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Analgesics in Pregnancy and Lactation

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The following chart includes information to help guide decisions regarding analgesic use in pregnancy and lactation. FDA pregnancy categories have several limitations and are not included. Topical analgesics are covered in our chart, *Topical Medications in Pregnancy and Lactation*.

NONOPIOIDS

Drug or Drug Class	Use in Pregnancy	Use in Lactation
Acetaminophen	• Generally considered the analgesic/antipyretic of choice in pregnant women, but use the lowest dose for the shortest duration necessary.[36] • For chronic use (e.g., >1 month), some (not all) limited observational studies in humans suggest an association with neurodevelopmental concerns (e.g., ADHD, autism).[1,4,11,12,22,28,29,34,35] • Some cohort evidence suggests an association with early puberty in girls, and cryptorchidism.[1,37]	• First-line analgesic for lactating patients.[17] • Amount in milk less than therapeutic doses given to infants.[2] • Case report of rash.[1]
NSAIDs and Aspirin	• Analgesic doses used around 20 weeks or later may cause perinatal renal impairment and/or oligohydramnios and its complications.[9,23] Consider ultrasound monitoring of amniotic fluid if used for >48 hours.[9] Increased risk of maternal and newborn hemorrhage.[1] • Third trimester use poses risk of premature closure of ductus arteriosus (30 weeks or later[9]) and inhibition of labor.[1] • Use of non-aspirin NSAIDs before week 20 possibly linked to miscarriage; data inconclusive.[6,7] • Modest association between use before 20 weeks and major birth defects, including heart defects, hypospadias, cleft palate +/- cleft lip, anencephaly, spina bifida, and gastroschisis.[6,8,31] If used, consider limiting use to <10 days.[31] • Low aspirin doses (e.g., 81 mg once daily) may have favorable risk/benefit for certain complicated pregnancies.[1,5,23] • There is no proof that topical NSAIDs are safter than systemic agents in pregnancy.	**Aspirin** • Hemolysis (in a glucose-6-phosphate dehydrogenase-deficient infant), metabolic acidosis, and thrombocytopenia reported.[2] • Theoretical risk of Reye's syndrome.[2] • Low-dose aspirin 81 mg once daily can be considered.[2] **NSAIDs** • Ibuprofen is the NSAID of choice: short half-life; amount in milk less than therapeutic doses given to infants.[2,17]

OPIOIDS IN PREGNANCY

- Opioids may pose teratogenic risks in the first trimester,[2] but absolute risk is generally considered low.[3,8,38] **See footnotes** b, d, and e for more information on birth defects from some large cohorts. Note there is no human data with tapentadol or oxymorphone.[1]
- Use the lowest dose that is effective for the shortest duration necessary.[3]
- Buprenorphine or methadone can be used during pregnancy for opioid use disorder.[24-26,32] Methadone has a higher risk of preterm birth than buprenorphine.[32]
- Opioid use during labor can cause fetal distress or neonatal respiratory depression.[1] Meperidine is not recommended during labor.[1] Newborns clear meperidine slowly and may experience respiratory depression or neurologic side effcts.[1]
- Although not a "typical" opioid, **tramadol** use near term is linked to respiratory depression and withdrawal in newborns.[1]
- Long-term opioid use during pregnancy may result in neonatal opioid withdrawal (abstinence) syndrome.[18] Symptoms of neonatal withdrawal include vomiting, diarrhea, poor feeding, irritability, tremor, and high-pitched crying.[18] Neonatal opioid withdrawal can be life-threatening and requires management according to protocols developed by neonatology experts.[19]

