FIRST TIME GENERIC APPROVAL

Brand Name	infliximab
Generic Name	infliximab
Drug Manufacturer	Janssen Biotech, Inc.

New Drug Approval

TYPE OF CLINICAL UPDATE

First Time Generic

FDA APPROVAL DATE

October 05, 2021

LAUNCH DATE

November 19, 2021

REVIEW DESIGNATION

N/A

TYPE OF REVIEW

Biologics License Application (BLA)

DISPENSING RESTRICTIONS

N/A

Overview

INDICATION FOR USE

Infliximab is a tumor necrosis factor (TNF) blocker indicated for:

- Crohn's Disease:
  - reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
  - reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing disease.
- Pediatric Crohn's Disease: reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.
- Ulcerative Colitis: reducing signs and symptoms, inducing and maintaining clinical remission and mucosal healing, and eliminating corticosteroid use in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy.
- Pediatric Ulcerative Colitis: reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy.

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- Rheumatoid Arthritis in combination with methotrexate: reducing signs and symptoms, inhibiting the progression of structural damage, and improving physical function in adult patients with moderately to severely active disease.
- Ankylosing Spondylitis: reducing signs and symptoms in adult patients with active disease.
- Psoriatic Arthritis: reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in adult patients.
- Plaque Psoriasis: treatment of adult patients with chronic severe (i.e., extensive and/or disabling) plaque psoriasis who are candidates for systemic therapy and when other systemic therapies are medically less appropriate.

MECHANISMS OF ACTION

Infliximab neutralizes the biological activity of TNFα by binding with high affinity to the soluble and transmembrane forms of TNFα and inhibits binding of TNFα with its receptors. Infliximab does not neutralize TNFβ (lymphotoxin-α), a related cytokine that utilizes the same receptors as TNFα. Biological activities attributed to TNFα include: induction of pro-inflammatory cytokines such as interleukins (IL) 1 and 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. Cells expressing transmembrane TNFα bound by infliximab can be lysed *in vitro* or *in vivo*. Infliximab inhibits the functional activity of TNFα in a wide variety of *in vitro* bioassays utilizing human fibroblasts, endothelial cells, neutrophils, B and T-lymphocytes and epithelial cells. The relationship of these biological response markers to the mechanism(s) by which Infliximab exerts its clinical effects is unknown. Anti-TNFα antibodies reduce disease activity in the cotton-top tamarin colitis model, and decrease synovitis and joint erosions in a murine model of collagen-induced arthritis. Infliximab prevents disease in transgenic mice that develop polyarthritis as a result of constitutive expression of human TNFα, and when administered after disease onset, allows eroded joints to heal.

DOSE FORM AND STRENGTH

For injection: 100 mg of infliximab as a lyophilized powder in a single-dose vial for reconstitution and dilution.

DOSE & ADMINISTRATION

- **Dosage in Adult Crohn's Disease**

The recommended dosage of Infliximab is 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter for the treatment of adults with moderately to severely active CD or fistulizing CD. For adult patients who respond and then lose their response, consideration may be given to treatment with 10 mg/kg every 8 weeks. Patients who do not respond by Week 14 are unlikely to respond with continued dosing and consideration should be given to discontinue Infliximab in these patients.

- **Dosage in Pediatric Crohn's Disease**

The recommended dosage of Infliximab for pediatric patients 6 years and older with moderately to severely active CD is 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks.

- **Dosage in Adult Ulcerative Colitis**

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The recommended dosage of Infliximab is 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter for the treatment of adult patients with moderately to severely active UC.

- **Dosage in Pediatric Ulcerative Colitis**

The recommended dosage of Infliximab for pediatric patients 6 years and older with moderately to severely active UC is 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks.

- **Dosage in Rheumatoid Arthritis**

The recommended dosage of Infliximab is 3 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 3 mg/kg every 8 weeks thereafter for the treatment of moderately to severely active RA. Infliximab should be given in combination with methotrexate. For patients who have an incomplete response, consideration may be given to adjusting the dosage up to 10 mg/kg every 8 weeks or treating as often as every 4 weeks bearing in mind that risk of serious infections is increased at higher doses per infusion or more frequent dosing.

- **Dosage in Ankylosing Spondylitis**

The recommended dosage of Infliximab is 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 6 weeks thereafter for the treatment of active AS.

- **Dosage in Psoriatic Arthritis**

The recommended dosage of Infliximab is 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter for the treatment of PsA. Infliximab can be used with or without methotrexate.

- **Dosage in Plaque Psoriasis**

The recommended dosage of Infliximab in adult patients is 5 mg/kg given as an intravenous induction regimen at 0, 2 and 6 weeks followed by a maintenance regimen of 5 mg/kg every 8 weeks thereafter for the treatment of chronic severe (i.e., extensive and/or disabling) Ps.