LOUISIANA BLUE

adalimumab Products

Policy # 00225
Original Effective Date: 03/19/2008
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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

unbranded adalimumab-adaz, adalimumab-ryvk (Simlandi®), adalimumab-ryvk*, adalimumab-adbm*

** These products are manufactured by Quallent Pharmaceuticals.*

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Rheumatoid Arthritis

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi®)‡ for the treatment of rheumatoid arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of rheumatoid arthritis when ALL of the following criteria are met:

Initial

- Patient has moderately to severely active rheumatoid arthritis; AND
- Patient is 18 years of age or older; AND
- Requested drug is NOT used in combination with other biologic disease-modifying anti-rheumatic drugs (DMARDs), such as etanercept (Enbrel®)‡ OR other drugs such as tofacitinib (Xeljanz®/XR)‡ or apremilast (Otezla®)‡; AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a negative tuberculosis (TB) test (e.g., purified protein derivative [PPD], blood test) prior to treatment.

Continuation

- Patient has received an initial authorization for the requested drug; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Note: The recommended dosing of adalimumab in rheumatoid arthritis is 40 mg every other week. Members unresponsive to 40 mg every other week after 12 weeks of therapy AND NOT on methotrexate may be approved for 40 mg once weekly dosing OR 80 mg every other week dosing.

Polyarticular Juvenile Idiopathic Arthritis

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of polyarticular juvenile idiopathic arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of polyarticular juvenile idiopathic arthritis when ALL of the following criteria are met:

Initial

- Patient is 2 years of age or older; AND
- Patient has moderately to severely active polyarticular juvenile idiopathic arthritis; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as improved range of motion, reduced joint pain or tenderness, decreased duration of morning

stiffness or fatigue, improved function or activities of daily living, reduced corticosteroid dosage, or improvement in inflammatory serum markers; AND
*(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*

- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Psoriatic Arthritis

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of psoriatic arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of psoriatic arthritis when ALL of the following criteria are met:

Initial

- Patient is 18 years of age or older; AND
- Patient has active psoriatic arthritis; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Ankylosing Spondylitis

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of active ankylosing spondylitis to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of active ankylosing spondylitis when ALL of the following criteria are met:

Initial

- Patient is 18 years of age or older; AND
- Patient has active ankylosing spondylitis; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with non-steroidal anti-inflammatory drugs (NSAIDs), such as naproxen, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., Ankylosing Spondylitis Disease Activity Score [ASDAS], Bath Ankylosing Spondylitis Disease Activity Index [BASDAI], inflammatory serum markers) or in clinical signs and symptoms such as reduced pain, stiffness, or improved daily functioning; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Crohn's Disease

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of Crohn's disease to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of Crohn's disease when ALL of the following criteria are met:

Initial

- Patient is 6 years of age or older; AND
- Patient has moderately to severely active Crohn's disease; AND

- Patient has failed treatment with conventional therapies such as corticosteroids, 6-mercaptopurine, or azathioprine unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or blood in stool; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Plaque Psoriasis

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of plaque psoriasis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of plaque psoriasis when ALL of the following criteria are met:

Initial

- Patient is 18 years of age or older; AND
- Patient has moderate to severe chronic plaque psoriasis; AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has greater than 10% of body surface area (BSA) or less than or equal to 10% BSA with plaque psoriasis involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck or genitalia); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

- Patient has failed to respond to an adequate trial of one of the following treatment modalities unless there is clinical evidence or patient history that suggests the use of these treatments will be ineffective or cause an adverse reaction to the patient:
    - Ultraviolet B; or
    - Psoralen positive Ultraviolet A; or
    - Systemic therapy (i.e., methotrexate, cyclosporine, acitretin).
      *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested adalimumab product) as evidenced by improvement in clinical signs and symptoms such as reduced estimated body surface area affected by psoriasis, decreased erythema, induration/thickness, or scaling, and/or improvement in symptoms such as pain, itching, or burning; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Ulcerative Colitis

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of ulcerative colitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of ulcerative colitis when ALL of the following criteria are met:

Initial

- Patient is 5 years of age or older; AND
- Patient has moderately to severely active ulcerative colitis; AND
- Patient has failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or rectal bleeding; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Hidradenitis Suppurativa

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of hidradenitis suppurativa to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of hidradenitis suppurativa when ALL of the following criteria are met:

Initial

- Patient has moderate to severe hidradenitis suppurativa; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with ONE other therapy (e.g., intralesional or oral corticosteroids, systemic antibiotics, isotretinoin) for hidradenitis suppurativa unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., Hurley staging, Sartorius score, Physician Global Assessment) or in symptoms such as pain or drainage of lesions, nodules, or cysts; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Uveitis

Based on review of available data, the Company may consider unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of uveitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for the treatment of uveitis when ALL of the following criteria are met:

Initial

- Patient has non-infectious intermediate uveitis, non-infectious posterior uveitis, or non-infectious panuveitis; AND
- Patient is 2 years of age or older; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with ONE other therapy for this condition (e.g., corticosteroids or immunosuppressive drugs) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., best-corrected visual acuity, assessment of chorioretinal and/or retinal vascular lesions) or in symptoms such as pain, redness, light sensitivity, visual acuity, or blurred vision; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) when any of the following criteria for their respective disease listed below (and denoted in the patient selection criteria above) are not met to be **not medically necessary**:**

- For rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, and psoriatic arthritis:
  - Patient has failed treatment to one or more traditional DMARDs, such as methotrexate

- For ankylosing spondylitis:
  - Patient has failed treatment with NSAIDs, such as naproxen
- For Crohn's disease:
  - Patient has failed treatment with conventional therapies such as corticosteroids, 6-mercaptopurine, or azathioprine
- For plaque psoriasis:
  - Patient has greater than 10% of BSA or less than or equal to 10% BSA with plaque psoriasis involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck or genitalia)
  - Patient has failed to respond to an adequate trial of one of the following treatment modalities:
    - Ultraviolet B
    - Psoralen positive Ultraviolet A
    - Systemic therapy (i.e. methotrexate, cyclosporine, acitretin)
- For ulcerative colitis:
  - Patient has failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine
- For hidradenitis suppurativa:
  - Patient has failed treatment with ONE other therapy (e.g., intralesional or oral corticosteroids, systemic antibiotics, isotretinoin)
- For uveitis:
  - Patient has failed treatment with ONE other therapy for this condition (e.g., corticosteroids or immunosuppressive drugs).

