Infliximab-abda

DESCRIPTION

Infliximab-abda is a chimeric IgG1κ monoclonal antibody specific for human tumor necrosis factor-alpha (TNFα). It is the second biosimilar agent approved by the FDA for infliximab. It has the same biological activities attributed to infliximab, which include induction of proinflammatory cytokines such as IL-1 and IL-6, enhancement of leukocyte migration by increasing endothelial layer permeability and expression of adhesion molecules by endothelial cells and leukocytes, activation of neutrophil and eosinophil functional activity, induction of acute phase reactants and other liver proteins, as well as tissue degrading enzymes produced by synoviocytes and/or chondrocytes.

POLICY

- Infliximab-abda for the treatment of the following is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**
  - Ankylosing spondylitis
  - Crohn's disease
  - Immune Checkpoint Inhibitor-Related Toxicity (Management of)
  - Plaque psoriasis
  - Psoriatic arthritis
  - Rheumatoid arthritis
  - Takayasu's arteritis (TAK)
  - Ulcerative colitis
  - Uveitis associated with Behçet's Syndrome
- Infliximab-abda for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

The proposal is to add text/statements in red and to delete text/statements with strikethrough:

INITIAL APPROVAL

- Infliximab-abda is considered medically appropriate if **ALL** of the following criteria are met:
  - Individual should be evaluated and screened/tested for presence of **ALL** of the following prior to beginning treatment
    - Serious active infection, including clinically important localized infections
    - Tuberculosis, latent infection
    - Hepatitis B virus (HBV) infection
  - Documentation of understanding of necessity of absence of **ALL** of the following:
    - Live vaccine product(s) during agent administration
    - Concurrent treatment with another TNF inhibitor, biologic response modifier or other non-biologic agent (i.e., apremilast, tofacitinib, baricitinib)
    - Physician has assessed baseline disease severity utilizing an objective measure/tool
  - Diagnosis of **ANY ONE** of the following:
    - Ankylosing spondylitis if **ALL** of the following:
      - Individual is 18 years of age or older
      - Disease is active
      - Adequate trial and failure of minimum of two (2) non-steroidal antiinflammatory agents (NSAIDS), unless use is contraindicated
    - Crohn's Disease if **ANY ONE** of the following:
      - Diagnosed with moderately to severely active Crohn's Disease if **ALL** of the following:
        - Individual is 6 years of age or older

- Documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial of corticosteroids or immunomodulators (e.g., azathioprine, 6-mercaptopurine, or methotrexate)
- Diagnosed with moderately to severely active Fistulizing Crohn's disease if **ALL** of the following:
  - Individual is 18 years of age or older
  - Documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial of corticosteroids or immunomodulators (e.g., azathioprine, 6-mercaptopurine, or methotrexate)

- Immune Checkpoint Inhibitor-Related Toxicity (Management of) and **ALL** of the following:
  - Individual has been receiving therapy with an immune checkpoint inhibitor (e.g. nivolumab, pembrolizumab, atezolizumab, avelumab, durvalumab, cemiplimab, ipilimumab, etc.)
  - Individual has **ANY ONE** of the following toxicities related to their immunotherapy:
    - Moderate (grade 2) to severe (grade 3-4) diarrhea or colitis
    - Severe pneumonitis (grade 3-4) refractory to methylprednisolone after 48 hours of therapy
    - Severe (grade 3) or life-threatening (grade 4) acute renal failure or elevated serum creatinine that is refractory after 1 week of therapy with corticosteroid therapy
    - Uveitis (grade 3-4) that is refractory to high-dose systemic corticosteroids
    - ~~o~~ Life-threatening (grade 4) myocarditis, pericarditis, arrhythmias or impaired ventricular function if no improvement within 24 hours of starting pulse-dose methylprednisolone
    - ~~o~~ Severe Inflammatory arthritis as additional disease-modifying therapy if refractory to high-dose corticosteroids after 14 days of treatment ~~refractory to corticosteroids or anti-inflammatory agents~~
- Plaque psoriasis if **ALL** of the following:
  - Individual is 18 years of age or older
  - Disease is documented moderate to severe for at least 6 months with at least one of the following:
    - Involvement of at least 10% of body surface area (BSA); OR
    - Psoriasis Area and Severity Index (PASI) score of 10 or greater; OR
    - Incapacitation due to plaque location (i.e. head and neck, palms, soles or genitalia)
  - Individual did not respond adequately (or is not a candidate) to a 3 month minimum trial of topical agents (i.e., anthralin, coal tar preparations, corticosteroids, emollients, immunosuppressives, keratolytics, retinoic acid derivatives, and/or vitamin D analogues)
  - Individual did not respond adequately (or is not a candidate) to a 3 month minimum trial of at least one systemic agent (i.e., immunosuppressives, retinoic acid derivatives, and/or methotrexate)
  - Individual did not respond adequately (or is not a candidate) to a 3 month minimum trial of phototherapy (i.e., psoralens with UVA light (PUVA) or UVB with coal tar or dithranol)
- Psoriatic arthritis if **ALL** of the following:
  - Individual is 18 years of age or older
  - Disease is documented moderately to severely active
  - Individual with **ANY ONE** of the following:
    - Predominantly axial disease OR active enthesitis and/or dactylitis, an adequate trial and failure of at least TWO (2) non-steroidal anti-inflammatory agents (NSAIDs), unless use is contraindicated
    - Peripheral arthritis, a trial and failure of at least a 3 month trial of ONE oral DMARD such as methotrexate, azathioprine, sulfasalazine, or hydroxychloroquine
- Rheumatoid arthritis if **ALL** of the following:
  - Individual is 18 years of age or older
  - Disease is moderately to severely active
  - Minimum of 3 month trial and failed previous therapy with ONE oral DMARD such as methotrexate, azathioprine, auranofin, hydroxychloroquine, penicillamine, sulfasalazine, or leflunomide
  - Previous failure with preferred self-injectable TNF antagonist
  - Used combined with methotrexate if tolerated unless contraindicated

