Ibalizumab (IBA, Trogarzo)

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Formulations
Single-Dose Vial for Intravenous Administration: 200 mg/1.33 mL (150 mg/mL) in a single-dose vial. Each single-dose vial contains the following inactive ingredients: L-histidine, polysorbate 80, sodium chloride, and sucrose. For additional information, see Drugs@FDA or DailyMed.

Dosing Recommendations	Selected Adverse Events
Child and Adolescent Dose • The safety and efficacy of using ibalizumab (IBA) in children and adolescents has not been established. Adult Dose • A single-loading dose infusion of IBA 2,000 mg administered intravenously (IV) over 30 minutes is followed by a maintenance dose of IBA 800 mg administered IV over 15 minutes every 2 weeks. • U.S. Food and Drug Administration approval of IBA is limited to heavily treatment-experienced adults with multidrug-resistant HIV infection who are experiencing treatment failure on their current regimen. • IBA is used in combination with other antiretroviral drugs.	• Diarrhea, dizziness, nausea, rash • Immune reconstitution inflammatory syndrome • In studies of cynomolgus macaque monkeys, IBA use during pregnancy was associated with reversible immunosuppression (CD4+ T and B cell lymphopenia) in offspring with IBA exposure *in utero*.[1] Whether this association exists for infants of women treated with IBA during pregnancy is unknown. • Potential for immunogenicity in the form of anti-IBA antibodies
	Special Instructions
	• The solution in the vial must be diluted in 0.9% sodium chloride injection and administered by IV infusion. • Using aseptic technique, withdraw 1.33 mL from each vial and transfer into a 250-mL bag of 0.9% sodium chloride for IV injection. Other IV diluents must not be used. • Once diluted, the solution should be administered immediately. If not used immediately, the solution can be stored at room temperature for up to 4 hours or refrigerated for up to 24 hours. Refrigerated solution should be allowed to stand at room temperature for at least 30 minutes but no more than 4 hours prior to administration. • Diluted solution is administered as an IV infusion, not as a bolus or IV push.
	Metabolism/Elimination
	• Monoclonal antibodies are metabolized to peptides and amino acids.

Drug Interactions

Additional information about drug interactions is available in the Adult and Adolescent Antiretroviral Guidelines and the HIV Drug Interaction Checker.

- Ibalizumab (IBA) is a humanized IgG4 monoclonal antibody that blocks HIV entry into CD4 T lymphocyte (CD4) cells. Based on IBA's mechanism of action and target-mediated drug

disposition, drug–drug interactions are not expected. However, no drug interaction studies have been conducted.[1]

Major Toxicities

- *More common:* Rash, diarrhea, headache, nausea, dizziness, depression[1,2]
- *Less common (more severe):* Immune reconstitution inflammatory syndrome (IRIS), hypersensitivity reaction[1]

Resistance

HIV has shown reduced susceptibility to IBA, as defined by a decrease in maximum percent inhibition, when HIV loses N-linked glycosylation sites in the V5 loop of glycoprotein 120.[1-3]

Phenotypic and genotypic test results showed no evidence of cross-resistance between IBA and any U.S. Food and Drug Administration (FDA)–approved classes of antiretroviral (ARV) drugs.[4] IBA exhibits ARV activity against R5-tropic, X4-tropic, and dual-tropic HIV.[4]

Pediatric Use

Approval

IBA is not approved by the FDA for use in pediatric patients. IBA was approved by the FDA in 2018 for use in adults in combination with other ARV drugs, with approval limited to heavily treatment-experienced adults with multidrug-resistant HIV who are experiencing treatment failure on their current regimen.[5] IBA has an orphan drug designation exempting the requirement for pediatric studies under the Pediatric Research Equity Act. The FDA requested that the company create a registry to collect prospective data in individuals exposed to IBA during pregnancy to monitor maternal and pregnancy outcomes, including adverse effects on the developing fetus, neonate, and infant. Healthcare providers are encouraged to report these adverse events to Theratechnologies by calling 1-833-23-THERA (1-833-23-4372).

Efficacy in Clinical Trials

Trial Tai Med Biologics (TMB-301) was conducted in 40 adults aged 23 to 65 years who had body weights ranging from 50 kg to 130 kg, had resistance to ARV drugs from three classes, had been treated for at least 6 months on stable ARV regimens, had viral loads >1,000 copies/mL, and had viral sensitivity to at least one ARV drug.[3,5] Participants continued their current ARV regimens and received a 2,000-mg loading dose of IBA on Day 7 of the study. One week after the loading dose, participants optimized their ARV regimens. Participants received IBA 800 mg on Day 21 and every 2 weeks thereafter. At Week 25, 43% of participants achieved suppressed viral loads[1,3] of <50 copies/mL. At Week 48 of an open-label extension study, 24 participants were taking IBA and their optimized ARV regimen. Sixteen of 27 participants (59%) had viral loads <50 copies/mL at 48 weeks.[6,7]

Mechanism of Action

IBA is a recombinant humanized monoclonal antibody that blocks HIV from infecting CD4 cells. It does this by binding to domain 2 of the CD4 receptor, which interferes with the post-attachment steps that allow HIV virus particles to enter host cells and prevent the viral transmission that occurs via cell–cell fusion.[1,7] IBA does not interfere with CD4-mediated immune functions because it binds to a conformational epitope located primarily in domain 2 of the extracellular portion of the CD4 receptor, away from Major Histocompatibility Complex II molecule binding sites.

Embryo-Fetal Toxicity

In an enhanced pre- and post-natal development study, pregnant cynomolgus monkeys were administered intravenous doses of IBA and significant changes in infant monkey immune cell levels were found (CD4+ T cell and B cell lymphocytopenia) that were attributed to *in utero* IBA exposure.[1] The lymphocyte changes correlated with infant monkey IBA serum concentrations and appeared to return to near normal levels when IBA concentrations were nearly undetectable. One treatment-group infant monkey died from a systemic viral infection with secondary superficial bacterial infection that was acquired during the postnatal period. Despite the low incidence of death (1 of 20 infant monkeys), the death may be related to IBA-induced immunosuppression.[1]

Based on these animal data, IBA may cause reversible immunosuppression (CD4+ T cell and B cell lymphocytopenia) in infants born to mothers treated with IBA during pregnancy. Immune phenotyping of the peripheral blood and expert consultation are recommended to provide guidance regarding monitoring and management of exposed infants based on the degree of immunosuppression observed. Furthermore, the safety of administering live or live-attenuated vaccines to infants with *in utero* IBA exposure and abnormal lymphocyte levels is unknown.

References

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