Based on the review of available data, the company considers the use of unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) for continued use when the patient has not experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective signs and/or symptoms of the requested indication to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, and adalimumab-ryvk (Simlandi) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) OR for use in any other indication than those listed above to be **investigational.***

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adalimumab (Humira®), adalimumab-atto (Amjevita™), adalimumab-afzb (Abrilada™), adalimumab-adbm (Cyltezo®), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima™), adalimumab-fkjp (Hulio®), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz®), adalimumab-aacf (Idacio®), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry™), adalimumab-aaty (Yuflyma®), unbranded adalimumab-aaty

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Rheumatoid Arthritis

Based on review of available data, the Company may consider adalimumab (Humira®)‡, adalimumab-atto (Amjevita™)‡, adalimumab-afzb (Abrilada™)‡, adalimumab-adbm (Cyltezo®)‡, unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima™)‡, adalimumab-fkjp (Hulio®)‡, unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz®)‡, adalimumab-aacf (Idacio®)‡, unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry™)‡, adalimumab-aaty (Yuflyma®)‡, and unbranded adalimumab-aaty for the treatment of rheumatoid arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of rheumatoid arthritis when ALL of the following criteria are met:

Initial

- Patient has moderately to severely active rheumatoid arthritis; AND
- Patient is 18 years of age or older; AND
- Requested drug is NOT used in combination with other biologic disease-modifying anti-rheumatic drugs (DMARDs), such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

- Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*), tofacitinib (Xeljanz/XR), upadacitinib (Rinvoq®)‡, or subcutaneous tocilizumab (Actemra®)‡ unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a negative tuberculosis (TB) test (e.g., purified protein derivative [PPD], blood test) prior to treatment.

Continuation

- Patient has received an initial authorization for the requested drug; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Note: The recommended dosing of adalimumab in rheumatoid arthritis is 40 mg every other week. Members unresponsive to 40 mg every other week after 12 weeks of therapy AND NOT on methotrexate may be approved for 40 mg once weekly dosing OR 80 mg every other week dosing.

Polyarticular Juvenile Idiopathic Arthritis

Based on review of available data, the Company may consider adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of polyarticular juvenile idiopathic arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry),-adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of polyarticular juvenile idiopathic arthritis when ALL of the following criteria are met:

Initial

- Patient has moderately to severely active polyarticular juvenile idiopathic arthritis; AND
- Patient is 2 years of age or older; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: adalimumab (Simlandi, unbranded adalimumab-adaz adalimumab-ryvk*, adalimumab-adbm*), etanercept (Enbrel), tofacitinib (Xeljanz), or subcutaneous tocilizumab (Actemra) unless there is clinical evidence or patient history that suggests that these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as improved range of motion, reduced joint pain or tenderness, decreased duration of morning stiffness or fatigue, improved function or activities of daily living, reduced corticosteroid dosage, or improvement in inflammatory serum markers; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Psoriatic Arthritis

Based on review of available data, the Company may consider adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of psoriatic arthritis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp,

adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of psoriatic arthritis when ALL of the following criteria are met:

Initial:

- Patient has active psoriatic arthritis; AND
- Patient is 18 years of age or older; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with one or more traditional DMARDs, such as methotrexate, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*), ustekinumab (Stelara®)‡, secukinumab (Cosentyx®)‡, tofacitinib (Xeljanz/XR), guselkumab (Tremfya®)‡, apremilast (Otezla), upadacitinib (Rinvoq), or risankizumab-rzaa (Skyrizi®)‡ unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in clinical signs and symptoms such as decreased joint pain, morning stiffness, or fatigue; improved function or activities of daily living; decreased soft tissue swelling in joints or tendon sheaths; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Ankylosing Spondylitis

Based on review of available data, the Company may consider adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of active ankylosing spondylitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), -adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of active ankylosing spondylitis when ALL of the following criteria are met:

Initial

- Patient has active ankylosing spondylitis; AND
- Patient is 18 years of age or older; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with non-steroidal anti-inflammatory drugs (NSAIDs), such as naproxen, unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*), secukinumab (Cosentyx), tofacitinib (Xeljanz/XR), or upadacitinib (Rinvoq) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., ASDAS, BASDAI, inflammatory serum markers) or in clinical signs and symptoms such as reduced pain, stiffness, or improved daily functioning; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Crohn's Disease

Based on review of available data, the Company may consider adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of Crohn's disease to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), -adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of Crohn's disease when ALL of the following criteria are met:

Initial

- Patient has moderately to severely active Crohn's disease; AND
- Patient is 6 years of age or older; AND
- Patient has failed treatment with conventional therapies such as corticosteroids, 6-mercaptopurine, or azathioprine unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests this product will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or blood in stool; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Plaque Psoriasis

Based on review of available data, the Company may consider adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of plaque psoriasis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry),-adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of plaque psoriasis when ALL of the following criteria are met:

Initial

- Patient has moderate to severe chronic plaque psoriasis; AND
- Patient is 18 years of age or older; AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has greater than 10% of body surface area (BSA) or less than or equal to 10% BSA with plaque psoriasis involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck or genitalia); AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*), etanercept (Enbrel), apremilast (Otezla), ustekinumab (Stelara), secukinumab (Cosentyx), guselkumab (Tremfya), risankizumab (Skyrizi), or deucravacitinib (Sotyktu®)‡ unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Patient has failed to respond to an adequate trial of one of the following treatment modalities unless there is clinical evidence or patient history that suggests the use of these treatments will be ineffective or cause an adverse reaction to the patient:
  - Ultraviolet B; or

- Psoralen positive Ultraviolet A; or
- Systemic therapy (e.g., methotrexate, cyclosporine, acitretin).
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested adalimumab product) as evidenced by improvement in clinical signs and symptoms such as reduced estimated body surface area affected by psoriasis, decreased erythema, induration/thickness, or scaling, and/or improvement in symptoms such as pain, itching, or burning; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met.)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Ulcerative Colitis

Based on review of available data, the Company may consider adalimumab (Humira), adalimumab-atto (Amjevita) adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of ulcerative colitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of ulcerative colitis when ALL of the following criteria are met:

Initial

- Patient has moderately to severely active ulcerative colitis; AND
- Patient is 18 years of age or older; AND
- Patient has failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*

- Patient has failed treatment with adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*) after at least TWO months of therapy unless there is clinical evidence or patient history that suggests this product will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or rectal bleeding; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Hidradenitis Suppurativa

Based on review of available data, the Company may consider adalimumab (Humira), adalimumab-atto (Amjevita) adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of hidradenitis suppurativa to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita) adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of hidradenitis suppurativa when ALL of the following criteria are met:

- Patient has moderate to severe hidradenitis suppurativa; AND
- Patient is 18 years of age or older; AND
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND

- Patient has failed treatment with ONE other therapy (e.g., intralesional or oral corticosteroids, systemic antibiotics, isotretinoin) for hidradenitis suppurativa unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has tried one preferred adalimumab product (unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*, Simlandi) for at least TWO months unless there is clinical evidence or patient history that suggests this product will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., Hurley staging, Sartorius score, Physician Global Assessment) or in symptoms such as pain or drainage of lesions, nodules, or cysts; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

Uveitis

Based on review of available data, the Company may consider adalimumab (Humira), adalimumab-atto (Amjevita) adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of uveitis to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira), adalimumab-atto (Amjevita) adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry),-adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for the treatment of uveitis when ALL of the following criteria are met:

Initial

- Patient has non-infectious intermediate uveitis, non-infectious posterior uveitis, or non-infectious panuveitis; AND
- Patient is 18 years of age or older; AND

- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has failed treatment with ONE other therapy for this condition (e.g., corticosteroids or immunosuppressive drugs) unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has tried one preferred adalimumab product (unbranded adalimumab-adaz, Simlandi, adalimumab-ryvk*, adalimumab-adbm*,) for at least TWO months unless there is clinical evidence or patient history that suggests this product will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met).*
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., best-corrected visual acuity, assessment of chorioretinal and/or retinal vascular lesions) or in symptoms such as pain, redness, light sensitivity, visual acuity, or blurred vision; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty when any of the following criteria for their respective disease listed below (and denoted in the patient selection criteria above) are not met to be **not medically necessary**:**

- For rheumatoid arthritis:
  - Patient has failed treatment with one or more traditional DMARDs, such as methotrexate
  - Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*), tofacitinib (Xeljanz/XR), upadacitinib (Rinvoq), or subcutaneous tocilizumab (Actemra)

- For polyarticular juvenile idiopathic arthritis:
    - Patient has failed treatment with one or more traditional DMARDs, such as methotrexate
    - Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*), etanercept (Enbrel), tofacitinib (Xeljanz), or subcutaneous tocilizumab (Actemra)
- For psoriatic arthritis:
    - Patient has failed treatment with one or more traditional DMARDs, such as methotrexate
    - Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Simlandi, unbranded adalimumab-adaz adalimumab-ryvk*, adalimumab-adbm*), ustekinumab (Stelara), secukinumab (Cosentyx), tofacitinib (Xeljanz/XR), guselkumab (Tremfya), apremilast (Otezla), upadacitinib (Rinvoq), or risankizumab-rzaa (Skyrizi)
- For ankylosing spondylitis:
    - Patient has failed treatment with NSAIDs, such as naproxen
    - Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: etanercept (Enbrel), adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*), secukinumab (Cosentyx), tofacitinib (Xeljanz/XR), or upadacitinib (Rinvoq)
- For Crohn's disease:
    - Patient has failed treatment with conventional therapies such as corticosteroids, 6-mercaptopurine, or azathioprine
    - Patient has failed treatment with adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*) after at least TWO months of therapy
- For plaque psoriasis:
    - Patient has greater than 10% of BSA or less than or equal to 10% BSA with plaque psoriasis involving sensitive areas or areas that would significantly impact daily function (such as palms, soles of feet, head/neck or genitalia)
    - Patient has failed treatment with TWO of the following after at least TWO months of therapy with EACH product: adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*), etanercept (Enbrel), apremilast (Otezla), ustekinumab (Stelara), secukinumab (Cosentyx), guselkumab (Tremfya), risankizumab (Skyrizi), or deucravacitinib (Sotyktu)
    - Patient has failed to respond to an adequate trial of one of the following treatment modalities:
        - Ultraviolet B
        - Psoralen positive Ultraviolet A
        - Systemic therapy (i.e. methotrexate, cyclosporine, acitretin)

- For ulcerative colitis:
  - Patient has failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine
  - Patient has failed treatment with adalimumab (Simlandi, unbranded adalimumab-adaz, adalimumab-ryvk*, adalimumab-adbm*) after at least TWO months of therapy
- For hidradenitis suppurativa:
  - Patient has failed treatment with ONE other therapy (e.g., intralesional or oral corticosteroids, systemic antibiotics, isotretinoin)
  - Patient has tried one preferred adalimumab product (unbranded adalimumab-adaz, Simlandi, adalimumab-ryvk*, adalimumab-adbm*) for at least TWO months
- For uveitis:
  - Patient has failed treatment with ONE other therapy for this condition (e.g., corticosteroids or immunosuppressive drugs).
  - Patient has tried one preferred adalimumab product (unbranded adalimumab-adaz, Simlandi, adalimumab-ryvk*, adalimumab-adbm*) for at least TWO months

Based on the review of available data, the company considers the use of adalimumab (Humira), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty for continued use when the patient has not experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective signs and/or symptoms of the requested indication to be **not medically necessary.****

** These products are manufactured by Quallent Pharmaceuticals.*

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of adalimumab (Humira), adalimumab-atto (Amjevita) adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and unbranded adalimumab-aaty when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) OR for use in any other indication than those listed above to be **investigational.***

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Ulcerative Colitis in Pediatric Patients

Based on review of available data, the Company may consider adalimumab (Humira) for the treatment of ulcerative colitis in pediatric patients to be **eligible for coverage.****

Patient Selection Criteria

Coverage eligibility will be considered for adalimumab (Humira) for the treatment of ulcerative colitis in pediatric patients when ALL of the following criteria are met:

Initial

- Patient has moderately to severely active ulcerative colitis; AND
- Patient is 5-17 years of age or older; AND
- Patient has failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine unless there is clinical evidence or patient history that suggests the use of these products will be ineffective or cause an adverse reaction to the patient; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla); AND
- Patient has a negative TB test (e.g., PPD, blood test) prior to treatment.

Continuation

- Patient has received an initial authorization; AND
- Patient has experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective measures (e.g., fecal or serum inflammatory markers, endoscopic findings, reduced corticosteroid use) or in symptoms such as pain, fatigue, stool frequency, or rectal bleeding; AND
  *(Note: This specific patient selection criterion is an additional Company requirement for coverage eligibility and will be denied as not medically necessary** if not met)*
- Requested drug is NOT used in combination with other biologic DMARDs, such as etanercept (Enbrel) OR other drugs such as tofacitinib (Xeljanz/XR) or apremilast (Otezla).