Drug	Use in LACTATION (also see footnote a)
Buprenorphine	• Poor oral absorption.[1] • Use considered "acceptable" based on use for opioid dependence.[2] • Extradural use for postpartum pain may suppress feeding.[2]
Butorphanol	• Poor oral absorption.[2] • Probably compatible with breastfeeding,[1] but no info with repeated, high, intravenous, or intranasal doses.[2] • Consider alternatives due to paucity of information, especially if nursing preterm infant or newborn.[2]
Codeine	• Not recommended (Canada: contraindicated).[15,21] Risk of fatal morphine (codeine metabolite) toxicity if the lactating person is an ultrarapid CYP2D6 metabolizer (**see footnote c**).[1]
Fentanyl	• Considered compatible with breastfeeding,[1] but try to limit use to only a few days at a low dose.[2] • Preterm infants have impaired fentanyl clearance.[2] • If used epidurally, may affect infant for first 24 hours and impair initial breastfeeding efforts if good support is not available.[2]
Hydrocodone	• Excessive sleepiness and cyanosis reported in two case reports.[2] • Active metabolite (hydromorphone) formed through CYP2D6 is more potent than oxycodone.[2] • Theoretical risk of hydromorphone (hydrocodone metabolite) toxicity if the lactating person is an ultrarapid CYP2D6 metabolizer (**see footnote c**).[2] • Limit daily dose 30 mg for 2 to 3 days.[2]
Hydromorphone	• Excreted in breast milk.[1] • Case report of excessive sleepiness, intermittent bradycardia, and apnea in infant.[2]
Meperidine	• Newborns have trouble clearing meperidine.[1] • Fentanyl preferred for intravenous or intramuscular use during lactation, especially if nursing a newborn or preterm infant.[2] • Higher risk vs morphine.[2] • Single dose for maternal anesthesia usually not problematic in older infants.[2] • Postpartum epidural PCA usually not sedating to breastfed infants.[2]
Methadone	• Probably compatible.[1] • Breast milk concentrations are too low to be relied upon to prevent neonatal abstinence syndrome.[1] • Other agents are preferred for pain control during breastfeeding.[2] • Initiation of methadone postpartum, or increasing the dose to >100 mg/day, poses a particular risk of infant sedation and respiratory depression, especially if the infant is opioid-naive.[2]
Morphine	• Newborns and young infants do not clear morphine as rapidly as adults.[2] Infant can have detectable morphine levels, which may be within the therapeutic range.[2] • Epidural administration leads to lower levels in milk than oral or intravenous administration.[2] • Limit use to 2 to 3 days at a low dose.[2]
Nalbuphine	• Poor oral absorption.[1] • Amount in milk less than therapeutic doses given to infants. Unlikely to affect infant.[2]
Oxycodone	• Accumulates in breast milk.[1] • May not be safer than codeine; one in five infants of moms taking oxycodone experience CNS depression, similar to codeine.[13] • Oxycodone elimination is impaired in young infants and varies interindividually.[2] • Theoretical risk of oxymorphone (oxycodone metabolite) toxicity if lactating person is a CYP2D6 ultrarapid metabolizer (see footnote c).[14] But oxycodone is metabolized mainly by CYP3A4 to a weak metabolite (noroxycodone).[13] • Limit daily dose to 30 mg for 2 to 3 days.[2]
Oxymorphone	• No data in humans.[1,2] • Probably excreted in breast milk.[2]
Tapentadol	• Potential to accumulate in breast milk based on physicochemical properties.[1]
Tramadol	• Not recommended (Canada: contraindicated) because tramadol and its active metabolite are excreted in breast milk.[20,30] • Tramadol has the same risks associated with ultrarapid CYP2D6 metabolism as codeine (**see codeine and footnote c**).[20,30]

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Footnotes

a. Reserve opioids for postpartum pain that can't be managed with acetaminophen or ibuprofen.[17] Use a low dose of a low-potency, short-acting opioid as needed for shortest time necessary.[17] Watch baby for limpness, difficulty feeding or breathing, or sleeping more than usual.[2]

b. Using data from the single-payer health system in Ontario, Canada, association was found between first trimester use of opioids and birth defects (2.8% vs 2% [unexposed]), including heart defects (e.g., ASD [tramadol], VSD [codeine], pulmonary artery stenosis) gastrointestinal malformations (e.g., hypertrophic pyloric stenosis), tongue tie, neoplasms (tramadol), urinary defects (tramadol), and genital defects (oxycodone).[33] Opioids represented in the study included **codeine, fentanyl, hydromorphone, meperidine, morphine, oxycodone, and tramadol**.[33]

c. Ultrarapid CYP2D6 metabolism occurs in up to 1% to 10% of white Europeans or North Americans; 3% to 4% of African Americans; 1% to 2% of Chinese, Japanese, and Koreans; and >10% of Oceanic, North African, Middle Eastern, and Puerto Rican populations, and Ashkenazi Jews.[20] In a US urban population, individuals identifying as Caucasian or Hispanic had an incidence of ~11%, with variability within subpopulations.[27]

d. The **Birth Defects Study (Pregnancy Health Interview Study)** found an odds ratio of 2.2 (95% CI 0.9 to 5.7) for risk of **neural tube defects** in women who took opioids in early pregnancy for pain.[9] The absolute risk of neural tube defects is low (four to six per 10,000 live births), so a two-fold increased risk would represent a small increase in absolute risk.[7] Opioids represented in the study included **buprenorphine, butorphanol, codeine, fentanyl, hydrocodone, hydromorphone, meperidine, morphine, nalbuphine, oxycodone, and tramadol**.[9]

e. In the **National Birth Defects Prevention Study**, associations were found between opioid use one and three months post-conception and heart defects, hydrocephaly, spina bifida, gastroschisis, glaucoma/anterior chamber defect, and cleft palate (hydrocodone).[8,10] However, the absolute risk is likely small (e.g., 0.06% increased risk of hypoplastic left heart syndrome).[10] Opioids represented in the study included **codeine, fentanyl, hydrocodone, hydromorphone, meperidine, methadone, morphine, oxycodone, and tramadol**.

