PREMERA | BLUE CROSS

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PHARMACY / MEDICAL POLICY – 5.01.647

Medical Necessity Criteria for Custom Incentive and Open Formularies

Effective Date:	Jan. 1, 2025
Last Revised:	Dec. 10, 2024
Replaces:	N/A

RELATED MEDICAL POLICIES:

5.01.550	Pharmacotherapy of Arthropathies
5.01.556	Rituximab: Non-oncologic and Miscellaneous Uses
5.01.563	Pharmacotherapy of Inflammatory Bowel Disease
5.01.564	Pharmacotherapy of Miscellaneous Autoimmune Diseases
5.01.629	Pharmacologic Treatment of Psoriasis

Select a hyperlink below to be directed to that section.

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

Introduction

Prior authorization and step therapy are a way to provide safe and effective drugs. In step therapy, at least one drug on the health plan's list of covered drugs (the formulary) needs to be tried first. This policy describes the plan's prior authorization and step therapy criteria for specific drugs in the plan's formulary. This policy applies only to certain custom Incentive and Open formulary plans. This policy contains separate criteria to be used only for members with these specific custom Incentive and Open formulary plans.

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

This policy applies only to one Open formulary (Formulary ID: 6062; Rx Plan F1) and one Incentive formulary (Formulary ID: 6064; Rx Plan G3). This policy contains separate criteria to be used only for members with these custom Open and Incentive formulary plans. Please check the member Plan booklet or member ID card to determine whether this policy criteria applies.

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

First-line Agents
TNF-α Inhibitors
Adalimumab-adaz (Hyrimoz unbranded) (SC)
Adalimumab-adbm (Cyltezo unbranded) (SC)
Adalimumab-ryvk (Simlandi unbranded) (SC)
Cyltezo (SC)
Humira (AbbVie) [NDCs starting with 00074] (SC)
Simlandi (adalimumab-ryvk) (SC)
Second-line Agents
TNF-α Inhibitors
Abrilada (SC)
Adalimumab-aacf (Idacio unbranded) (SC)
Adalimumab-aaty (Yuflyma unbranded) (SC)
Adalimumab-fkjp (Hulio unbranded) (SC)
Amjevita (SC)
Hadlima (SC)
Hulio (SC)
Humira (Cordavis) [NDCs starting with 83457] (SC)
Hyrimoz (Cordavis) [NDCs starting with 83457] (SC)
Hyrimoz (Sandoz) [NDCs starting with 61314] (SC)
Idacio (SC)
Yuflyma (SC)
Yusimry (SC)

Drug	Medical Necessity
First-line TNF-α Antagonists	
• **Adalimumab-adaz (Hyrimoz unbranded) SC**	**Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie)**

Drug	Medical Necessity
• **Adalimumab-adbm (Cyltezo unbranded) SC** • **Adalimumab-ryvk (Simlandi unbranded) SC** • **Cyltezo (adalimumab-adbm) SC** • **Humira (adalimumab) (AbbVie) [NDCs starting with 00074] SC** • **Simlandi (adalimumab-ryvk) SC**	**[NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of ankylosing spondylitis when:** • Medication is being prescribed by or in consultation with a rheumatologist **Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of Crohn's disease when:** • The individual has tried one corticosteroid (e.g., methylprednisolone, prednisone, prednisolone, dexamethasone, budesonide, etc.) or is currently taking a corticosteroid medication **OR** • Has tried one other agent for Crohn's disease (e.g., azathioprine, 6-mercaptopurine, methotrexate, mesalamine extended-release [Pentasa formulation], etc.) **OR** • Has enterocutaneous (perianal or abdominal) or rectovaginal fistulas **OR** • Has had ileocolonic resection (to reduce the chance of Crohn's disease recurrence) **AND** • Medication is being prescribed by or in consultation with a gastroenterologist **Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk)**

Drug	Medical Necessity

	may be considered medically necessary for the treatment of hidradenitis suppurativa when:
	• The individual is aged 12 years or older
	AND
	• Has tried at least one other therapy (e.g., intralesional or oral corticosteroids, systemic antibiotics)
	AND
	• The medication is prescribed by or in consultation with a dermatologist
	
	Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) 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
	  ▪ 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