When Services Are Considered Not Medically Necessary

Based on review of available data, the Company considers the use of adalimumab (Humira) for ulcerative colitis in pediatric patients when the patient has not failed treatment with conventional therapies such as corticosteroids, azathioprine, or 6-mercaptopurine to be **not medically necessary****

Based on the review of available data, the company considers the continued use of adalimumab (Humira) for ulcerative colitis in pediatric patients when the patient has not experienced a beneficial clinical response from baseline (prior to therapy with the requested drug) as evidenced by improvement in objective signs and/or symptoms to be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers the use of adalimumab (Humira) when the patient selection criteria are not met (with the exception of those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Adalimumab is a recombinant human IgG1 monoclonal antibody specific for human tumor necrosis factor (TNF). Adalimumab binds specifically to TNF-alpha and blocks its interaction with the p55 and p75 cell. TNF is a naturally occurring cytokine that is involved in normal inflammatory and immune responses. Adalimumab is available as Humira and several biosimilars, including adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), adalimumab-aqvh (Yusimry), adalimumab-aaty (Yuflyma), and adalimumab-ryvk (Simlandi). Some biosimilars are also produced by private label manufacturing companies, such as Quallent Pharmaceuticals, Cordavis, and Nuvaila. Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product known as a reference product and that there are no clinically meaningful differences between the biosimilar product and the reference product. The biosimilarity of the available biosimilars to Humira has been demonstrated for the condition(s) of use [e.g., indication(s), dosing regimen(s), strength(s), dosage form(s), and route(s) of administration] described in their package inserts. Adalimumab products are available with varying formulations, including high concentration and original concentration products, presentations, including products that are citrate free and/or interchangeable, and pricing strategies, including higher and lower cost options. The original adalimumab product, Humira, currently has indications for the treatment of rheumatoid arthritis, juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis, Crohn's disease, ulcerative colitis, plaque psoriasis, hidradenitis suppurativa, and uveitis. The biosimilars have most of the same indications as Humira, except for three that are currently protected by Orphan Drug Exclusivity patents. The three indications that are not seen in any of the biosimilar package inserts are pediatric uveitis, adolescent hidradenitis suppurativa, and pediatric ulcerative colitis. Dosing information can be found in the products' package inserts.

Rheumatoid Arthritis

Rheumatoid arthritis is a chronic (long-term) disease that causes inflammation of the joints and surrounding tissues. It can also affect other organs. It is considered an autoimmune disease. In an

autoimmune disease, the immune system confuses healthy tissue for foreign substances. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Polyarticular Juvenile Idiopathic Arthritis
Polyarticular juvenile idiopathic arthritis includes the inflammation of joints and presence of arthritis in children. Polyarticular juvenile idiopathic arthritis typically occurs in a symmetrical manner with knees, wrists, and ankles most frequently affected. However, certain subgroups of children do have predominantly asymmetrical involvement. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Psoriatic Arthritis
Psoriatic arthritis is an arthritis that is often associated with psoriasis of the skin. Typically, first line treatments such as traditional DMARDs are used to treat this condition. An example of a traditional DMARD would include methotrexate.

Ankylosing Spondylitis
Ankylosing spondylitis is a chronic inflammatory disease that affects the joints between the vertebrae of the spine, and the joints between the spine and the pelvis. It eventually causes the affected vertebrae to fuse or grow together. Nonsteroidal anti-inflammatory drugs, such as ibuprofen or naproxen, are used to reduce inflammation and pain associated with the condition. Corticosteroid therapy or medications to suppress the immune system may be prescribed to control various symptoms.

Crohn's Disease
Crohn's disease is a chronic autoimmune disease that can affect any part of the gastrointestinal tract but most commonly occurs in the ileum. As a result of the immune attack, the intestinal wall becomes thick, and deep ulcers may form. In addition to the bowel abnormalities, Crohn's disease can also affect other organs in the body. Typically, first line treatments such as corticosteroids, 6-mercaptopurine and azathioprine are used to treat this condition.

Plaque Psoriasis
Psoriasis is a common skin condition that is caused by an increase in production of skin cells. It is characterized by frequent episodes of redness, itching and thick, dry silvery scales on the skin. It is most commonly seen on the trunk, elbows, knees, scalp, skin folds and fingernails. This condition can appear suddenly or gradually and may affect people of any age; it most commonly begins between the ages of 15 and 35. Psoriasis is not contagious. It is an inherited disorder related to an inflammatory response in which the immune system produces too much TNF-alpha. It may be severe in immunosuppressed people or those who have other autoimmune disorders such as rheumatoid arthritis. Typical treatments for severe cases of plaque psoriasis include ultraviolet therapy or systemic therapies such as methotrexate or cyclosporine.

Ulcerative Colitis
Ulcerative colitis is a chronic, episodic, inflammatory disease of the large intestine and rectum characterized by bloody diarrhea. This disease usually begins in the rectal area and may eventually extend through the entire large intestine. Repeated episodes of inflammation lead to thickening of the wall of the intestine and rectum with scar tissue. Death of colon tissue or sepsis may occur with severe disease. The goals of treatment are to control the acute attacks, prevent recurrent attacks and promote healing of the colon. Hospitalization is often required for severe attacks. Typically, first line treatments such as corticosteroids, 6-mercaptopurine and azathioprine are used to treat this condition.

Disease-Modifying Anti-Rheumatic Drugs
Traditional DMARDS are typically used for the treatment of inflammatory conditions. These drugs slow the disease process by modifying the immune system.

- methotrexate
- cyclosporine
- sulfasalazine
- mercaptopurine
- gold compounds

Hidradenitis Suppurativa
Hidradenitis suppurativa is a chronic inflammatory skin condition, also known as acne inversa. Hidradenitis suppurativa is a chronic, suppurative process involving the skin and subcutaneous tissues. The initial presentation of the disease typically includes recurrent, painful, and inflamed nodules. The pathogenesis of hidradenitis suppurativa is somewhat unknown, but it is thought that follicular occlusion, follicular rupture, and an associated immune response appear to be important events in the clinical manifestations of this disease. Hidradenitis suppurativa typically occurs on intertriginous skin. The most common site is usually the axilla. Non-intertriginous skin can be affected as well. Humira is the first agent to be approved by the Food and Drug Administration for the treatment of moderate to severe hidradenitis suppurativa. Other agents typically used for the treatment of hidradenitis suppurativa include systemic antibiotics, intralesional or oral corticosteroids, or isotretinoin products.

