo IV (spesolimab-sbzo) to site of service requirement.
10/01/24	Interim Review, approved September 10, 2024. The following changes are effective January 3, 2025, following a 90-day provider notification, Changed Inflectra (infliximab-dyyb) to a first-line agent. Changed Avsola (infliximab-axxq) to a second-line agent. Updated coverage criteria for Avsola and Renflexis to require the individual to have an adequate trial and failure with Inflectra, Infliximab (Janssen – unbranded), or Remicade. Updated Hyrimoz (Sandoz) (adalimumab-adaz) [NDCs starting with 61314] from a preferred product to a non-preferred product. Updated Humira (AbbVie)

Date	Comments
	(adalimumab) [NDCs starting with 00074] to require that the individual has had an inadequate response or intolerance to a preferred product for new starts.
12/01/24	Interim Review, approved November 12, 2024. Updated Bimzelx (bimekizumab-bkzx) brand step therapy requirement from trial and inadequate response or intolerance to two agents to trial and inadequate response or intolerance to one agent.
01/01/25	Interim Review, approved December 23, 2024. Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Added the following to note to all criteria for adalimumab products: This medical necessity criteria does not apply to one Open formulary (Formulary ID: 6062; Rx Plan F1) and one Incentive formulary (Formulary ID: 6064; Rx Plan G3). The criteria for members with these custom Open and Incentive formulary plans can be found in policy 5.01.647 Medical Necessity Criteria for Custom Incentive and Open Formularies. Please check the member Plan booklet or member ID card to determine whether this policy criteria applies. Added new HCPCS codes J0139, Q5140, Q5141, Q5142, Q5143, Q5144, Q5145.
02/01/25	Annual Review, approved January 27, 2025. Policy updated to indicate that Site of Service Medical Necessity criteria does not apply to Alaska fully-insured members; only Medical Necessity criteria for the infusion drug applies pursuant to Alaska HB 226 (link added). Clarified that non-formulary exception review authorizations for all drugs listed in this policy may be approved up to 12 months. Added an exception to the site-of-service requirements for certain individuals receiving treatment for cytokine release syndrome (CRS).
03/01/25	Interim Review, approved February 11, 2025. The following policy changes are effective July 1, 2025, following a 90-day provider notification. Updated Humira (adalimumab) (AbbVie) [NDCs starting with 00074] from a preferred to a non-preferred adalimumab product.
05/01/25	Interim Review, approved April 8, 2025. Updated re-authorization duration of approval from 3 years to 12 months.

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.