Drug	Medical Necessity
	Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when: • The individual has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine **OR** • Is being started on adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], or Simlandi (adalimumab-ryvk) concurrently with leflunomide, methotrexate, or sulfasalazine **AND** • Medication is being prescribed by or in consultation with a rheumatologist **Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a rheumatologist or dermatologist **Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of pyoderma gangrenosum when:**

Drug	Medical Necessity
	• The individual has not responded to one standard non-biologic therapy (e.g., oral corticosteroids, systemic cyclosporine, topical tacrolimus, etc.) **AND** • The medication is prescribed by or in consultation with a dermatologist **Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:** • The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine **AND** • Medication is being prescribed by or in consultation with a rheumatologist **Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of sarcoidosis when:** • The individual has tried and had an inadequate response or intolerance to one corticosteroid **AND** • Has tried and had an inadequate response or intolerance to one immunosuppressive medication (e.g., methotrexate, leflunomide, azathioprine, mycophenolate, cyclosporine, chlorambucil, cyclophosphamide, thalidomide, or chloroquine) **AND** • The medication is prescribed by or in consultation with a pulmonologist, ophthalmologist, or dermatologist

Drug	Medical Necessity

	Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of ulcerative colitis when:
	• Medication is being prescribed by or in consultation with a gastroenterologist
	
	Adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-ryvk (Simlandi unbranded), Cyltezo (adalimumab-adbm), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], and Simlandi (adalimumab-ryvk) may be considered medically necessary for the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis when:
	• The individual is aged 2 years or older
	AND
	• Has tried one of the following therapies:
	  ○ Periocular, intraocular, or systemic corticosteroids
	  ○ Immunosuppressives
	AND
	• The medication is prescribed by or in consultation with an ophthalmologist

Second-line TNF-α Antagonists	
• **Abrilada (adalimumab-afzb) SC** • **Adalimumab-aacf (Idacio unbranded) SC** • **Adalimumab-aaty (Yuflyma unbranded) SC** • **Adalimumab-fkjp (Hulio unbranded) SC** • **Amjevita (adalimumab-atto) 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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered**

Drug	Medical Necessity

• **Hadlima (adalimumab-bwwd) SC**
• **Hulio (adalimumab-fkjp) SC**
• **Humira (adalimumab) (Cordavis) [NDCs starting with 83457] SC**
• **Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457] SC**
• **Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314] SC**
• **Idacio (adalimumab-aacf) SC**
• **Yuflyma (adalimumab-aaty) SC**
• **Yusimry (adalimumab-aqvh) SC**
	medically necessary for the treatment of ankylosing spondylitis when:
	• Medication is being prescribed by or in consultation with a rheumatologist
	AND
	• The individual has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)
	
	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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of Crohn's disease when:
	• The individual has tried one corticosteroid (e.g., methylprednisolone, prednisone, prednisolone, dexamethasone, budesonide, etc.) or is currently taking a corticosteroid medication
	OR
	• Has tried one other agent for Crohn's disease (e.g., azathioprine, 6-mercaptopurine, methotrexate, mesalamine extended-release [Pentasa formulation], etc.)
	OR
	• Has enterocutaneous (perianal or abdominal) or rectovaginal fistulas
	OR

Drug	Medical Necessity

	• Has had ileocolonic resection (to reduce the chance of Crohn's disease recurrence)
	AND
	• Has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)
	AND
	• Medication is being prescribed by or in consultation with a gastroenterologist
	
	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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of hidradenitis suppurativa when:
	• The individual is aged 12 years or older
	AND
	• Has tried at least one other therapy (e.g., intralesional or oral corticosteroids, systemic antibiotics)
	AND
	• Has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)

Drug	Medical Necessity
	○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074] ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded) **AND** • The medication is prescribed by or in consultation with a dermatologist **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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], 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** ▪ 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**

Drug	Medical Necessity

	• Has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)
	AND
	• Medication is being prescribed by or in consultation with a dermatologist
	
	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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of polyarticular juvenile idiopathic arthritis when:
	• The individual has had an inadequate response or intolerance to leflunomide, methotrexate, or sulfasalazine
	AND
	• Has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)
	AND

Drug	Medical Necessity
	• Medication is being prescribed by or in consultation with a rheumatologist **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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of active psoriatic arthritis when:** • Medication is being prescribed by or in consultation with a dermatologist or a rheumatologist **AND** • The individual has had an inadequate response or intolerance to ALL the following agents: o Adalimumab-adaz (Hyrimoz unbranded) o Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded) o Humira (adalimumab) (AbbVie) [NDCs starting with 00074] o Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded) **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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) considered medically necessary for the treatment of pyoderma gangrenosum when:**

