Infliximab (Remicade®)

Biosimilars:
- **Infliximab-dyyb (Inflectra)**
- **Infliximab-axxq (Avsola)**
- **Infliximab-abda (Renflexis)**
- **Infliximab-qbtx (Ixifi®)***

Formulation of infliximab is generally insurance driven based on patient's coverage and plan.

Infliximab (and biosimilars) is a chimeric (part mouse, part human) monoclonal antibody that blocks activity of a key biologic response mediator called "tumor necrosis factor alpha (TNF-α). The action of infliximab is to bind to and neutralize TNF-α on the cell membrane as well as soluble TNF-α and to destroy TNF-α producing cell, thus inhibiting inflammation.

Resources from Manufacturer

Remicade®
Patient Medication Guide
Full Prescribing Information
Janssen CarePath
Financial Assistance

Inflectra®
Patient Medication Guide
Full Prescribing Information
Pfizer enCompass Co-pay Enrollment

Avsola®
Patient Medication Guide
Full Prescribing Information
Avsola Co-pay Program
Financial Assistance through Amgen

Renflexis®
Patient Medication Guide
Full Prescribing Information
The Organon Co-pay Assistance Program
Financial Assistance

Ifixi®
Full prescribing information

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FDA-Approved Indications and Dosing in Rheumatology

- Crohn's Disease in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy
- Pediatric Crohn's Disease in patients 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy
- Ulcerative Colitis in adult patients with moderately to severely active disease who have had an inadequate response to conventional therapy
- Pediatric Ulcerative Colitis in 6 years of age and older with moderately to severely active disease who have had an inadequate response to conventional therapy
- Rheumatoid Arthritis in combination with methotrexate in adult patients with moderately to severely active disease
- Ankylosing Spondylitis in adult patients with active disease
- Psoriatic Arthritis 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

Intravenous Dosing

- Crohn's Disease: 5 mg/kg IV at 0, 2 and 6 weeks, then every 8 weeks. Some adult patients may benefit from doses up to10 mg/kg every 8 weeks
- Pediatric Crohn's Disease (≥ 6 years old): 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks
- Ulcerative Colitis: 5 mg/kg IV at 0, 2 and 6 weeks, then every 8 weeks.
- Pediatric Ulcerative Colitis (≥ 6 years old): 5 mg/kg at 0, 2 and 6 weeks, then every 8 weeks
- Rheumatoid Arthritis: 3 mg/kg IV at 0, 2 and 6 weeks, then every 8 weeks, in conjunction with methotrexate. Some patients may benefit from doses up to 10 mg/kg or treating as often as every 4 weeks.
- Ankylosing Spondylitis: 5 mg/kg IV at 0, 2 and 6 weeks, then every 6 weeks.
- Psoriatic Arthritis and Plaque Psoriasis: 5 mg/kg IV at 0, 2 and 6 weeks, then every 8 weeks

Contraindications

- Doses greater than 5 mg/kg in patients with moderate to severe heart failure (New York Heart Association Functional Class III/IV).
- Previous severe hypersensitivity reaction to infliximab or known hypersensitivity to any component of infliximab or to any murine proteins.

Black Box Warnings

- Increased risk of serious infections leading to hospitalization or death, including tuberculosis (TB), bacterial sepsis, invasive fungal infections (such as histoplasmosis) and infections due to other opportunistic pathogens.
- Discontinue infliximab if a patient develops a serious infection.
- Perform test for latent TB; if positive, start treatment for TB prior to starting infliximab. Monitor all patients for active TB during treatment, even if initial latent TB test is negative.
- Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with tumor necrosis factor (TNF) blockers, including infliximab products.
- Postmarketing cases of fatal hepatosplenic T-cell lymphoma (HSTCL) have been reported in patients treated with TNF blockers, including infliximab products. Almost all had received azathioprine or 6-mercaptopurine concomitantly with a TNF blocker at or prior to diagnosis. The majority of cases were reported in patients with Crohn's disease or ulcerative colitis, most of whom were adolescent or young adult males

Warnings and Precautions

- Serious infections–do not administer if active infection is present. Patient greater than 65 years of age, those with comorbid conditions or on concomitant immunosuppressant or corticosteroids may be at greater risk for infection.
- Invasive fungal infections–for patients who develop a systemic illness on infliximab, consider empiric antifungal therapy for those who reside or travel to regions where mycoses are endemic
- Malignancies–the incidence of malignancies, including invasive cervical cancer and lymphoma, was greater in REMICADE treated patients than in controls. Due to the risk of HSTCL carefully assess the risk/benefit especially if the patient has Crohn's disease or ulcerative colitis, is male, and is receiving azathioprine or 6-mercaptopurine treatment.
- Reactivation of hepatitis B virus–test HBV infection before starting infliximab and monitor for HBV carriers.
- Rare hepatotoxicity leading to death or liver transplantation; monitor for marked liver enzyme elevations and for the presence of jaundice.
- Lymphoma and other malignancies have been reported in patients receiving TNF blockers.
- New or worsening of heart failure may occur, particularly with infliximab 5 mg/kg/dose or higher.
- Hypersensitivity–infusion reactions, including anaphylaxis or serious allergic reactions may occur.
- Cytopenias
- Cardiovascular and Cerebrovascular Reactions – Cerebrovascular accidents, myocardial infarctions (some fatal), and arrhythmias have been reported during and within 24 hours of initiation of infliximab infusion. Monitor patients during infliximab infusion and if serious reaction occurs, discontinue infusion.
- Demyelinating disease–exacerbation or new onset
- Lupus-like syndrome
- Live vaccines or therapeutic infectious agents should not be given with concurrent infliximab use. At least a six month waiting period following birth is recommended before the administration of live vaccines to infants exposed in utero to infliximab
- Drug interactions–avoid use with anakinra or abatacept, which may increase risk of serious infections.

