AVSOLA® INFUSION GUIDE



DOSING, PREPARATION, AND ADMINISTRATION IDENTICAL TO REMICADE®1,2,*

*When storing AVSOLA®, protect from light.¹

INDICATIONS

AVSOLA® is indicated for:

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 ulcerative colitis who have had an inadequate response to conventional therapy.

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 rheumatoid arthritis.



RECOMMENDED DOSING AND SCHEDULES¹

For patients transitioning to AVSOLA® from Remicade®, similarities in dosing, schedule, and storage and handling help to establish a seamless experience.



• Intravenous (IV) infusions are administered over at least a 2-hour period.

*For patients with incomplete response, consideration may be given to adjusting the dose up to 10 mg/kg every 8 weeks or treating as often as every 4 weeks (bearing in mind that the risk of serious infections increases with higher doses per infusion or more frequent dosing).

*AVSOLA® can be used with or without methotrexate.

[‡]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 AVSOLA® in these patients.

FAMILIAR STORAGE AND HANDLING¹



Store unopened AVSOLA[®] in the refrigerator at 36°F to 46°F (2°C to 8°C). If needed, unopened AVSOLA[®] vials may be stored at room temperature up to a maximum of 86°F (30°C) for a single period of up to 6 months, but not exceeding the original expiration date. AVSOLA[®] contains no preservative.



Protect from light.



Once removed from the refrigerator, AVSOLA® cannot be returned to the refrigerator.



If you have any questions about the reconstitution and preparation of AVSOLA®, refer to the package insert. For additional information and resources, please visit **AVSOLA.com**

SELECT IMPORTANT SAFETY INFORMATION

Serious and sometimes fatal side effects have been reported with infliximab products. Infections due to bacterial, mycobacterial, invasive fungal, viral, or other opportunistic pathogens (eg, TB, histoplasmosis) have been reported. Lymphoma, including cases of fatal hepatosplenic T-cell lymphoma (HSTCL), and other malignancies have been reported, including in children and young adult patients. Due to the risk of HSTCL, mostly reported in Crohn's disease and ulcerative colitis, assess the risk/benefit, especially if the patient is male and is receiving azathioprine or 6-mercaptopurine treatment. AVSOLA® is

contraindicated at doses >5 mg/kg in patients with moderate or severe heart failure and in patients with severe hypersensitivity reactions to infliximab. Other serious side effects reported include melanoma, Merkel cell carcinoma, invasive

cervical cancer, hepatitis B reactivation, hepatotoxicity, hematological events, hypersensitivity, cardiovascular and cerebrovascular reactions during and after infusion, neurological events, and lupus-like syndrome.



PREPARING FOR AN INFUSION¹

AVSOLA® is intended for use under the guidance and supervision of a healthcare provider. The supplied lyophilized powder must be reconstituted and diluted prior to administration. The infusion solution should be prepared and administered by a trained medical professional using aseptic technique as outlined in the Prescribing Information and summarized below:



Calculate the dose, total volume of reconstituted AVSOLA[®] solution required, and the number of vials needed. More than one vial may be needed for a full dose.



Reconstitute each 100 mg AVSOLA® vial with 10 mL Sterile Water for Injection, USP (SWFI) to obtain a concentration of 10 mg/mL using a syringe equipped with a 21-gauge needle, or smaller if needed.

Remove the flip-top from the vial and wipe the top with an alcohol swab. Insert the syringe needle into the vial through the center of the rubber stopper, and direct the stream of SWFI to the glass wall of the vial.

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Gently swirl (rotate) the vial to dissolve the lyophilized powder, which has a cake-like appearance. Avoid prolonged or vigorous agitation. DO NOT SHAKE.

- Foaming of the solution on reconstitution is not unusual. Allow the reconstituted solution to stand for 5 minutes.
- Visually inspect the reconstituted solution for particulate matter and discoloration. The solution should be colorless to light yellow and opalescent, and the solution might develop a few translucent particles, as infliximab-axxq is a protein.
- Do not use if the lyophilized powder has not fully dissolved or if opaque particles, discoloration, or other foreign particles are present.
- Do not store unused reconstituted AVSOLA® solution.



Dilute the total volume of reconstituted AVSOLA® solution to 250 mL* with sterile 0.9% Sodium Chloride Injection, USP (do not dilute with any other diluent), by withdrawing a volume from the 0.9% Sodium Chloride Injection, USP, 250 mL bottle or bag equal to the total volume of reconstituted AVSOLA® required for a dose.

• Discard any unused portion of the reconstituted AVSOLA® solution remaining in the vial(s).