Drug	Medical Necessity

	• The individual has not responded to one standard non-biologic therapy (e.g., oral corticosteroids, systemic cyclosporine, topical tacrolimus, etc.)
	AND
	• Has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)
	AND
	• The medication is prescribed by or in consultation with a dermatologist
	
	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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of moderate to severe rheumatoid arthritis when:
	• The individual has not responded to or does not tolerate methotrexate, leflunomide, sulfasalazine or hydroxychloroquine
	AND
	• Medication is being prescribed by or in consultation with a rheumatologist
	AND
	• Has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)

Drug	Medical Necessity
	○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded) ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074] ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded) **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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of sarcoidosis when:** • The individual has tried and had an inadequate response or intolerance to one corticosteroid **AND** • Has tried and had an inadequate response or intolerance to one immunosuppressive medication (e.g., methotrexate, leflunomide, azathioprine, mycophenolate, cyclosporine, chlorambucil, cyclophosphamide, thalidomide, or chloroquine) **AND** • Has had an inadequate response or intolerance to ALL the following agents: ○ Adalimumab-adaz (Hyrimoz unbranded) ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded) ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074] ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded) **AND** • Medication is prescribed by or in consultation with a pulmonologist, ophthalmologist, or dermatologist

Drug	Medical Necessity

	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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of ulcerative colitis when:
	• The individual has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)
	AND
	• Medication is being prescribed by or in consultation with a gastroenterologist
	
	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) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) may be considered medically necessary for the treatment of non-infectious intermediate uveitis, posterior uveitis, or panuveitis when:

Drug	Medical Necessity

	• The individual is aged 2 years or older
	AND
	• Has tried one of the following therapies:
	  ○ Periocular, intraocular, or systemic corticosteroids
	  ○ Immunosuppressives
	AND
	• Has had an inadequate response or intolerance to ALL the following agents:
	  ○ Adalimumab-adaz (Hyrimoz unbranded)
	  ○ Cyltezo (adalimumab-adbm) OR adalimumab-adbm (Cyltezo unbranded)
	  ○ Humira (adalimumab) (AbbVie) [NDCs starting with 00074]
	  ○ Simlandi (adalimumab-ryvk) OR adalimumab-ryvk (Simlandi unbranded)
	AND
	• The medication is prescribed by or in consultation with an ophthalmologist

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 are considered investigational.**

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

Length of Approval	
Approval	**Criteria**
Initial authorization	**All drugs listed in policy may be approved up to 12 months.**

Length of Approval	
Approval	**Criteria**
Re-authorization criteria	**Future re-authorization of all drugs listed in policy may be approved up to 3 years 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 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 diagnosis, relevant history, physical evaluation and medication history

Coding

Code	Description
HCPCS	
J0135	Injection, adalimumab (Humira), 20 mg
J3590	Unclassified biologics (use to report Amjevita, Cyltezo, Hadlima, Hulio, Hyrimoz, Simlandi, Yuflyma, Yusimry)
Q5131	Injection, adalimumab-aacf (Idacio), biosimilar, 20 mg
Q5132	Injection, adalimumab-afzb (Abrilada), biosimilar, 10 mg (new code effective 1/1/2024)

Related Information

Consideration of Age

Age limits specified in this policy are determined according to FDA-approved indications, where applicable.

Medical / Pharmacy Benefit

Abrilada (adalimumab-afzb), adalimumab-aacf (Idacio unbranded), adalimumab-aaty (Yuflyma unbranded), adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-fkjp (Hulio unbranded), adalimumab-ryvk (Simlandi unbranded), Amjevita (adalimumab-atto), Cyltezo (adalimumab-adbm), Hadlima (adalimumab-bwwd), Hulio (adalimumab-fkjp), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], Humira (adalimumab) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Simlandi (adalimumab-ryvk), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh) are managed through both the pharmacy and medical benefit.