- Takayasu's arteritis uncontrolled with glucocorticoids
- Ulcerative colitis if **ALL** of the following:
  - Individual is 18 years of age or older
  - Disease is moderately to severely active
  - Documented failure, contraindication, or ineffective response at maximum tolerated doses to a minimum (3) month trial of corticosteroids or immunomodulators (e.g., azathioprine, 6-mercaptopurine, or methotrexate)
- Uveitis associated with Behçet's Syndrome if **ALL** of the following:
  - Disease is refractory to immunosuppressive therapy (e.g., corticosteroids, etc.)
  - Inadequate response to a self-administered biologic therapy (e.g., adalimumab)

RENEWAL CRITERIA

- Infliximab-abda is considered **medically appropriate** for renewal therapy if **ALL** of the following criteria are met:
  - Individual continues to meet ALL the initial approval criteria
  - Absence of unacceptable toxicity from the agent, e.g., severe hypersensitivity reactions, malignancy, significant hematologic abnormalities, serious infections, cardiovascular/cerebrovascular reactions, ~~accidents~~, cardiotoxicity/heart failure, neurotoxicity, hepatotoxicity, lupus-like syndrome, demyelinating disease, etc.
  - Continued monitoring for tuberculosis and other serious infections
  - Disease response as indicated by **ANY ONE** of the following:
    - Ankylosing spondylitis with improvement in signs and symptoms compared to baseline such as total back pain, physical function, and/or morning stiffness, and/or an improvement on a disease activity scoring tool (e.g. ≥ 1.1 improvements on the Ankylosing Spondylitis Disease Activity Score [ASDAS] or an improvement of ≥ 2 on the Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]).
    - Crohn's disease with improvement in signs and symptoms compared to baseline such as endoscopic activity, number of liquid stools, presence and severity of abdominal pain, presence of abdominal mass, body weight compared to IBW, hematocrit, presence of extraintestinal complications, tapering or discontinuation of corticosteroid therapy, use of anti-diarrheal drugs, and/or an improvement on a disease activity scoring tool (e.g. an improvement on the Crohn's Disease Activity Index [CDAI] score or the Harvey-Bradshaw Index score.)
    - Fistulizing Crohn's disease with improvement in signs and symptoms compared to baseline such as a reduction in number of enterocutaneous fistulas draining upon gentle compression, and/or an improvement on a disease activity scoring tool (e.g. an improvement on the Crohn's Disease Activity Index [CDAI] score or the Harvey-Bradshaw Index score).
    - Management of Immune Checkpoint Inhibitor-Related Toxicity - May not be renewed.
    - Plaque psoriasis with improvement in signs and symptoms compared to baseline such as redness, thickness, scaliness, and/or the amount of surface area involvement (a total BSA involvement ≤1%), and/or an improvement on a disease activity scoring tool [e.g. a 75% reduction in the PASI score from when treatment started (PASI 75) or a 50% reduction in the PASI score (PASI 50) and a four-point reduction in the DLQI from when treatment started.
    - Psoriatic arthritis with improvement in signs and symptoms compared to baseline such as the number of tender and swollen joint counts and/or an improvement on a disease activity scoring tool (e.g. defined as an improvement in at least 2 of the 4 Psoriatic Arthritis Response Criteria [PsARC], 1 of which must be joint tenderness or swelling score, with no worsening in any of the 4 criteria.)
    - Rheumatoid arthritis with improvement in signs and symptoms compared to baseline such as the number of tender and swollen joint counts, reduction of C-reactive protein, improvement of patient global assessment, and/or an improvement on a disease activity scoring tool (e.g. an improvement on a composite scoring index such as Disease Activity Score-28 [DAS28] of 1.2 points or more or a ≥20% improvement on the American College of Rheumatology-20 (ACR20) criteria).