Gently invert the bag to mix the solution. The resulting infusion concentration should range between 0.4 mg/mL (minimum recommended concentration) and 4 mg/mL (maximum recommended concentration) of infliximab-axxq.

*For volumes greater than 250 mL, either use a larger infusion bag (eg, 500 mL) or multiple 250 mL infusion bags to ensure that the concentration of the infusion solution does not exceed 4 mg/mL



DURING AN INFUSION¹

Patients taking AVSOLA[®] should adhere to a specific schedule and the infusion requirements as outlined in the Prescribing Information and included below.



The AVSOLA® infusion should begin within 3 hours of reconstitution and dilution.



The infusion must be administered intravenously for at least 2 hours with an infusion set with an in-line, sterile, non-pyrogenic, low-protein-binding filter (pore size of 1.2 μ m or less).

Given that the vials do not contain antibacterial preservatives, discard any unused portion of the infusion solution (do not store for reuse).



AVSOLA[®] should not be infused concomitantly in the same IV line with other agents.

No physical biochemical compatibility studies have been conducted to evaluate the co-administration of AVSOLA® with other agents.

Assessment for Latent and Active Tuberculosis

Prior to initiating AVSOLA[®] and periodically during therapy, patients should be evaluated for active tuberculosis and tested for latent infection.

Administration Instructions Regarding Infusion Reactions

Prior to treatment, ensure appropriate personnel and medication are available to treat reactions (eg, hypersensitivity, other reactions) that occur during infusion and shortly after infusion. Prior to infusion with AVSOLA®, patients may be premedicated with histamine-1 receptor antagonists, histamine-2 receptor antagonists, acetaminophen, and/or corticosteroids.

For mild to moderate reactions during the infusion, consider slowing or stopping the infusion. Upon resolution of these reactions, may reinitiate at a lower infusion rate and/or with histamine-1 receptor antagonists, histamine-2 receptor antagonists, acetaminophen, and/or corticosteroids. Discontinue the infusion if the mild to moderate reactions reoccur.

Discontinue the infusion if severe hypersensitivity reactions occur during the infusion.



FOR MORE INFORMATION AND SUPPORT

AMGEN[®]Support⁺

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Benefit Verifications via the Amgen SupportPlus Customer Portal

A tool for managing patient benefits verification and more. Submit, store, and retrieve benefit verifications electronically. Visit myAmgenPortal.com to register and submit forms online



Financial Support

We know every patient has unique needs. And we're here to provide financial support information and resources, regardless of current financial situation or type of insurance. Visit AmgenSupportPlus.com to learn more



Amgen® SupportPlus Representatives

Our Amgen® SupportPlus Representatives can assist with issues around patient coverage, prior authorizations, co-pay programs, and more. Call **(866) 264-2778** Monday-Friday 9am-8pm ET

Call (866) 264-2778 Monday to Friday, 9:00 am to 8:00 pm ET

AMGEN[®] Safety Net Foundation

The Amgen Safety Net Foundation is a nonprofit patient assistance program sponsored by Amgen that helps qualifying patients access Amgen medicines at no cost.



AMGEN[®] SUPPORTPLUS CO-PAY PROGRAM*

May help eligible patients with private or commercial insurance lower their out-of-pocket costs.

***SUMMARY OF TERMS AND CONDITIONS**

It is important that every patient read and understand the full Amgen SupportPlus Co-Pay Card Terms and Conditions. The following summary is not a substitute for reviewing the Terms and Conditions in their entirety.

These terms and conditions apply to the following products:

BLINCYTO® (blinatumomab), IMLYGIC® (talimogene laherparepvec), KANJINTI® (trastuzumab-anns), KYPROLIS® (carfilzomib), LUMAKRAS® (sotorasib), MVASI® (bevacizumab-awwb), NEULASTA® (pegfilgrastim), NEUPOGEN® (filgrastim), NPLATE® (romiplostim), PROLIA® (denosumab), RIABNI® (rituximab-arrx), VECTIBIX® (panitumumab), XGEVA® (denosumab), EVENITY® (romosozumab-aqqg), and AVSOLA® (infliximab-axxq)

As further described below, in general:

- The Amgen SupportPlus Co-Pay Card is open to patients with commercial insurance that covers an Amgen SupportPlus product listed above, regardless of financial need. The program is not valid for patients whose prescription for an Amgen SupportPlus product is paid for in whole or in part by Medicare, Medicaid, or any other federal or state healthcare program. It is not valid for cash paying patients or where prohibited by law. (See ELIGIBILITY section in the full Terms & Conditions.)
- The Amgen SupportPlus Co-Pay Card may help lower your Amgen SupportPlus product out-of-pocket medication costs. Out-of-pocket costs may include co-payment, co-insurance, and deductible out-of-pocket costs. The Amgen SupportPlus Co-Pay Card does not cover any other costs related to office visits or administration of the product. The Amgen SupportPlus Co-Pay Card provides support up to the Maximum Program Benefit or Patient Total Program Benefit. If a patient's commercial insurance plan imposes different or additional requirements on patients who receive Amgen SupportPlus Co-Pay Card benefits, Amgen has the right to modify or eliminate those benefits. Whether you are eligible to receive the Maximum Program Benefit or Patient Total Program Benefit is determined by the type of plan coverage you have. Please ask your Amgen SupportPlus Support Representative to help you understand eligibility for the Amgen SupportPlus Co-Pay Card, whether your reaching the Maximum Program Benefit or your Patient Total Program Benefit amount by calling (866) 264-2778. (See PROGRAM BENEFITS section in the full Terms & Conditions.)
- Amgen SupportPlus patients may pay as little as:
- \$0 out-of-pocket for each dose or cycle of the Amgen SupportPlus product (excluding Prolia® and EVENITY®)
- \$25 out-of-pocket for each dose of Prolia® or EVENITY®

Amgen will pay the remaining eligible out-of-pocket costs on behalf of the patient until the Amgen payments have reached either the Maximum Program Benefit and/or the Patient Total Program Benefit. Patients are responsible for all amounts that exceed this limit. Please ask your Amgen SupportPlus Support Representative to help you understand eligibility for the Amgen SupportPlus Co-Pay Card by calling (866) 264-2778. (See PROGRAM DETAILS section in the full Terms & Conditions.)

Program coverage through the Amgen SupportPlus Co-Pay Card is contingent on (1) the submission of the required Explanation of Benefits (EOB) form within 180 days of the date of approval documented on the EOB for medical benefit claims or (2) the submission of the claim within 180 days of the date of service for pharmacy benefit claims. (See PROGRAM DETAILS section in the full Terms & Conditions.)

See Amgensupportplus.com/copay for full Terms and Conditions. Please see full <u>Indications</u> and <u>Important Safety Information</u> on

pages 10-13 and *full Prescribing Information*.



IMPORTANT SAFETY INFORMATION

SERIOUS INFECTIONS: Patients treated with infliximab products are at increased risk for developing serious infections that may lead to hospitalization or death. Most patients who developed these infections were taking concomitant immunosuppressants such as methotrexate or corticosteroids. Discontinue AVSOLA® if a patient develops a serious infection or sepsis.

Reported infections include:

- Active tuberculosis (TB), including reactivation of latent TB. Patients frequently presented with disseminated or extrapulmonary disease. Patients should be tested for latent TB before AVSOLA[®] use and during therapy. Treatment for latent infection should be initiated prior to AVSOLA[®] use.
- Invasive fungal infections including histoplasmosis, coccidioidomycosis, candidiasis, aspergillosis, blastomycosis, pneumocystosis and cryptococcosis. Patients may present with disseminated, rather than localized, disease. Empiric anti-fungal therapy should be considered in patients at risk for invasive fungal infections who develop severe systemic illness.
- Bacterial, viral, and other infections due to opportunistic pathogens, including Legionella, Listeria, and Salmonella.

The risks and benefits of treatment with AVSOLA® should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection. Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with AVSOLA®, including the possible development of TB in patients who tested negative for latent TB infection prior to initiating therapy, who are on treatment for latent TB, or who were previously treated for TB infection.

Risk of infection may be higher in patients greater than 65 years of age, pediatric patients, patients with co-morbid conditions and/or patients taking concomitant immunosuppressant therapy. In clinical trials, other serious infections observed in patients treated with infliximab products included pneumonia, cellulitis, abscess, and skin ulceration.

MALIGNANCIES

Lymphoma and other malignancies, some fatal, have been reported in children and adolescent patients treated with TNF blockers, including infliximab products. Approximately half of these cases were lymphomas, including Hodgkin's and non-Hodgkin's lymphoma. The other cases represented a variety of malignancies, including rare malignancies that are usually associated with immunosuppression and malignancies that are not usually observed in children and adolescents. The malignancies occurred after a median of 30 months after the first dose of therapy. Most of the patients were receiving concomitant immunosuppressants.