Uveitis
Uveitis is characterized by inflammation of the uvea, which is the middle portion of the eye. Most cases are idiopathic, but identifiable causes include various infections and systemic diseases, often autoimmune. Symptoms include decreased vision, pain, redness, photophobia, and floaters. Treatment of the non-infectious type of uveitis typically includes steroids, immunosuppressants, etc. The different types of uveitis are named based on their location in the eye. Intermediate uveitis refers to inflammation localized to the vitreous humor and peripheral retina. Posterior uveitis refers to inflammation of the choroid, or the back part of the uvea. Anterior uveitis affects the front part of the eye. Panuveitis is defined as simultaneous inflammation of the anterior chamber (AC), vitreous humor, and the retina or choroid.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

Humira (adalimumab) is the first adalimumab product to be approved for the treatment of rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, polyarticular juvenile idiopathic arthritis, ulcerative colitis (including pediatric ulcerative colitis), plaque psoriasis, Crohn's disease (including pediatric Crohn's disease), hidradenitis suppurativa, and non-infectious uveitis. Adalimumab biosimilars, Amjevita, Cyltezo, Hadlima, Hulio, Idacio, Yusimry, Simlandi and Yuflyma, are all indicated for rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, juvenile idiopathic arthritis, ulcerative colitis in adults, plaque psoriasis, Crohn's disease, hidradenitis suppurativa in adults, and uveitis in adult patients. Hyrimoz is indicated for all of the previously mentioned indications except for uveitis.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Rheumatoid Arthritis

The efficacy and safety of Adalimumab were assessed in five randomized, double-blind studies in patients ≥ 18 years of age with active rheumatoid arthritis diagnosed according to American College of Rheumatology (ACR) criteria. Adalimumab was administered in combination with methotrexate (12.5 to 25 mg, Studies RA-I, RA-III and RA-V) or as monotherapy (Studies RA-II and RA-V) or with other DMARDs (Study RA-IV). The results of Study RA-I were similar to Study RA-III; patients receiving Adalimumab 40 mg every other week in Study RA-I also achieved ACR 20, 50 and 70 response rates of 65%, 52% and 24%, respectively, compared to placebo responses of 13%, 7% and 3% respectively, at 6 months ($p < 0.01$). In Study RA-IV, 53% of patients treated with Adalimumab 40 mg every other week plus standard of care had an ACR 20 response at week 24 compared to 35% on placebo plus standard of care ($p < 0.001$). In Study RA-V with methotrexate naïve patients with recent onset rheumatoid arthritis, the combination treatment with Adalimumab plus methotrexate led to greater percentages of patients achieving ACR responses than either methotrexate monotherapy or Adalimumab monotherapy at week 52 and responses were sustained at week 104. Adalimumab/methotrexate treated patients demonstrated less radiographic progression than patients receiving methotrexate alone at 52 weeks.

Polyarticular Juvenile Idiopathic Arthritis

The safety and efficacy of Adalimumab were assessed in a multicenter, randomized, withdrawal, double-blind, parallel-group study in 171 children (4 to 17 years of age) with polyarticular juvenile idiopathic arthritis. The study included four phases: an open-label lead in phase (OL-LI; 16 weeks), a double-blind randomized withdrawal phase (DB; 32 weeks), an open-label extension phase (OLE-BSA; up to 136 weeks), and an open-label fixed dose phase (OLE-FD; 16 weeks). In the first three

phases of the study, Adalimumab was administered based on BSA at a dose of 24 mg/m2 up to a maximum total body dose of 40 mg every other week. In the OLE-FD phase, the patients were treated with 20 mg of Adalimumab every other week if their weight was less than 30 kg and with 40 mg of Adalimumab every other week if their weight was 30 kg or greater. Patients remained on stable doses of NSAIDs and or prednisone (≤ 0.2 mg/kg/day or 10 mg/day maximum). At the end of the 16-week OL-LI phase, 94% of the patients in the methotrexate stratum and 74% of the patients in the non-methotrexate stratum were pediatric ACR 30 responders. In the double-blind phase significantly fewer patients who received Adalimumab experienced disease flare compared to placebo, both without methotrexate (43% vs. 71%) and with methotrexate (37% vs. 65%). More patients treated with Adalimumab continued to show pediatric ACR 30/50/70 responses at week 48 compared to patients treated with placebo. Pediatric ACR responses were maintained for up to two years in the OLE phase in patients who received Adalimumab throughout the study.

Adalimumab was assessed in an open-label, multicenter study in 32 patients who were 2 to < 4 years of age or 4 years of age and older weighing < 15 kg with moderately to severely active polyarticular juvenile idiopathic arthritis. Most patients (97%) received at least 24 weeks of Adalimumab treatment dosed 24 mg/m2 up to a maximum of 20 mg every other week as a single injection up to a maximum of 120 weeks duration. During the study, most patients used concomitant methotrexate, with fewer reporting use of corticosteroids or NSAIDs. The primary objective of the study was evaluation of safety.

Psoriatic Arthritis
The safety and efficacy of Adalimumab was assessed in two randomized, double-blind, placebo controlled studies in 413 patients with psoriatic arthritis. Compared to placebo, treatment with Adalimumab resulted in improvements in the measures of disease activity. Similar responses were seen in patients with each of the subtypes of psoriatic arthritis, although few patients were enrolled with the arthritis mutilans and ankylosing spondylitis-like subtypes. Patients with psoriatic involvement of at least three percent BSA were evaluated for Psoriatic Area and Severity Index (PASI) responses. At 24 weeks, the proportions of patients achieving a 75% or 90% improvement in the PASI were 59% and 42% respectively, in the Adalimumab group (N = 69), compared to 1% and 0% respectively, in the placebo group. Adalimumab-treated patients demonstrated greater inhibition of radiographic progression compared to placebo-treated patients and this effect was maintained at 48 weeks. In Study PsA-I, physical function and disability were assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI) and the SF-36 Health Survey. Patients treated with 40 mg of Adalimumab every other week showed greater improvement from baseline in the HAQ-DI score (mean decreases of 47% and 49% at weeks 12 and 24 respectively) in comparison to placebo (mean decreases of 1% and 3% at weeks 12 and 24 respectively). At weeks 12 and 24, patients treated with Adalimumab showed greater improvement from baseline in the SF-36 Physical Component Summary score compared to patients treated with placebo, and no worsening in the SF-36 Mental Component Summary score.

Ankylosing Spondylitis
The safety and efficacy of Adalimumab 40 mg every other week was assessed in 315 adult patients in a randomized, 24 week double-blind, placebo-controlled study in patients with active ankylosing spondylitis who had an inadequate response to glucocorticoids, NSAIDs, analgesics, methotrexate, or sulfasalazine. The blinded period was followed by an open-label period during which patients received Adalimumab 40 mg every other week for up to an additional 28 weeks. Improvement in measures of disease activity was first observed at week 2 and maintained through 24 weeks. At 12 weeks, the Ankylosing Spondylitis Assessment (ASAS) 20/50/70 responses were achieved by 58%, 38%, and 23%, respectively, of patients receiving Adalimumab, compared to 21%, 10%, and 5% respectively, of patients receiving placebo ($p < 0.001$). Similar responses were seen at week 24 and were sustained in patients receiving open-label Adalimumab for up to 52 weeks.