- Takayasu's arteritis with improvement in signs and symptoms compared to baseline such as control of the inflammatory phase.
- Ulcerative colitis with improvement in signs and symptoms compared to baseline such as stool frequency, rectal bleeding, and/or endoscopic activity, tapering or discontinuation of corticosteroid therapy, and/or an improvement on a disease activity scoring tool (e.g. an improvement on the Ulcerative Colitis Endoscopic Index of Severity [UCEIS] score, or the Mayo Score).
- Uveitis associated with Behçet's Syndrome with disease response as indicated by improvement in signs and symptoms of uveitis compared to baseline (e.g. reduction in inflammation and/or lesions, dose reduction of oral glucocorticoids and/or immunosuppressive agents, improvement in vitreous haze, improvement in best corrected visual acuity [BCVA], disease stability and/or reduced rate of decline)

INDICATION(S)	LOADING DOSE	MAINTENANCE DOSE	Maximum Dose & Frequency
Ankylosing Spondylitis	5mg/kg at weeks 0, 2, 6	5mg/kg every 6 weeks thereafter	Up to 10 mg/kg every 4 weeks
Crohn's Disease Ulcerative Colitis	5mg/kg at weeks 0, 2, 6	5mg/kg every 8 weeks thereafter	5 mg/kg every 6 weeks
Plaque Psoriasis, Psoriatic Arthritis, Behçet's Uveitis	5mg/kg at weeks 0, 2, 6	5mg/kg every 8 weeks thereafter	Up to 10 mg/kg every 8 weeks
Rheumatoid Arthritis	3mg/kg at weeks 0, 2, 6	3mg/kg every 8 weeks thereafter	5 mg/kg every 8 weeks
Takayasu's Arteritis	5mg/kg at weeks 0, 2, 6	5mg/kg every 8 weeks thereafter; 3 to 5mg/kg every 6 weeks as steroid-sparing agent	5 mg/kg every 8 weeks
Management of Immune Checkpoint Inhibitor Related Toxicity	5 mg/kg at weeks 0, 2	N/A	N/A

- Dose escalation (up to the maximum dose and frequency specified above) may occur upon clinical
- review on a case by case basis provided that the patient has:
  - o Shown an initial response to therapy
  - o Received the three loading doses at the dose **AND** interval specified above
  - o Received a minimum of one maintenance dose at the dose **AND** interval specified above
  - o Responded to therapy (by treatment week 16) with subsequent loss of response
  - o Dose escalation may either increase the dose **OR** decrease the interval provided it does not exceed the following limits:
    - Dose increase by no more than 2.5 mg/kg **OR**
    - Interval decrease by no more than 2 weeks

Note:

- Prior to escalating doses a patient's neutralizing IFX-antibodies should be assessed and addition of a DMARD (e.g., thiopurine or MTX), if not already on such therapy, should be considered.
- Criteria for disease-specific response to therapy are noted in section IV. Patients with moderate to severe heart failure (NYHA Functional Class III/IV; LVEF ≤35%) should not receive doses in excess of 5 mg/kg.

***Due to proprietary considerations, FDA approval was NOT granted to pediatric ulcerative colitis**

LENGTH OF AUTHORIZATION

Coverage will be provided for six months and may be renewed.

Therapy for the management of Immune-Checkpoint Inhibitor Related Toxicity may **not** be renewed.

Refer to **DOSAGE LIMITS** below

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

MICROMEDEX Healthcare Series, Drugdex Drug Evaluations. (2018, February). *Infliximab*. Retrieved March 9, 2018 from MICROMEDEX Healthcare Series.

National Comprehensive Cancer Network. (2018). NCCN Drugs & Biologics Compendium®. *Infliximab.* Retrieved December 14, 2018 from the National Comprehensive Cancer Network.

U. S. Food and Drug Administration. (2017, April). Center for Drug Evaluation and Research. *Renflexis™ (infliximab-abda) for injection, for intravenous use.* Retrieved March 16, 2018 from https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/761054Orig1s000lbledt.pdf.

EFFECTIVE DATE

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