Postmarketing cases of hepatosplenic T-cell lymphoma, a rare type of T-cell lymphoma, have been reported in patients treated with TNF blockers, including infliximab products. These cases have had a very aggressive disease course and have been fatal. The majority of reported cases have occurred in patients with Crohn's disease or ulcerative colitis and most were in adolescent and young adult males. Almost all patients had received treatment with azathioprine or 6-mercaptopurine concomitantly with a TNF-blocker at or prior to diagnosis. Carefully assess the risks and benefits of treatment with AVSOLA®, especially in these patient types.

IMPORTANT SAFETY INFORMATION (continued)

In clinical trials of all TNF inhibitors, more cases of lymphoma were observed compared with controls and the expected rate in the general population. However, patients with Crohn's disease, rheumatoid arthritis, or plaque psoriasis may be at higher risk for developing lymphoma. In clinical trials of some TNF inhibitors, including infliximab products, more cases of other malignancies were observed compared with controls. The rate of these malignancies among patients treated with infliximab products was similar to that expected in the general population, whereas the rate in control patients was lower than expected. Cases of acute and chronic leukemia have been reported with postmarketing TNF-blocker use. As the potential role of TNF inhibitors in the development of malignancies is not known, caution should be exercised when considering treatment of patients with a current or a past history of malignancy or other risk factors such as chronic obstructive pulmonary disease (COPD).

Melanoma and Merkel cell carcinoma have been reported in patients treated with TNF-blocker therapy, including infliximab products. Periodic skin examination is recommended for all patients, particularly those with risk factors for skin cancer.

A population-based retrospective cohort study found a 2- to 3-fold increase in the incidence of invasive cervical cancer in women with rheumatoid arthritis treated with infliximab compared to biologics-naïve patients or the general population, particularly those over 60 years of age. A causal relationship between infliximab products and cervical cancer cannot be excluded. Periodic screening should continue in women treated with AVSOLA[®].

CONTRAINDICATIONS

The use of AVSOLA® at doses >5 mg/kg is contraindicated in patients with moderate or severe heart failure. AVSOLA® is contraindicated in patients with a previous severe hypersensitivity reaction to infliximab or any of the inactive ingredients of AVSOLA® or any murine proteins (severe hypersensitivity reactions have included anaphylaxis, hypotension, and serum sickness).

HEPATITIS B REACTIVATION

TNF inhibitors, including infliximab products, have been associated with reactivation of hepatitis B virus (HBV) in patients who are chronic carriers. Some cases were fatal. Patients should be tested for HBV infection before initiating AVSOLA®. For patients who test positive, consult a physician with expertise in the treatment of hepatitis B. Exercise caution when prescribing AVSOLA® for patients identified as carriers of HBV and monitor closely for active HBV infection during and following termination of therapy with AVSOLA®. Discontinue AVSOLA® in patients who develop HBV reactivation and initiate antiviral therapy with appropriate supportive treatment. Exercise caution when considering resumption of TNF-blocker therapy and monitor patients closely.

HEPATOTOXICITY

Severe hepatic reactions, including acute liver failure, jaundice, hepatitis, and cholestasis have been reported in patients receiving infliximab products postmarketing. Some cases were fatal or required liver transplant. Aminotransferase elevations were not noted prior to discovery of liver injury in many cases. Patients with symptoms or signs of liver dysfunction should be evaluated for evidence of liver injury.



IMPORTANT SAFETY INFORMATION (continued)

If jaundice and/or marked liver enzyme elevations (eg, \geq 5 times the upper limit of normal) develop, AVSOLA[®] should be discontinued, and a thorough investigation of the abnormality should be undertaken.

HEART FAILURE

In a randomized, placebo-controlled study in patients with moderate or severe heart failure (NYHA Functional Class III/IV), higher mortality rates and a higher risk of hospitalization were observed at Week 28 at a dose of 10 mg/kg and higher rates of cardiovascular events were observed at both 5 mg/kg and 10 mg/kg. There have been postmarketing reports of new onset and worsening heart failure, with and without identifiable precipitating factors. Patients with moderate or severe heart failure taking infliximab (≤5 mg/kg) or patients with mild heart failure should be closely monitored and treatment should be discontinued if new or worsening symptoms appear.

HEMATOLOGIC REACTIONS

Cases of leukopenia, neutropenia, thrombocytopenia, and pancytopenia (some fatal) have been reported in patients receiving infliximab products. The causal relationship to infliximab product therapy remains unclear. Exercise caution in patients who have ongoing or a history of significant hematologic abnormalities. Advise patients to seek immediate medical attention if they develop signs and symptoms of blood dyscrasias or infection. Consider discontinuation of AVSOLA® in patients who develop significant hematologic abnormalities.

