Doravirine (Pifeltro, DOR)

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Animal Studies

Carcinogenicity

Doravirine (DOR) was not carcinogenic in long-term oral carcinogenicity studies in mice and rats at exposures up to six times and seven times, respectively, the exposure seen in humans who received the recommended dose. A statistically significant incidence of thyroid parafollicular cell adenoma and carcinoma was observed among female rats that received the high dose (which produced the sevenfold increase in exposure) of DOR; however, the incidence was similar to the incidence observed among historical controls that did not receive DOR. DOR was not genotoxic in a battery of *in vitro* or *in vivo* mutagenicity assays.[1]

Reproduction/Fertility

In rats, DOR did not affect fertility, reproductive performance, or early embryonic development at exposures (based on area under the curve [AUC]) that were approximately seven times the exposure seen in humans who received the recommended dose.[1]

Teratogenicity/Adverse Pregnancy Outcomes

No adverse embryo-fetal effects were observed in rats and rabbits at DOR exposures (based on AUC) that were approximately nine times (in rats) and eight times (in rabbits) the exposures seen in humans who received the recommended dose. Similarly, no adverse developmental findings were reported in a prenatal/postnatal study in rats at DOR exposures that were approximately nine times the exposure seen in humans who received the recommended dose.[1]

Placental and Breast Milk Passage

Embryo-fetal studies in rats and rabbits demonstrate placental passage of DOR. Fetal plasma concentrations observed on gestation Day 20 were up to 40% (in rabbits) and 52% (in rats) of maternal concentrations. DOR was excreted into the milk of lactating rats at concentrations that were approximately 1.5 times the maternal concentrations measured 2 hours post-dose on lactation Day 14.[1]

Human Studies in Pregnancy

Pharmacokinetics

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

Placental and Breast Milk Passage

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

Teratogenicity/Adverse Pregnancy Outcomes

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

Excerpt from Table 10

Note: When using FDC tablets, refer to other sections in Appendix B and Table 10 for information about the dosing and safety of the individual drug components of the FDC tablet during pregnancy.

Generic Name (Abbreviation) *Trade Name*	**Formulation**	**Dosing Recommendations**[a]	**Use in Pregnancy**
Doravirine (DOR) *Pifeltro* (DOR/3TC/TDF) *Delstrigo*	**DOR (Pifeltro):** • 100 mg tablet **DOR/3TC/TDF (Delstrigo):** • DOR 100 mg/3TC 300 mg/TDF 300 mg tablet	**Standard Adult Doses** *DOR* (*Pifeltro*): • DOR 100 mg once daily with or without food *DOR/3TC/TDF* (*Delstrigo*): • One tablet once daily with or without food **Pregnancy** *PKs in Pregnancy:* • No PK studies in human pregnancy *Dosing in Pregnancy:* • Insufficient data to make dosing recommendations For guidance about use of combination products in pregnancy, please see the specific sections on other components (i.e., 3TC, TDF).	No data are available on the placental transfer of DOR in humans, but animal studies suggest that DOR crosses the placenta. 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 10).

Key: 3TC = lamivudine; ARV = antiretroviral; DOR = doravirine; FDC = fixed-dose combination; PK = pharmacokinetic; TDF = tenofovir disoproxil fumarate

References

1. Doravirine (Pifeltro) [package insert]. Food and Drug Administration. 2019. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/210806s003lbl.pdf.