Evidence Review

Crohn's Disease (CD)

The American College of Gastroenterology indicates current therapeutic recommendations depend on disease location, disease severity, and the presence of disease-associated complications. Pharmacologic approaches include various 5-aminosalicylates (5-ASAs), corticosteroids, and immunosuppressants. While the effectiveness of the 5-ASAs is less than corticosteroids, their side effect profile is more favorable. Azathioprine and sulfasalazine are also associated with clinically significant long-term toxicity, according to the National Cooperative Crohn's Disease Study. Azathioprine, sulfasalazine, and prednisone have not been demonstrated to prevent recurrence of disease flares.

Surgical resection is a common occurrence in CD, with up to 57% of individuals requiring at least one surgery in any given year. Within 10 years of disease onset, 71% of individuals undergo this therapy.

The safety and efficacy of adalimumab (Humira) for the induction and/or maintenance of remission in individuals with moderately to severely active CD (Crohn's Disease Activity Index

[CDAI] ≥220 and ≤450) was evaluated in four randomized placebo-controlled studies. Two of these studies evaluated Humira for induction of remission (defined as a CDAI <150), one study in individuals who were TNF antagonist naïve (CLASSIC-I) and the other in individuals who had lost response or were intolerant to Remicade (GAIN). Two of these studies evaluated Humira for maintenance of remission, both studies in individuals who were TNF antagonist naïve (CLASSIC-II and CHARM).

In CLASSIC-I, 299 individuals with moderately to severely active CD, including individuals with draining fistulas, were randomized to two subcutaneous injections at Weeks 0 and 2 with Humira 40 mg/20 mg, 80 mg/40 mg, or 160 mg/80 mg or placebo. Enrollees were also able to maintain existing therapy with immunomodulatory agents, corticosteroids, and/or aminosalicylates. The primary efficacy endpoint was induction of remission (CDAI <150) at Week 4. The rate of remission was significantly higher in the 160 mg/80 mg group (36%, p=0.001), but not for the 40 mg/20 mg (18%, p=0.36) or 80 mg/40 mg (24%, p=0.06) groups compared with placebo (12%). Injection site reactions occurred more frequently in Humira-treated individuals; otherwise, adverse events occurred at similar frequencies in all four treatment groups.

In GAIN, 325 individuals with moderately to severely active CD who were intolerant of, who had lost response, or who had an inadequate response to Remicade were randomized to two subcutaneous injections at Weeks 0 and 2 with Humira 160 mg/80 mg or placebo. Primary efficacy endpoint was induction of remission (CDAI <150) at Week 4. Clinical response (decrease in CDAI score ≥70 or 100) at Week 4 was also assessed. More Humira-treated individuals (21%, p<0.001) achieved clinical remission compared to those treated with placebo (7%). More Humira-treated individuals (52%, p<0.01) achieved a clinical response-70 compared with the placebo group (34%).

A total of 276 individuals participating in CLASSIC-I enrolled in CLASSIC-II and received open-label Humira 40 mg subcutaneously at Weeks 0 (Week 4 of CLASSIC-I) and 2. Those individuals (n=55) in remission at both Week 0 and Week 4 were re-randomized to Humira 40 mg QOW, 40 mg QW, or placebo for 52 additional weeks. Individuals who were not in remission at both Weeks 0 and 4 were treated with open-label Humira 40 mg QOW. These individuals were allowed to have their dose increase to 40 mg QW for non-response or disease flare. The re-randomized individuals were also allowed to "escape" into this open-label arm with disease flare. The primary efficacy endpoint was maintenance of remission (CDAI <150) in randomized individuals through week 56. Of the 55 individuals randomized at Week 4, a greater proportion receiving Humira (79% of the Humira 40 mg QOW group and 83% of the 40 mg QW group, both p<0.05) were in remission compared to the placebo group (44%). Of 204 individuals entering the open-label arm, 46% were in remission at Week 56. Humira was generally well-tolerated.

