

Safety of Drugs Used for Inflammatory Bowel Disease in Special Populations

Drug	FDA pregnancy category	Use in pregnancy	Lactation risk ^{1*}	Use in lactation**
Mesalamine	Oral B, Rectal C	No increased risk of fetal malformations. Possible risk of preterm delivery, but this is confounded by the disease process. ²⁻⁴	L3	RID is 0.1-8%. Observe for vomiting and watery diarrhea. ⁵⁻⁸
Sulfasalazine	B	No apparent increase in risk of fetal malformations. Sporadic reports of neural tube defects, fetal anemia, and neutropenia exist in the literature. Folate supplementation recommended with this drug. ⁹⁻¹³ No increased risk of neonatal hyperbilirubinemia when exposed to this drug in the 3 rd trimester. ¹⁴⁻¹⁶	L3	RID is 0.3-1%. Observe for vomiting and watery diarrhea. ^{6, 17-20}
Prednisone	C	Small increase (approx. 1 % above baseline) in the risk for cleft lip and/or palate with oral steroid use in the first trimester. Rare cases of premature birth and congenital cataracts associated with oral steroid use throughout gestation. Neonates should be screened for adrenal insufficiency at birth. ²¹⁻²³	L2	RID is 2-5%. Observe for poor feeding, decline in linear growth rate. Pump and discard milk for 4 hours after oral dose to decrease infant exposure by 50%. ²⁴⁻²⁶
Budesonide	C	Causes fetal loss, low birth weight in animals. No human studies published. Neonates should be screened for adrenal insufficiency at birth. ²⁷	L3	No studies available. Brief half-life and low oral bioavailability (after the enteric coating is stripped off) support it being safe for breastfeeding. ²⁷
Azathioprine	D	Existing literature is conflicted regarding congenital malformations; no specific pattern of malformation has been reported.	L3	RID is 0.07-0.3%. Multiple trials suggest infant exposure is minimal with no adverse effects reported. ³²⁻⁴⁰ Monitor

		Increased risk of premature delivery, low birth weight, and depressed immunologic status in newborns following maternal treatment with azathioprine. Since untreated IBD also carries fetal risk, the benefits of the drug might exceed risk to the fetus. ^{11, 28-31}		infant for immunosuppression.
Infliximab	B	No controlled human studies or animal research available. Large case studies conclude there are no adverse effects. Discontinue use by the third trimester to prevent most trans-placental transfer. ^{31, 41, 42}	L3	RID is 0.3-0.7%. Infliximab has a very large molecular weight and very poor oral bioavailability, both properties that support its safety in breastfeeding. Studies show that little to none enters breastmilk with no adverse effects reported. Possible absorption pathway via neonatal Fc receptor. ⁴³⁻⁴⁶
Adalimumab	B	No controlled human studies or animal research available. Several small case reports suggest no adverse effects from this drug. Both the FDA and the European Crohn's Colitis Organisation consider adalimumab safe for pregnancy. ⁴⁷⁻⁵¹	L3	Same as Infliximab. ⁴⁴
Golimumab	B	No controlled human studies available. Drug was non-teratogenic in monkey models. ⁵²	L3	No human studies available. Drug detected in the milk of lactating monkeys. ⁵² Large molecular weight and poor oral bioavailability support its safety in breastfeeding. Possible absorption pathway via neonatal Fc receptor.
Methotrexate	X	Teratogen and abortifacient. Contraindicated in pregnancy. ^{53, 54}	L4	RID is 0.1%. Evidence of long-term tissue retention and toxicity. Pump and discard milk for 2-4 days to reduce infant exposure. Consider leucovorin prophylaxis in the infant. ^{11, 30, 55, 56}

Cyclosporin	C	May cause maternal nephrotoxicity and systemic hypertension; monitor renal function. Small studies suggest no increased risk of congenital anomalies. Cyclosporine suppresses the neonatal cellular immune system but does not appear to cause clinical immunosuppression. ^{31, 57-61}	L3	RID is 0.4-3%. A small number of case studies report milk levels of cyclosporine to be uniformly low and the dose transferred to the infant subclinical and undetectable. Infant drug monitoring is appropriate. ⁶²⁻⁶⁷
Tacrolimus	C	No increase in birth defects. Oral use associated with maternal nephrotoxicity and systemic hypertension; monitor renal function. Also linked to prematurity, low birth weight, hyperkalemia, and transient, decreased renal function in neonates. ⁶⁸⁻⁷³	L2	RID is 0.1-0.5%. Numerous case studies show very little transfers into milk and no adverse effects were reported in nursing infants. Product has poor oral bioavailability. ⁷⁴⁻⁷⁹
Ciprofloxacin	C	Studies conflict as to whether ciprofloxacin causes birth defects in humans. Consider using other antibiotics first. ⁸⁰⁻⁸⁴	L3	RID is 2-6%. The majority of infant exposure cases report no adverse effects. One case exists of pseudomembranous colitis associated with non-prescribed use of the drug. ⁸⁵⁻⁸⁹
Metronidazole	B	No increase in birth defects if taken in typically prescribed doses. ^{90, 91}	L2	RID is 12-24%. Typical adult doses produce breastmilk levels that are below the therapeutic dose for infants. No adverse effects have been reported at these levels. ⁹²⁻⁹⁵

*Lactation risk is divided into 5 categories: L1 = "Safest," L2 = "Safer," L3 = "Probably compatible," L4 = "Possibly hazardous," L5 = "Hazardous." Any medication without data and thought to be theoretically safe is an L3.

**The Relative Infant Dose (RID) is the percentage of the mother's daily medication dose that will be ingested by the baby. This calculation uses a maternal weight of 70 kg and a daily milk intake of 150 mL/kg/day by the infant. Toddlers consume markedly less milk relative to their body weight. Oral bioavailability of the drug in the infant is not a part of the RID

calculation. Many experts agree that most drugs with an RID <10% are generally considered compatible with breastfeeding. Toxicity (or non-toxicity) of the medication in infants should also be considered.

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