# Status of studies on monoclonal antibody therapies (biologics) and asthma during pregnancy

American Academy of Allergy Asthma & Immunology

Monoclonal antibodies are known to be transported across the placenta during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy. This table presents the available human and animal safety data for biologics used for asthma and allergic diseases during pregnancy and lactation.

| | Mode of Action | Human Studies | Animal Studies | Lactation Studies | Registries |
|---|---|---|---|---|---|
| Omalizumab (XOLAIR)<br>Approved by FDA in 2003<br>**Moderate to severe asthma, nasal polyps, chronic urticaria** | Blocks IgE binding to mast cell, basophil, dendritic cells and downregulate IgE receptor | EXPECT Registry: observational study published in 2014 with 188 women exposed to omalizumab during the first trimester. There were 160 live births, 11 spontaneous abortions, 1 elective termination and 1 still birth out of 169. There were a total of 20 total congenital anomalies and 7 with single major defect. There was no pattern of anomalies. A follow-up study in 2019 with 250 women and 1153 disease matched comparators found there was no evidence of increased risk of major congenital anomalies for women exposed to omalizumab compared to unexposed control group with moderate to severe asthma. | | A case report showed that omalizumab can cross the placenta and when compared to maternal serum, 12 weeks after last dose of omalizumab, the breast milk contained 1/10,000 to 1/1000 of omalizumab | Registries closed |
| Mepolizumab (NUCALA)<br>Approved by FDA in 2015<br>**Severe eosinophilic asthma, eosinophilic granulomatosis with polyangiitis, hypereosinophilic syndrome, nasal polyps** | Interleukin 5 (IL-5) antagonist monoclonal antibody | There are 2 case reports of first trimester exposure with mepolizumab. In the first case, the mother decided to stop mepolizumab therapy, experienced increasing severity of asthma with poor control requiring systemic corticosteroids but delivered a healthy baby. The second case involved the mother deciding to terminate the pregnancy due to unknown teratogenic risk.<br>Lactation: Levels of mepolizumab in milk were <0.5% of maternal serum concentration | Pregnant cynomolgus monkeys receiving mepolizumab from gestation days 20 to 140 at doses that produced exposures up to 9 times the maximum recommended human dose had no adverse effects on fetal or neonatal growth up to 9 months post-delivery. There were also no teratogenic effects observed. Mepolizumab crosses the placenta in cynomolgus monkeys and persist in infant circulation at 2.4 times higher levels compared to mothers.<br>CD-1 mice with wild type mice given murine IL-5 at IV dose of 50 mg/kg were noted to have no observed effect on fertility, early embryonic development. | | No longer enrolling |
| Reslizumab (CINQAIR)<br>Approved by FDA in 2016<br>**Severe eosinophilic asthma** | Humanized interleukin 5 (IL-5) monoclonal antibody | 24 days | Two embryo-fetal development studies of pregnant mice and rabbits receiving a single dose of reslizumab during organogenesis at 2, 10, and 50 mg/kg demonstrated that the drug was not teratogenic in mice or rabbits. Developmental studies of IL-5 deficient mice when compared to wild-type mice. Pregnant CD-1 mice receiving reslizumab during organogenesis on gestation days 6 and 18 and on postnatal day 14 at 10 or 50 mg/kg, did not have any effect on fetal development up to 3 approximately 4 months after birth. Reslizumab crossed the placenta of pregnant mice. Serum concentrations in pups were approximately 6 to 8% of those in the dams (parental female mice) on postnatal day 14. | Reslizumab is excreted in milk of lactating CD-1 mice that received reslizumab at 10 or 50 mg/kg during pregnancy on gestation days 6 and 18 and on postnatal day 14. Levels of reslizumab in milk were approximately 5-7% of maternal serum concentrations. It is not known whether reslizumab is present in human milk, and the effects of reslizumab on the breast fed infant and on milk production are not known. | Not enrolling |