Crohn's Disease
The safety and efficacy of multiple doses of Adalimumab were assessed in adult patients with moderately to severely active Crohn's disease in randomized, double-blind, placebo-controlled studies. Induction of clinical remission (defined as Crohn's Disease Activity Index [CDAI] < 150) was evaluated in two studies. In Study CD-I, 299 TNF-blocker naïve patients were randomized to one of four treatment groups: the placebo group received placebo at weeks 0 and 2, the 160/80 group received 160 mg Adalimumab at week 0 and 80 mg at week 2, the 80/40 group received 80 mg at week 0 and 40 mg at week 2, and the 40/20 group received 40 mg at week 0 and 20 mg at week 2. Clinical results were assessed at week 4. In the second induction study, Study CD-II, 325 patients who had lost response to, or were intolerant to, previous infliximab therapy were randomized to receive either 160 mg of Adalimumab at week 0 and 80 mg at week 2, or placebo at weeks 0 and 2. Clinical results were assessed at week 4. A greater percentage of the patients treated with 160/80 mg Adalimumab achieved induction of clinical remission versus placebo at week 4 regardless of whether the patients were TNF blocker naïve (CD-I), or had lost response to or were intolerant to infliximab.

Maintenance of clinical remission was evaluated in Study CD-III. In this study, 854 patients with active disease received open-label Adalimumab 80 mg at week 0 and 40 mg at week 2. Patients were then randomized at week 4 to 40 mg Adalimumab every other week, 40 mg Adalimumab every week, or placebo. The total study duration was 56 weeks. Patients in clinical response (decrease in CDAI ≥ 70) at week 4 were stratified and analyzed separately from those not in clinical response at week 4. In Study CD-III at week 4, 58% (499/854) of patients were in clinical response and were assessed in the primary analysis. At weeks 26 and 56, greater proportions of patients who were in clinical response at week 4 achieved clinical remission in the Adalimumab 40 mg every other week maintenance group compared to patients in the placebo maintenance group. The group that received Adalimumab therapy every week did not demonstrate significantly higher remission rates compared to the group that received Adalimumab every other week.

Ulcerative Colitis
The safety and efficacy of Adalimumab were assessed in adult patients with moderately to severely active ulcerative colitis despite concurrent or prior treatment with immunosuppressants such as corticosteroids, azathioprine, or 6-mercaptopurine in two randomized, double-blind, placebo-controlled clinical studies (Studies UC-I and UC-II). Induction of clinical remission at week 8 was evaluated in both studies. Clinical remission at week 52 and sustained clinical remission (defined as clinical remission at both weeks 8 and 52) were evaluated in Study UC-II. In both Studies UC-I and UC-II, a greater percentage of the patients treated with 160/80 mg of Adalimumab compared to patients treated with placebo achieved induction of clinical remission. In Study UC-II, a greater percentage of the patients treated with 160/80 mg of Adalimumab compared to patients treated with placebo achieved sustained clinical remission (clinical remission at both weeks 8 and 52).

Plaque Psoriasis
The safety and efficacy of Adalimumab were assessed in randomized, double-blind, placebo controlled studies (Ps-I and Ps-II) in 1696 adult patients with moderate to severe chronic plaque psoriasis who were candidates for systemic therapy or phototherapy. The studies evaluated the proportion of patients who achieved “clear” or “minimal” disease on the 6-point Physician's Global Assessment (PGA) scale and the proportion of patients who achieved a reduction in PASI score of at least 75% (PASI 75) from baseline at week 16. At week 16 In PS-I, 4% of patients in the placebo group vs. 62% in the Adalimumab 40mg every other week group had a PGA of “clear or minimal”. Seven percent of patients in the placebo group achieved a PASI 75 vs. 71% in the Adalimumab group. At week 16 in Ps-II 10% of patients in the placebo group vs. 71% in the Adalimumab 40mg every other week group had a PGA of “clear or minimal”. Nineteen percent of patients in the placebo group achieved a PASI 75 vs. 78% in the Adalimumab group.

Pediatric Crohn’s Disease
The safety and efficacy of Adalimumab for pediatric patients with Crohn’s disease was assessed in a randomized, double-blind, 52-week clinical study in 192 pediatric patients (6 to 17 years of age). Enrolled patients had over the previous two year period an inadequate response to corticosteroids or an immunomodulator (i.e., azathioprine, 6-mercaptopurine, or methotrexate). Patients who had previously received a TNF blocker were allowed to enroll if they had previously had loss of response or intolerance to that TNF blocker. Patients received open-label induction therapy at a dose based on their body weight (≥ 40 kg and < 40 kg). Patients weighing ≥ 40 kg received 160 mg (at week 0) and 80 mg (at week 2). Patients weighing < 40 kg received 80 mg (at week 0) and 40 mg (at week 2). At week 4, patients within each body weight category (≥ 40 kg and < 40 kg) were randomized 1:1 to one of two maintenance dose regimens (high dose and low dose). The high dose was 40 mg every other week for patients weighing ≥ 40 kg and 20 mg every other week for patients weighing < 40 kg. The low dose was 20 mg every other week for patients weighing ≥ 40 kg and 10 mg every other week for patients weighing < 40 kg. Concomitant stable dosages of corticosteroids (prednisone dosage ≤ 40 mg/day or equivalent) and immunomodulators (azathioprine, 6-mercaptopurine, or methotrexate) were permitted throughout the study. At week 4, 28% (52/188) of patients were in clinical remission [defined as Pediatric Crohn’s Disease Activity Index (PCDAI ≤ 10)]. The proportions of patients in clinical remission (defined as PCDAI ≤ 10) and clinical response (defined

as reduction in PCDAI of at least 15 points from baseline) were assessed at weeks 26 and 52. At both weeks 26 and 52, the proportion of patients in clinical remission and clinical response was numerically higher in the high dose group compared to the low dose group. The recommended maintenance regimen is 20 mg every other week for patients weighing < 40 kg and 40 mg every other week for patients weighing ≥ 40 kg. Every week dosing is not the recommended maintenance dosing regimen.

Hidradenitis Suppurativa
The safety and efficacy of Adalimumab for patients with hidradenitis suppurativa was assessed in two randomized, double-blind, placebo controlled studies in 633 adult subjects. In both studies, subjects received placebo or Adalimumab at an initial dose of 160 mg at week 0, 80 mg at week 2, and 40 mg every week starting at week 4 through week 11. Both studies evaluated the HS 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. In both studies, a higher proportion of Adalimumab than placebo treated patients achieved HiSCR. In Study 1, 42% of subjects receiving Adalimumab achieved the HiSCR versus 26% in the placebo group. In Study 2, 59% of subjects receiving Adalimumab achieved the HiSCR versus 28% in the placebo group.