HYPERSENSITIVITY

Infliximab products have been associated with hypersensitivity reactions that differ in their time of onset. Anaphylaxis, urticaria, dyspnea, and hypotension have occurred in association with infusions of infliximab products. Medications for the treatment of hypersensitivity reactions should be available.

CARDIOVASCULAR AND CEREBROVASCULAR REACTIONS DURING AND AFTER INFUSION

Serious cerebrovascular accidents, myocardial ischemia/infarction (some fatal), hypotension, hypertension, and arrhythmias have been reported during and within 24 hours of initiation of infliximab product infusion. Cases of transient visual loss have been reported during or within 2 hours of infusion of infliximab. Monitor patients during infusion and if a serious reaction occurs, discontinue infusion. Manage reactions according to signs and symptoms.

NEUROLOGIC REACTIONS

Agents that inhibit TNF have been associated with CNS manifestation of systemic vasculitis, seizure, and new onset or exacerbation of CNS demyelinating disorders, including multiple sclerosis and optic neuritis, and peripheral demyelinating disorders, including Guillain-Barré syndrome. Exercise caution when considering AVSOLA® in patients with these disorders and consider discontinuation if these disorders develop.

CONCURRENT ADMINISTRATION WITH OTHER BIOLOGICS

Concomitant use of AVSOLA® with anakinra, abatacept, tocilizumab, or other biologics used to treat the same conditions as AVSOLA® is not recommended because of the possibility of an increased risk of infection. Care should be taken when switching from one biologic to another, since overlapping biological activity may further increase the risk of infection.

AUTOIMMUNITY

Treatment with infliximab products may result in the formation of autoantibodies and in the development of a lupus-like syndrome. Discontinue treatment with AVSOLA® if symptoms of a lupus-like syndrome develop.

IMPORTANT SAFETY INFORMATION (continued)

VACCINATIONS AND USE OF LIVE VACCINES/THERAPEUTIC INFECTIOUS AGENTS

Bring patients up to date with all vaccinations prior to initiating AVSOLA®. Live vaccines or therapeutic infectious agents should not be given with AVSOLA® due to the possibility of clinical infections, including disseminated infections.

At least a 6-month waiting period following birth is recommended before the administration of any live vaccine to infants exposed *in utero* to infliximab products.

ADVERSE REACTIONS

In clinical trials with infliximab products, the most common adverse reactions occurring in >10% of patients included infections (eg, upper respiratory, sinusitis, and pharyngitis), infusion-related reactions, headache, and abdominal pain.

INDICATIONS

AVSOLA[®] is indicated for:

Crohn's Disease: Reducing signs and symptoms and inducing and maintaining clinical remission in adult patients with moderately to severely active Crohn's disease who have had an inadequate response to conventional therapy. AVSOLA® is indicated for reducing the number of draining enterocutaneous and rectovaginal fistulas and maintaining fistula closure in adult patients with fistulizing Crohn's disease.

Pediatric Crohn's Disease: Reducing signs and symptoms and inducing and maintaining clinical remission in pediatric patients 6 years of age or older with moderately to severely active Crohn's 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 ulcerative colitis 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 ulcerative colitis who have had an inadequate response to conventional therapy.

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 rheumatoid arthritis.

Ankylosing Spondylitis: Reducing signs and symptoms in adult patients with active ankylosing spondylitis.

Psoriatic Arthritis: Reducing signs and symptoms of active arthritis, inhibiting the progression of structural damage, and improving physical function in adult patients with psoriatic arthritis.

Plaque Psoriasis: The 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.

AVSOLA[®] should only be administered to patients who will be closely monitored and have regular follow-up visits with a physician.



BEHIND AVSOLA® THE AMGEN EXPERIENCE YOU CAN TRUST





AVSOLA[®] is proven biosimilar to Remicade[®] based on a totality of evidence with no clinically meaningful differences¹



AVSOLA® is FDA approved for all Remicade® indications through extrapolation^{1,2}



Backed by Amgen: At the forefront of biologics for **over 40 years**



Dedicated support and resources for you and your patients

TO LEARN MORE, VISIT AVSOLA.COM

References: 1. AVSOLA^{*} (infliximab-axxq) Prescribing Information, Amgen. **2.** Remicade^{*} (infliximab) Prescribing Information, Janssen Biotech.

Please see Important Safety Information on pages 10-13 and full Prescribing Information. Please visit AVSOLA.com for additional information and resources. Call (866) 264-2778 if you have questions about ordering and accessing AVSOLA[®].

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