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| Benralizumab (FASENRA)<br>Approved by FDA in 2017<br>**Eosinophilic asthma** | Binds to IL-5 alpha receptor on eosinophils, signals natural killer cells to induce eosinophilic apoptosis | Case report in human: A single case of unexpected pregnancy while on treatment with benralizumab resulted in a late preterm birth with normal APGAR. Eosinophil count of the baby persisted to be 0 until 7 months of age. | In prenatal and postnatal developmental studies of cynomolgus monkeys exposed to 310 times higher doses of benralizumab approved for use in humans did not demonstrate any fetal harm. | Benralizumab is a humanized monoclonal antibody (IgG1/k) and IgG is present in breast milk. If benralizumab is transferred to breast milk, the effect of local exposure in the gastrointestinal tract and potential limited systemic exposure in the infant to benralizumab are unknown.<br>There is no information regarding the presence of benralizumab in human or animal milk, and the effects are not known. | www.mothertobaby.org |
| Dupilumab (DUPIXENT)<br>Approved by FDA 2017 for Atopic dermatitis, 2018 for asthma, 2019 for CRSwNP, 2022 for eosinophilic esophagitis | Fully human monoclonal antibody (IgG4) directed against IL-4R alpha subunit, leading to inhibition of IL-4 and IL-13 cytokine response and suppressing TH2 inflammation including the release of proinflammatory cytokines, chemokines, and IgE | Available data from case reports and case series with dupilumab use in pregnant women have not identified a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes. Human IgG antibodies are known to cross the placental barrier; therefore, dupilumab may be transmitted from the mother to the developing fetus<br>In a case series of males and female treated with dupilumab for atopic dermatitis and concurrent asthma during conception, pregnant patients decided male or female parent on the medication. All were prescribed the medication for atopic dermatitis, but when reported most had asthma and allergic rhinitis as well. Some described continued use from conception to delivery. Others describe cessation upon learning they were pregnant, still others continued but stopped prior to the 3rd trimester. Of those that reported it, none breastfeed the infant while on the medication. Reassuringly none reported teratogenic effects. All describe the infant as healthy. Of those that report the delivery, all babies were born at term | Pregnant cynomolgus monkeys administered weekly subcutaneous doses of homologous antibody against IL-4R up to 10 times the MRHD from the beginning of organogenesis to parturition showed no treatment-related adverse effects on embryo-fetal toxicity or malformations, or on morphological, functional, or immunological development were observed in the infants from birth through 6 months of age. | There is no data on the presence of dupilumab in human milk, the effects on the breastfed infant, or the effects on milk production. | www.mothertobaby.org |
| Tezepelumab (TEZSPIRE)<br>Approved by FDA in 2021<br>**Severe asthma** | A thymic stromal lymphopoietin (TSLP) blocker human monoclonal antibody | There are no available data on tezepelumab use in pregnant women to evaluate for any drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes. Placental transfer of monoclonal antibodies such as tezepelumab is greater during the third trimester of pregnancy; therefore, potential effects on a fetus are likely to be greater during the third trimester of pregnancy | In the ePPND study, pregnant cynomolgus monkeys received tezepelumab from GD20 to GD22, at the beginning of organogenesis, and once every 7 days until the end of gestation at doses that produced exposures up to 168 times that achieved with the MRHD. There were no tezepelumab related adverse effects on maternal health, pregnancy outcome, embryo-fetal development, or neonatal growth and development up to 6.5 months of age. Tezepelumab crossed the placenta in cynomolgus monkeys and tezepelumab serum concentrations were 0.5- to 6.7-fold higher in infants relative to maternal animals. | There is no information regarding the presence of tezepelumab in human milk, its effects on the breastfed infant, or its effects on milk production. Tezepelumab is a human monoclonal antibody immunoglobulin G2 (IgG2), and immunoglobulin G (IgG) is present in human milk in small amounts. Tezepelumab was present in the milk of cynomolgus monkeys postpartum following dosing during pregnancy | No registry |

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