Uveitis
The safety and efficacy of Adalimumab were assessed in adult patients with non-infectious intermediate, posterior, and panuveitis, excluding patients with isolated anterior uveitis, in two randomized, double-masked, placebo-controlled studies (UV I and II). Patients received placebo or Adalimumab at an initial dose of 80 mg followed by 40 mg every other week starting one week after the initial dose. The primary efficacy endpoint in both studies was ´time to treatment failure´. Treatment failure was a multi-component outcome defined as the development of new inflammatory chorioretinal and/or inflammatory retinal vascular lesions, an increase in AC cell grade or vitreous haze (VH) grade or a decrease in best corrected visual acuity (BCVA). Study UV I evaluated 217 patients with active uveitis while being treated with corticosteroids (oral prednisone at a dose of 10 to 60 mg/day). All patients received a standardized dose of prednisone 60 mg/day at study entry followed by a mandatory taper schedule, with complete corticosteroid discontinuation by week 15. Study UV II evaluated 226 patients with inactive uveitis while being treated with corticosteroids (oral prednisone 10 to 35 mg/day) at baseline to control their disease. Patients subsequently underwent a mandatory taper schedule, with complete corticosteroid discontinuation by week 19. Results from both studies demonstrated statistically significant reduction of the risk of treatment failure in patients treated with Adalimumab versus patients receiving placebo. In both studies, all components of the primary endpoint contributed cumulatively to the overall difference between Adalimumab and placebo groups.

The safety and efficacy of Adalimumab were assessed in a randomized, double-masked, placebo-controlled study of 90 pediatric patients from 2 to < 18 years of age with active juvenile idiopathic arthritis-associated non-infectious uveitis (PUV-I). Patients received either placebo or 20 mg Adalimumab (if < 30 kg) or 40 mg Adalimumab (if ≥ 30 kg) every other week in combination with

a dose of methotrexate. Concomitant dosages of corticosteroids were permitted at study entry followed by a mandatory reduction in topical corticosteroids within 3 months. The primary endpoint was time to treatment failure. The criteria determining treatment failure were worsening or sustained non-improvement in ocular inflammation or worsening of ocular co-morbidities. Adalimumab significantly decreased the risk of treatment failure by 75% relative to placebo (HR = 0.25 [95% CI: 0.12, 0.49]).

Pediatric Ulcerative Colitis
The safety and efficacy of Adalimumab were assessed in a multicenter, randomized, double-blind trial in 93 pediatric patients 5 years to 17 years of age with moderately to severely active ulcerative colitis who had an inadequate response or intolerance to therapy with corticosteroids and/or an immunomodulator (i.e., azathioprine, 6mercaptopurine, or methotrexate). Fifteen out of 93 patients (16%) in the study had prior experience with a TNF blocker. Patients who received corticosteroids at enrollment were allowed to taper their corticosteroid therapy after week 4.

Seventy-seven patients were initially randomized 3:2 to receive double-blind treatment with one of two dosages of Adalimumab. Patients in both dosage groups received 2.4 mg/kg (maximum of 160 mg) at week 0, 1.2 mg/kg (maximum of 80 mg) at week 2, and 0.6 mg/kg (maximum of 40 mg) at weeks 4 and 6. The higher dosage group also received an additional dosage of 2.4 mg/kg (maximum of 160 mg) at week 1. Following an amendment to the study design, 16 additional patients were enrolled and received open-label treatment with Adalimumab at the higher dosage.

At week 8, 62 patients who demonstrated clinical response per Partial Mayo Score (PMS; a subset of the Mayo score with no endoscopic component and defined as a decrease in PMS ≥ 2 points and ≥ 30% from baseline) were randomized equally to receive double-blind treatment with Adalimumab 0.6 mg/kg(maximum of 40 mg) every other week (lower dosage group), or 0.6 mg/kg (maximum of 40 mg) every week (higher dosage group). Prior to an amendment to the study design, 12 additional patients who demonstrated clinical response per PMS were randomized to receive placebo.

There are no anticipated clinically relevant differences in efficacy between the studied higher dosage administered during this trial and the recommended dosage of Adalimumab.

Patients who met criteria for disease flare at or after week 12 were randomized to receive a reinduction dose of 2.4 mg/kg (maximum of 160 mg) or a dose of 0.6 mg/kg (maximum of 40 mg) and then continued the dose to which they were randomized at week 8.

The co-primary endpoints of the study were clinical remission per PMS (defined as PMS ≤ 2 and no individual subscore > 1) at week 8, and clinical remission per the Mayo Score (defined as Mayo Score ≤ 2 and no individual subscore > 1) at week 52 in patients who achieved clinical response per PMS at week 8. Secondary endpoints included Mayo Score response (defined as a decrease in Mayo Score of ≥ 3 points and ≥ 30% from baseline) at week 52 in week 8 PMS responders, endoscopic improvement (defined as a Mayo endoscopy subscore ≤ 1) at week 52 in week 8 PMS responders, and Mayo Score remission at week 52 in week 8 PMS remitters.

At week 8, PMS remission was achieved by 60% [28/47; 95% confidence interval (CI): (44%, 74%)] of patients in the higher dosage group (not including the 16 patients receiving open-label higher dosage) and 43% [13/30; 95% CI: (25%, 63%)] of patients in the lower dosage group. Results from the higher dosage group are representative of the results expected with the recommended dosage.

At week 52, endpoints were assessed in the population of patients who received double-blind placebo, Adalimumab 0.6 mg/kg (maximum of 40 mg) every other week, or Adalimumab 0.6 mg/kg (maximum of 40 mg) every week between week 8 and week 52. At 52 weeks, clinical remission in week 8 PMS responders was 33% in the placebo group [4/12; 95% CI: (10%, 65%)], 29% in the Adalimumab 0.6 mg/kg (max of 40 mg) every week group [9/31; 95% CI: (14%, 48%)], and 45% in the Adalimumab 0.6 mg/kg (max of 40 mg) every week group [14/31; 95% CI: (27%, 64%)].