In CHARM, a total of 854 individuals with moderately to severely active CD were treated with open-label Humira 80 mg at Week 0 followed by 40 mg at Week 2 as induction therapy. At Week 4, individuals were stratified by clinical response (decrease of CDAI ≥70) and randomized to double-blind treatment with subcutaneous Humira 40 mg QOW, Humira 40 mg QW, or placebo weekly for 52 additional weeks. The proportion of randomized clinical responders achieving clinical remission at Weeks 26 and 56 were coprimary endpoints. At Week 4, 499/854 (58%) of individuals achieved a clinical response-70 and were randomized to Humira or placebo. The percentage of randomized responders in remission was significantly greater in the Humira 40 mg QOW and 40 mg QW groups compared to the placebo group at Week 26 (40%, 47%, and 17%, respectively; $p<0.001$) and at Week 56 (36%, 41%, and 12%, respectively; $p<0.001$). No significant differences in efficacy were observed between the two active treatment groups. Individuals who did not achieve clinical response after 12 weeks were unlikely to achieve response. The safety profile for Humira was consistent with previous experience with the drug. More individuals receiving placebo (13.4%) discontinued treatment for an adverse event than those receiving Humira (6.9% in the 40 mg QOW and 4.7% in the 40 mg QW group).

Hidradenitis Suppurativa

Hidradenitis Suppurativa (HS) is an inflammatory skin disease affecting an estimated 1 to 4% of the world population. The main features of HS include painful and chronically recurring, deep-seated follicular nodules, papules, pustules, and abscesses, scarring, sinus tracts, and recurrent discharge. The area's most commonly affected are the under the arms, groin, buttocks, and under the breasts. The disease is variable and recurrent. It may occur as solitary or multiple lesions in one area, or in many areas. In more severe cases, there may be large areas of skin affected by recurrent, draining lesions.

The FDA approved Humira (adalimumab) to treat individuals with HS.

Two randomized, double-blind, placebo-controlled studies (Studies HS-I and II) evaluated the safety and efficacy of Humira in a total of 633 adult subjects with moderate to severe hidradenitis suppurativa (HS) with Hurley Stage II or III disease and with at least 3 abscesses or inflammatory nodules. In both studies, subjects received placebo or Humira at an initial dose of 160 mg at Week 0, 80 mg at Week 2, and 40 mg every week starting at Week 4 and continued through Week 11. Subjects used topical antiseptic wash daily. Concomitant oral antibiotic use was allowed in Study HS-II.

Both studies evaluated Hidradenitis Suppurativa Clinical Response (HiSCR) at Week 12. HiSCR was defined as at least a 50% reduction in total abscess and inflammatory nodule count with no

increase in abscess count and no increase in draining fistula count relative to baseline (see Table below). Reduction in HS-related skin pain was assessed using a Numeric Rating Scale in individuals who entered the study with an initial baseline score of 3 or greater on a 11-point scale.

In both studies, a higher proportion of Humira than placebo-treated subjects achieved HiSCR (see **Table 1** below).

Table 1. Efficacy Results at 12 Weeks in Subjects with Moderate to Severe Hidradenitis Suppurativa

	HS Study I		HS Study II*	
	Placebo	Humira 40 mg Weekly	Placebo	Humira 40 mg Weekly
Hidradenitis Suppurativa Clinical Response (HiSCR)	N=154, 40 (26%)	N=153, 64 (42%)	N=163, 45 (28%)	N=163, 96 (59%)

*19.3% of subjects in Study HS-II continued baseline oral antibiotic during the study.

In both studies, from Week 12 to Week 35 (Period B), subjects who had received Humira were re-randomized to 1 of 3 treatment groups (Humira 40 mg every week, Humira 40 mg every other week, or placebo). Subjects who had been randomized to placebo were assigned to receive Humira 40 mg every week (Study HS-I) or placebo (Study HS-II).

During Period B, flare of HS, defined as ≥25% increase from baseline in abscesses and inflammatory nodule counts and with a minimum of 2 additional lesions, was documented in 22 (22%) of the 100 subjects who were withdrawn from Humira treatment following the primary efficacy time point in two studies.

Juvenile Idiopathic Arthritis

Juvenile Idiopathic Arthritis (JIA) is the most common type of arthritis in children under the age of 17. It causes persistent joint pain, swelling, and stiffness. Some children may experience symptoms for only a few months, while others have symptoms for the rest of their lives. In some cases this disease can cause complications, such as growth problems and eye inflammation. Treatment usually focuses on controlling pain, improving function, and preventing joint damage.

JIA occurs when the body's immune system attacks its own cells and tissues. It is not clear why this happens, however, both heredity and environment seem to play a role. Many different blood tests are used to diagnose JIA. Examples of some are: erythrocyte sedimentation rate (ESR), anti-nuclear antibody, rheumatoid factor, cyclic citrullinated peptide (CCP).