Adverse Reactions (>10%)

- Infections (e.g. upper respiratory, n sinusitis, and pharyngitis)
- Infusion-related reactions
- Headache
- Abdominal pain

Medication Strength and Preparations

The infliximab formulations are all supplied as 100mg lyophilized powder for reconstitution. Reconstituted infliximab infusion solution should be prepared by a trained medical professional using aseptic technique

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Medication Administration and Storage

- Unopened vials must be refrigerated at 2ºC to 8ºC [36ºF to 46ºF]

Intravenous Administration

1. Vital Signs Monitoring: Obtain vital signs [patient temperature, blood pressure and pulse] upon arrival, after start of medication, upon discontinuing infusion and before the patient departs the facility. However, if prior history of an acute infusion reaction, monitor vitals every 10 minutes for 30 minutes then every 30 minutes and for 30 minutes after infusion.
2. Review Orders and Obtain IV Access:
   - Check for pre-medication orders. Give pre-medications if ordered. Pre-medications may include antihistamines, acetaminophen and/or corticosteroids.
   - Infliximab infusion should be administered over a period of not less than 2 hours. Below is an example of an infusion rate schedule for infliximab diluted in a 250mL volume:
     - ❑ 40mL/hr. for 15 minutes, then if tolerated, increase to:
     - ❑ 80mL/hr. x 30 minutes, then if tolerate, increase to:
     - ❑ 160mL/hr. for the duration of infusion
     - ❑ Flush to ensure all medication in the IV tubing is administered.
     - ❑ Total infusion time is 2 hours, plus 15 minutes for the flush.

Intravenous Administration Pre-infusion Checklist

- Tuberculosis Screening
  - ❑ Verify that latent tuberculosis infection screening has been performed
  - ❑ Detailed history of patient tuberculosis exposure risk factors
  - ❑ Confirm the following:
    - Negative tuberculin skin test/PPD and/or Negative Interferon Gamma Release Assay [Quantiferon or TSpot TB test]. Consider chest x-ray in patients with TB risk factors but negative screening tests.
    - Positive tuberculin skin test/PPD or positive Quantiferon/TSpot TB test with negative chest x-ray.
- Patient is at least 4 weeks post initiation of INH or other TB therapy.
  - ❑ Consider repeating screening tests if a patient has subsequently traveled to TB endemic countries or there has been a change in risk factors for TB exposure.
- Confirm that the patient is hepatitis B negative [particularly HepB Surface Antigen].
- If patient has a history of moderate to severe heart failure, infliximab has been associated with an exacerbation of heart failure; doses >5 mg/kg are contraindicated. Close monitoring is recommended.
- If patient has demyelinating diseases, such as multiple sclerosis, infliximab is contraindicated.
- Ask the patient if:
  - ❑ Has a current or recent infection or illness
  - ❑ Is taking any anti-infective treatment
  - ❑ Is taking antibiotics
  - ❑ Has an upcoming surgery
  - ❑ Has had any recent live vaccines

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Intravenous Medication Preparation

1. Calculate the dose per providers order, total volume of reconstituted infliximab solution required and the number of infliximab vials needed. Each vial contains 100 mg of infliximab.
2. Reconstitute each infliximab vial with 10 mL of Sterile Water using a syringe equipped with a 21-gauge or smaller needle as follows:
   - Insert the syringe needle into the vial through the center of the rubber stopper and direct the stream of Sterile Water gently to the glass wall of the vial.
   - GENTLY swirl the solution by rotating the vial to dissolve the lyophilized powder. Avoid shaking, which may inactivate infliximab. Foaming of the solution is not unusual.
   - Allow the reconstituted solution to stand for 5 minutes. The solution should be colorless to light yellow and opalescent. The solution may develop a few translucent particles.
   - Do not use if the lyophilized cake has not fully dissolved or if opaque particles, discoloration, or other foreign particles are present.
3. Dilute the total volume of the reconstituted infliximab solution dose to a total volume of 250 mL with sterile 0.9% Sodium Chloride Injection, USP, by withdrawing a volume equal to the volume of reconstituted infliximab from the 0.9% Sodium Chloride Injection, USP, 250 mL bottle or bag.
4. Slowly add the total volume of reconstituted infliximab solution to the 250 mL infusion bottle or bag. Gently mix.
5. The infusion solution must be administered over a period of no less than 2 hours utilizing an infusion set with an in-line, sterile, non-pyrogenic, low-protein-binding filter (pore size of 1.2 µm or less).

No physical biochemical compatibility studies have been conducted to evaluate the co-administration of infliximab with other agents. Infliximab should not be infused concomitantly in the same intravenous line with other agents.

Managing Infusion Reactions

- Patients who became positive for antibodies to infliximab were more likely (approximately two-to three-fold) to have an infusion reaction than were those who were negative. Use of concomitant immunosuppressant agents appeared to reduce the frequency of both antibodies to infliximab and infusion reactions
- Acute infusion reaction or anaphylaxis can occur at any time during the administration of this agent and include flu-like symptoms, headache, dyspnea, hypotension, transient fever, chills, gastrointestinal symptoms, and skin rashes.
- If patient reports mild reactions (such as flushing, chills, etc.)
  - ❑ Stop the infusion and assess patient.
- For more severe reactions (such as hives, difficulty breathing, chest pain, high or low blood pressure, swelling of face and hands, fever, chills or anaphylaxis) or where mild reactions persist
  - ❑ Stop the infusion and treat the acute reaction. Then notify the supervising provider immediately to coordinate next plan of action. For mild reactions, consider adding additional pre-medications for subsequent doses.

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