Ibalizumab-uiyk (Trogarzo, IBA)

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Summary

- Pharmacokinetic (PK) data are insufficient to make dosing recommendations for ibalizumab (IBA) during pregnancy.
- Clinical data are insufficient to characterize the risk for congenital anomalies associated with *in utero* exposure to IBA. No reproductive toxicity or teratogenicity concerns were identified in animal studies.
- Results from an enhanced pre- and postnatal development (ePPND) study conducted in cynomolgus monkeys suggest IBA may cause reversible immunosuppression in infants born to mothers exposed to this drug during pregnancy.

Human Studies in Pregnancy

Pharmacokinetics

No PK studies of IBA in pregnant women have been reported.

Placental and Breast Milk Passage

No data are available on placental or breast milk passage of IBA in humans. However, because monoclonal antibodies are transported across the placenta during pregnancy, IBA has the potential to be transmitted from the birthing parent to the developing fetus. Human immunoglobulin G also is present in human milk, although published data indicate that antibodies in breast milk do not enter the neonatal or infant circulation system in substantial amounts.[1]

Teratogenicity/Adverse Pregnancy Outcomes

No data are available on the risk of birth defects in infants born to women who received IBA during pregnancy.

The U.S. Food and Drug Administration requires collection of 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.

Animal Studies

Carcinogenicity

Carcinogenicity and mutagenicity studies of IBA have not been conducted.[1]

Reproduction/Fertility

Reproductive toxicology studies of IBA have not been conducted.[1]

Teratogenicity/Adverse Pregnancy Outcomes

Results from an ePPND study conducted in cynomolgus monkeys suggest IBA may cause reversible immunosuppression in infants born to mothers exposed to this drug during pregnancy. Decreases in CD4 T lymphocyte (CD4) T cells and B cells and increases in CD8 T cells were observed within the first 4 weeks after birth in cynomolgus monkeys with *in utero* exposure; lymphocyte counts returned to near-normal levels by 3 months of age in these infant monkeys. No data are available for human infants with *in utero* exposure. However, based on these animal data, immune phenotyping of the peripheral blood, including CD4 lymphocyte T cell and B cell counts, is recommended for infants with *in utero* exposure to IBA. If immune suppression is observed, expert consultation also is recommended to provide guidance on monitoring and management (e.g., need for antibiotics or immunoprophylaxis) of exposed infants based on the degree of immunosuppression observed. The safety of administering live or live-attenuated vaccines in exposed infants who have significant immune suppression is unknown. Of note, no malformations or premature births were observed in the ePPND study.[1]

Placental and Breast Milk Passage

No data are available on placental or breast milk passage of IBA in animals.

Excerpt from Table 14

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations[a]	Use in Pregnancy
Ibalizumab-uiyk (IBA) *Trogarzo*	IV Solution • 150 mg/mL	Pregnancy *PK in Pregnancy* • No PK studies in human pregnancy *Dosing in Pregnancy* • Insufficient data to make dosing recommendations Standard Adult Doses • IBA 2,000-mg loading dose, followed by IBA 800-mg maintenance doses administered every 2 weeks	No human data are available, but placental transfer of IBA, a monoclonal antibody, is possible and documented in monkeys. Based on data in cynomolgus monkeys with *in utero* exposure, the potential exists for reversible immunosuppression (CD4 T cell and B cell lymphocytopenia) in infants born to mothers exposed to IBA during pregnancy. The FDA requires collection of 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. Insufficient data to assess for teratogenicity in humans.

[a] Individual ARV drug doses may need to be adjusted in patients with renal or hepatic insufficiency (for details, see the Adult and Adolescent Antiretroviral Guidelines, Appendix B, Table 12).

Key: ARV = antiretroviral; CD4 = CD4 T lymphocyte; FDA = U.S. Food and Drug Administration; IBA = ibalizumab-uiyk; IV = intravenous; PK = pharmacokinetic

References

1. Trogarzo (ibalizumab-uiyk) [package insert]. Food and Drug Administration. 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761065s013lbl.pdf.