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5. Cyltezo [package insert]. Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, Connecticut. Updated June 2023.
6. Adalimumab-adbm [package insert]. Boehringer Ingelheim Pharmaceuticals, Inc. Ridgefield, Connecticut. Updated September 2023.
7. Abrilada [package insert]. Pfizer, Inc. New York, New York. Updated August 2023.
8. Hulio [package insert]. Biocon Biologics, inc. Cambridge, Massachusetts. Updated August 2023.
9. Hadlima [package insert]. Organon and Co. Jersey City, New Jersey. Updated July 2023.
10. Idacio [package insert]. Fresenius Kabi USA, LLC. Lake Zurich, Illinois. Updated October 2023.
11. Yusimry [package insert]. Coherus BioSciences, Inc. Redwood City, California. Updated September 2023.
12. Yuflyma [package insert]. Celltrion, Inc. Jersey City, New Jersey. Updated December 2023.
13. Hyrimoz [package insert]. Sandoz Inc. Princeton, New Jersey. Updated April 2023.
14. Simlandi [package insert]. Alvotech USA Inc. Lessburg Virginia. Updated February 2024.

Policy History

Original Effective Date: 03/19/2008
Current Effective Date: 01/01/2026

03/12/2008	Medical Director review
03/19/2008	Medical Policy Committee approval
03/04/2009	Medical Director review
03/18/2009	Medical Policy Committee approval. Added FDA Black Box Warning to section. No change to coverage eligibility. FDA
07/01/2010	Medical Policy Committee approval

07/21/2010	Medical Policy Implementation Committee approval. Added a Note stating the recommended dosing from the Humira package insert for the treatment of rheumatoid arthritis, which is 40mg every other week. The Note also states that those members unresponsive to this dosing after 12 weeks of therapy AND NOT on Methotrexate may be approved for 40mg once weekly dosing. Changed the verbiage of the Note after each set of Patient Selection Criteria to read that "all members must have a negative cancer history prior to approval", instead of a "negative cancer screening".
07/07/2011	Medical Policy Committee review
07/20/2011	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/28/2012	Medical Policy Committee review
07/27/2012	Medical Policy Implementation Committee approval. Deleted SangCya (an international brand name) and replaced it with cyclosporine (the generic name). Added a Note to the criteria for rheumatoid arthritis, juvenile rheumatoid arthritis/juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis and plaque psoriasis stating that patients must have failed conventional therapies specific to the condition such as NSAIDS, DMARDS, phototherapy, psoralens and hydroxyurea before using adalimumab (Humira). The reason for denial will be not medically necessary if this criterion is not met. The not medically necessary denial statement is also incorporated into the Investigational and Not Medically Necessary coverage sections. Deleted the investigational statement regarding non-FDA approved indications, since it is duplicative given the additions to the coverage section.
11/01/2012	Medical Policy Committee review
11/28/2012	Medical Policy Implementation Committee approval. Added a new indication for ulcerative colitis to be eligible for coverage with criteria.
05/02/2013	Medical Policy Committee review
05/22/2013	Medical Policy Implementation Committee approval. Removed the criteria under Ulcerative Colitis that the patient is unresponsive or intolerant to TNF blockers. Opened age to 4 and older on polyarticular juvenile idiopathic arthritis. Changed language for DMARD usage to match other similar policies. Changed language on therapy for plaque psoriasis to match other similar policies. Updated the investigational and not medically necessary sections. Removed the requirement for a negative cancer history.
05/01/2014	Medical Policy Committee review
05/21/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
11/06/2014	Medical Policy Committee review
11/21/2014	Medical Policy Implementation Committee approval. Added a new indication for pediatric Crohn's following the package insert. Changed age to 2 years of age for polyarticular juvenile idiopathic arthritis per change of indication in package insert.

08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
12/03/2015	Medical Policy Committee review
12/16/2015	Medical Policy Implementation Committee approval. Added new indication, criteria, background, and rationale for hidradenitis suppurativa.
09/08/2016	Medical Policy Committee review
09/21/2016	Medical Policy Implementation Committee approval. Added indication of uveitis to this policy.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
09/07/2017	Medical Policy Committee review
09/20/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/07/2017	Medical Policy Committee review
12/20/2017	Medical Policy Implementation Committee approval. Clarified that this drug should not be used in combination with other biologics or other drugs like Otezla or Xeljanz/XR.
12/06/2018	Medical Policy Committee review
12/19/2018	Medical Policy Implementation Committee approval. Changed age for uveitis to 2 years of age or older to coincide with the package insert update. Updated rationale.
12/05/2019	Medical Policy Committee review
12/11/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/14/2020	Coding update
12/03/2020	Medical Policy Committee review
12/09/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/01/2021	Medical Policy Committee review
04/14/2021	Medical Policy Implementation Committee approval. Updated the age for ulcerative colitis to 5 years (previously 18 years). Consolidated the pediatric and adult Crohn's disease sections. Updated relevant background and rationale/source sections. Trial and failure of traditional medication denials for Crohn's disease and ulcerative colitis have been changed from investigational to not medically necessary due to a package insert update.
10/01/2021	Coding update
04/07/2022	Medical Policy Committee review
04/13/2022	Medical Policy Implementation Committee approval. Updated certain DMARDs language to specify the term "traditional".
04/06/2023	Medical Policy Committee review
04/12/2023	Medical Policy Implementation Committee approval. No change to coverage.
05/02/2024	Medical Policy Committee review
05/08/2024	Medical Policy Implementation Committee approval. Changed title of policy from "adalimumab (Humira®)" to "adalimumab Products". Added the following biosimilar products to policy: unbranded adalimumab-adaz, and adalimumab-ryvk

	(Simlandi), adalimumab-atto (Amjevita), adalimumab-afzb (Abrilada), adalimumab-adbm (Cyltezo), unbranded adalimumab-adbm, adalimumab-bwwd (Hadlima), adalimumab-fkjp (Hulio), unbranded adalimumab-fkjp, adalimumab-adaz (Hyrimoz), adalimumab-aacf (Idacio), unbranded adalimumab-aacf, adalimumab-aqvh (Yusimry), and adalimumab-aaty (Yuflyma) with criteria. Added section to delineate the preferred adalimumab products criteria from the non-preferred products criteria. Changed "Humira" to "Adalimumab" in rationale section.
05/01/2025	Medical Policy Committee review
05/13/2025	Medical Policy Implementation Committee approval. Added unbranded adalimumab-aaty to policy with criteria. Added Sotyktu to the list of prerequisites to be tried prior to therapy with any of the non-preferred adalimumab products for plaque psoriasis.
10/02/2025	Medical Policy Committee review
10/08/2025	Medical Policy Implementation Committee approval. Updated coverage eligibility for Humira to require trial and failure of preferred alternatives. Added products, adalimumab-adbm and adalimumab-ryvk, manufactured by Quallent Pharmaceuticals, to the policy with criteria. Added continuation criteria to each indication for all products. Added "When Services are Eligible for Coverage, " "When Services are Considered Not Medically Necessary," and "When Services are Considered Investigational" sections for Humira for the use of ulcerative colitis in pediatric patients.

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.