Treatment modalities depend on the extent of the disease, and individual child's needs. Some children benefit from one medication; others may need a combination of a few different medications. Each drug comes with its own side-effect potential which needs to be taken into consideration based on the child's overall health condition and needs. First-line therapy includes the nonsteroidal anti-inflammatory drugs (NSAIDs)-examples of which are: ibuprofen, naproxen, and others. NSAIDs help to reduce pain and swelling of the joints. Disease-modifying antirheumatic drugs (DMARDs) is another option for drug therapy and include methotrexate, sulfasalazine, and others may be used when NSAIDs alone fail. Their purpose is to slow the progression of JIA. Tumor necrosis factor (TNF) blockers, such as etanercept and adalimumab can help reduce pain, morning stiffness, and swollen joints.

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 who's 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.

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.

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.

Psoriatic Arthritis

Psoriatic Arthritis (PsA) is characterized as a spondyloarthropathy associated with psoriasis. The true incidence is unknown and is variably reported to occur in 6-42% (25% is considered a reasonable estimate) of individuals with psoriasis, an immunologic skin disease which occurs in 2-3% of the general population. There is similarity in the histopathogenesis of PsA and RA, including the role of cytokines such as tumor necrosis factor alpha (TNF- α), although there are important differences as well. Several subsets of PsA have also been described. PsA is characterized by stiffness - both peripheral and spine inflammation and pain - joint deformities related to joint destruction, dactylitis, enthesitis (inflammation at insertion sites of tendons, ligaments, and joint capsule fibers), and psoriasis skin plaques. The course of PsA is variable, but the majority of individuals develop a chronic progressive form of the disease resulting in joint destruction, unless treated effectively. Although less well characterized than in RA, similar levels of disability, decreased quality of life, increased co-morbidities, and premature mortality are now being noted in long term registry studies.

Pharmacologic therapy combined with a physical rehabilitation program is the most effective available treatment for psoriatic arthritis (PsA). As with RA, early initiation of pharmacologic therapy is needed to avoid joint damage and disability.

NSAIDs have customarily been used in milder disease along with corticosteroids or traditional DMARDs. Moderate to severe disease requires the use of traditional DMARDs such as MTX, sulfasalazine, or the anti-TNF agents. Azathioprine and cyclosporine are rarely used. Retinoids, phototherapy, and topical and systemic corticosteroids have also been used to treat the skin

manifestations of PsA. In January 2002, etanercept, a TNF-α inhibitor became the first therapy to be approved for the indication.

Other Spondyloarthropathies

The spondyloarthropathies (SpAs) are a heterogeneous set of disorders characterized by axial skeletal involvement and frequent association with the HLA-B27 antigen. Ankylosing spondylitis (AS) is probably the most familiar spondyloarthropathy, which is characterized predominantly by progressive vertebral enthesitis and facet joint inflammation of the spine and sacroiliac joints, leading to eventual spine fusion and decreased range of motion, as well as peripheral joint synovitis, although much less than is seen in RA. Variations in incidence among different racial groups support the hypothesis of a genetic role in AS, as is also postulated in other arthropathies. In the United States, AS is believed to affect approximately 1-3 persons/1000, or about 350,000 to 1 million individuals.

While peripheral arthritis is commonly seen in association with psoriasis, approximately 20-40% of individuals with PsA may have some degree of sacroiliitis with paravertebral ossification. The skin manifestations associated with the arthropathy are not necessarily widespread and may be localized.

About 20% of individuals with inflammatory bowel disease may have evidence of sacroiliitis and some 20% of these individuals may progress to spondylitis. The course of the spondylitis does not necessarily correlate with bowel inflammatory activity.

Treatment of mild spondyloarthropathy may be benefited by symptomatic therapy with NSAIDs, corticosteroids, or sulfasalazine. These agents have shown to have little clinical benefit in individuals with moderate to severe or progressive disease. The paucity of treatment options contrasts with the treatment of RA where there are several different categories of DMARDs (disease-modifying anti-rheumatic drugs) that are used alone or in combination to try and alter the natural history of the disease. Like PsA, etanercept became the first therapy approved by the FDA for the treatment of AS, followed by infliximab and adalimumab.

