Fostemsavir (Rukobia, FTR)

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Fostemsavir (FTR) is a prodrug of the active drug temsavir, a gp120-directed attachment inhibitor.

Summary

- Pharmacokinetic data are insufficient to make dosing recommendations for fostemsavir (FTR) during pregnancy.
- Clinical data are insufficient to characterize the risk for congenital anomalies associated with *in utero* exposure to FTR. No reproductive toxicity or teratogenicity concerns were identified in animal studies.

Human Studies in Pregnancy

Pharmacokinetics

No pharmacokinetic studies of FTR have been reported in pregnant women.

Placental and Breast Milk Passage

No data are available on placental or breast milk passage of FTR in humans.

Teratogenicity/Adverse Pregnancy Outcomes

Two live births of infants who were exposed to FTR during the first trimester have been reported to the Antiretroviral Pregnancy Registry; no birth defects were reported. These data are insufficient to draw conclusions about the risk of birth defects among infants who were exposed to FTR.[1]

Animal Studies

Carcinogenicity

Temsavir was not genotoxic or mutagenic *in vitro*.[2]

Reproduction/Fertility

FTR did not adversely affect the fertility of male or female rats at temsavir exposures approximately 10 times (males) and 186 times (females) higher than those achieved in humans at the recommended dose.[2]

Teratogenicity/Adverse Pregnancy Outcomes

No adverse embryo-fetal effects were observed in rats and rabbits at temsavir exposures of approximately 180 times (rats) and 30 times (rabbits) the exposure in humans at the recommended dose. Maternal toxicity and increased embryonic death were observed in rabbits at temsavir exposures approximately 60 times those in humans. In a rat study conducted at drug exposures

approximately 200 times those in humans, fetal abnormalities (cleft palate, open eyes, shortened snout, microstomia, misaligned mouth/jaw, and protruding tongue) and reductions in fetal body weights occurred in the presence of maternal toxicity.[2]

Placental and Breast Milk Passage

When FTR was administered to pregnant rats, FTR-related drug materials (e.g., temsavir or metabolites) crossed the placenta and were detectable in fetal tissue. Temsavir is excreted in rat milk and was present at concentrations similar to those measured in maternal plasma on Day 11 postpartum.[2]

Excerpt from Table 14

Generic Name (Abbreviation) *Trade Name*	Formulation	Dosing Recommendations[a]	Use in Pregnancy
Fostemsavir (FTR) *Rukobia*	Extended-release tablet: 600 mg	Pregnancy *PKs in Pregnancy:* • No PK studies in human pregnancy *Dosing in Pregnancy* Insufficient data to make dosing recommendation Standard Adult Doses *(FTR) Rukobia* • FTR 600 mg twice daily with or without food	No human data are available regarding placental passage. A study in rats demonstrates placental passage of temsavir or other metabolites. Insufficient data to assess for teratogenicity in humans. No evidence of teratogenicity in rats or rabbits.

[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 11).

Key: ARV = antiretroviral; FTR = fostemsavir; PK = pharmacokinetic

References

1. Antiretroviral Pregnancy Registry Steering Committee. Antiretroviral Pregnancy Registry international interim report for 1 January 1989–31 January 2022. Wilmington, NC: Registry Coordinating Center; 2022. Available at: http://www.apregistry.com/forms/interim_report.pdf.

2. Fostemsavir (Rukobia) [package insert]. Food and Drug Administration. 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212950s000lbl.pdf.