Pyoderma Gangrenosum

Pyoderma gangrenosum is an inflammatory disease with dermatologic manifestations including painful ulcerations with erythematous borders. It is presumed to be autoimmune in origin, though the mechanism is not well understood. Lesions usually develop at sites of minor skin

injury, usually on the lower extremities. These lesions can grow in size and become necrotic. Underlying fasciitis may occasionally develop from them. Some individuals develop pustular, bullous or vegetative lesions. Other common sites are colostomies and paraneoplastic lesions in individuals with hematologic malignancies. Progress of the lesions is highly variable, and individual response to treatment is heterogeneous. Obesity, diabetes or edema may be contributing factors.

Due to the infrequent occurrence and heterogeneity of pyoderma gangrenosum, the treatment approach is empiric and individual specific. First-line options include topical tacrolimus, nicotine, and 5-ASA, systemic corticosteroids and immunosuppressant agents such as azathioprine, cyclosporine, methotrexate and mycophenolate. When these approaches fail, biologic therapy is usually tried. Successful treatment with TNF inhibitors (etanercept, adalimumab, infliximab) has been reported.

Rheumatoid Arthritis

Rheumatoid Arthritis (RA) is a chronic, progressive, inflammatory, autoimmune disease affecting about 1% of the US adult population and occurs approximately three times more frequently in women than in men (ACR Subcommittee on Rheumatoid Arthritis Guidelines, 2002). Almost 80% of RA cases occur in individuals between 35 and 50 years of age (Kavanaugh and Lipsky, 1996); usually a time of peak social productivity. The underlying cause of RA is unknown, but the disease is characterized by persistent inflammation of the synovium, cartilage loss, and bone erosion in peripheral joints, usually in a symmetric fashion. This inflammation is believed to be mediated by both B- and T-cells and a variety of cytokines (messenger proteins), including tumor necrosis factor-alpha (TNF-α). Research has shown that joint damage occurs within the first two years of symptoms and diagnosis and progresses rapidly if not treated. Although RA primarily affects the joints, it is a systemic disease and does cause systemic and extra-articular clinical features (e.g., fever, fatigue, anorexia, weight loss, and anemia), which contribute to the significant work disability and impaired quality of life which occur. Individuals with RA also have earlier mortality than the general population averaging 7-10 years, primarily due to an increased risk of cardiovascular disease, infection, and lymphoma associated with more severe inflammation.

The American College of Rheumatology (ACR) has established clinical guidelines for the treatment of RA. While both non-pharmacologic (e.g., individual education, exercise, and physical and occupational therapy) and pharmacologic therapies are recommended, the mainstay of RA treatment is pharmacologic therapy. Pharmacologic management often consists of nonsteroidal anti-inflammatory drugs (NSAIDs), disease-modifying antirheumatic drugs

(DMARDs) (including biologic response modifiers/cytokine antagonists), and/or corticosteroids. Because of the evidence showing that joint damage can occur early in the disease process, physicians are now encouraged to treat individuals more aggressively earlier by initiating a DMARD (or combinations of DMARDs) within three months of diagnosis.

Emerging evidence also suggests that the DMARD subclass of tumor necrosis factor-alpha (TNF-α) antagonists retard radiographic progression of the disease better than methotrexate (MTX), particularly in individuals with rapidly progressive disease. The predictive risk factor found to be most associated with this subset of individuals was a CRP ≥4.1 mg/dl. Other predictors are currently being investigated. This should lead to improved ability for the clinician to determine the best DMARD for an individual; however, the choice will continue to be influenced by numerous factors, including but not limited to relative efficacy, convenience of administration, adverse effects, monitoring requirements, comorbidities, and cost.

Ulcerative Colitis (UC)

After positive reports in small open-label trials, the safety and efficacy of adalimumab (Humira) was assessed in a multicenter, double-blinded randomized controlled trial in individuals with moderate to severe ulcerative colitis who were anti-TNF naïve and on stable suppressive therapy with oral corticosteroids and/or immunomodulators. A total of 576 individuals were randomized to receive either placebo, high dose (HD), or low dose (LD) adalimumab. HD was 180/60/40/40mg and LD was 80/40/40/40mg of adalimumab at Weeks 0, 2, 4, 6, respectively. Clinical remission was defined as a Mayo score ≤ 2 with subscores no greater than 1. Secondary outcomes included absolute score decrease plus decrease in rectal bleeding subscore, proportion with mucosal healing, and proportion with mild disease (including physician global assessment [PGA], rectal bleeding, and stool frequency subscores). Because the European regulatory authorities wanted to include a LD of adalimumab, there were two parts to the study, a 1:1 with HD (n=186) and a 1:1:1 portion of the study (n=390); results were pulled from the latter.

Twice as many individuals reached clinical remission at Week 8 with HD (p=0.031) therapy, while LD individuals were not significantly different versus placebo. Of the secondary outcomes, subscores in rectal bleeding and PGA showed improvement with significance vs. placebo in the HD arm. Individuals with higher baseline CRP levels had less instances of remission, and higher placebo rates were seen in Canadian and Eastern European centers than those in the US. Discontinuation rates were similar in each arm, with UC being the most common reason. Injection site pain was minimal, and infection incidence was similar across groups, and malignancy was only seen in the placebo arm.

Toxicities of TNF-α Antagonists

All TNF-α antagonists have treatment-limiting toxicities. Some of the toxicities associated with these agents include Concomitant use of TNF-α inhibitors and MTX consistently scored better with respect to ACR scores, disease activity in 28 joints (DAS28) scores, radiographical progression and health assessment questionnaire (HAQ) scores compared to TNF-α inhibitor monotherapy. The ACR70 scores ranged from 15-20% for all agents, with etanercept showing the highest treatment effect over the control group at three years in the TEMPO trial. While infliximab showed high efficacy at both 3mg/kg and 10mg/kg dosing every eight weeks, the ACR50, ACR70 scores, HAQ scores were slightly higher with 10mg/kg dosing. The DAS28 scores and HAQ scores varied from study to study, but over-all showed improvement over controls across the TNF-α inhibitor class at 12 weeks and greater. Radiographical changes are subject to interpretation by the individual investigator, even with standardized scoring, so comparing across the TNF-α inhibitor trials is not practical. However, of the studies that did assess radiographical progression of the disease, the overall rate of radiographical progression was slowed significantly with adalimumab, certolizumab, etanercept and infliximab compared to MTX therapy alone. In the three-year TEMPO trial, the scores for the etanercept + MTX arm showed reversal of radiographical progression, but this is debatable and requires further investigation. There is no radiographical progression data for golimumab, as they did not assess this in their clinical trials.

There have been no prospective trials evaluating safety among the TNF-α inhibitors. The risk of malignancies and serious infections has been studied to some depth retrospectively with the three older agents (adalimumab, etanercept and infliximab). The FDA did a meta-analysis of the available data in 2006 and found that the malignancy rates of individuals on TNF-α inhibitors are no higher than what is to be expected in this individual population. Another study done in 2007 found a higher incidence of cutaneous cancers among the TNF-α inhibitor treated individuals, irrespective of the agent. The newer agents are limited in their data breadth to demonstrate safety with respect to malignancies, but so far, they compare similarly to the older agents. Long-term safety evaluations are necessary to validate this finding.

With regards to serious infections and tuberculosis, there are higher rates of serious infections while on the TNF-α inhibitors, compared to MTX alone. However, the retrospective studies do not come to an agreement on the actual risk.

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History

Date	Comments
01/01/25	New policy, approved December 10, 2024. Added coverage criteria for Abrilada (adalimumab-afzb), adalimumab-aacf (Idacio unbranded), adalimumab-aaty (Yuflyma unbranded), adalimumab-adaz (Hyrimoz unbranded), adalimumab-adbm (Cyltezo unbranded), adalimumab-fkjp (Hulio unbranded), adalimumab-ryvk (Simlandi unbranded), Amjevita (adalimumab-atto), Cyltezo (adalimumab-adbm), Hadlima

Date	Comments
	(adalimumab-bwwd), Hulio (adalimumab-fkjp), Humira (adalimumab) (AbbVie) [NDCs starting with 00074], Humira (adalimumab) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Cordavis) [NDCs starting with 83457], Hyrimoz (adalimumab-adaz) (Sandoz) [NDCs starting with 61314], Idacio (adalimumab-aacf), Simlandi (adalimumab-ryvk), Yuflyma (adalimumab-aaty), and Yusimry (adalimumab-aqvh). Clarified that the medications listed in this policy are subject to the product's FDA dosage and administration prescribing information. Added HCPCS codes J0135, J3590, Q5131, Q5132.

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.