Abbreviations: ASD = atrial septal defect; VSD = ventricular septal defect

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Glossary of Study Design and Statistical Terms

Absolute risk reduction: The absolute difference in rates of an outcome between treatment and control groups.[1] Example: A hypothetical clinical trial compares the effect of a new statin and placebo on the incidence of stroke. Over the course of the study, the incidence of stroke is 4% with the statin and 6% with placebo. The absolute risk reduction with the statin is 6% - 4% = 2%.

Bias: Flaws in the design or operation of a study that lead to results that are not truth.[2] Bias can occur at any point of a study. Some types include:[5]

- *Information bias*: systematic differences in collection and handling of data.
- *Confounding bias*: additional factors distort the interaction between the treatment and the outcome.
- *Selection bias*: Differences between treatment and control groups that result from the way patients were selected. Randomization and blinding should help prevent selection bias.

Blinding or Masking: May help reduce bias in a study. Blinding can be double-blind (where neither the investigator nor the patient knows who is assigned to which treatment group), single-blinded (one party is aware of treatment groups), or open-label. In an open-label study, patients and investigators know the treatment group assignments.[3,4]

Case-control study: Compares patients who have the outcome of interest (cases; often rare conditions) and patients without that outcome (controls) to look for causes or characteristics that are linked to the outcome. Case-control studies are retrospective and observational.[6]

Cohort study: Compares two groups (cohorts) of patients, one with exposure or risk factor and one which does not (control group). Cohort studies are observational studies.[6]

Composite endpoint: A combination of endpoints that each have a low incidence but together provide a single measure of effect. Individual outcomes within a composite endpoint should have similar value (e.g., cardiovascular death, myocardial infarction, and stroke.) Each component should be analyzed individually. Improvement in a single component can be responsible for statistical significance of a composite endpoint. A negative outcome for one component can negate or dilute the positive outcome for another component.[7]

Confidence Interval (CI): An estimate of the range within which the true treatment effect lies. The 95% CI is the range of values within which we are 95% certain that the true value lies. If the confidence interval for the difference in efficacy (a difference in means or proportions) between two treatments includes zero, then you cannot exclude the possibility that there is no difference in efficacy between treatments. The width of the CI is determined by the number of patients studied, the variability of the data, and the pre-set confidence level. The confidence level is usually set at 95%, but can range from 90% to 99%.[2]

Confounding factor: An additional factor (other than the treatment/intervention) in a study that affects the statistical outcome of a treatment/intervention. A confounding factor can make it appear that there is a direct relationship between two factors when, in reality, the confounder is responsible for the relationship.[2]

Crossover study: Two groups receive both interventions/treatments. Each group serves as their own control. Reduced variability means a smaller sample size is needed than for a parallel-group trial. The two treatments/interventions are usually separated by a washout period.[3,6]

Cross-sectional study: This type of study looks at a defined population at a single point in time; it is a snapshot of what is happening at that moment in time.[6]

Effectiveness: How well a drug or intervention works in every-day real-world use.[8]

Efficacy: How well a drug or intervention works under ideal circumstances, such as in a randomized controlled trial.[8]

Endpoint: Pre-determined outcome used to measure an outcome of benefit or safety. The primary endpoint addresses the most important question the study attempts to answer. Secondary endpoints address supportive questions.[8]

Heterogeneity: Measure of variability among studies in a meta-analysis or systematic review. Heterogeneity occurs when there is more variation between the study results than would be expected to occur by chance alone. Testing for heterogeneity helps determine if it's appropriate to combine studies.[2]

Incidence: The rate of newly diagnosed cases of a disease occurring in the population at risk during a specified period of time.[8]

Intention-to-treat analysis: A statistical analysis for randomized trials that includes all of the patients who were randomized to a treatment arm regardless of whether or not they finished the study. An intention-to-treat analysis is considered to mimic clinical practice more closely than an analysis that includes just the patients who completed the study.[2]

Meta-analysis: An analysis of pooled data from several studies, which all address the same clinical question. Criteria for study inclusion in the analysis are established beforehand. Meta-analysis can be used to increase sample size, statistical power, and/or allow for increased subgroup analysis. Analysis is considered reliable with rigorous methods and appropriate study inclusion.[8]

Non-inferiority study: Looks to see if a new treatment works not worse than an existing treatment based on prespecified outcomes. Often used when it would be considered unethical to randomize patients take a placebo. This type of study requires fewer patients to show a significant difference compared to a superiority study.[8]

Null hypothesis: Hypothesis that there is no statistical difference between treatment groups in a study.[9]

Number needed to harm (NNH): The number of patients treated with a specified therapy/intervention in order for one of them to have a bad outcome (i.e., harm), over a specified time period. Round calculation down to a whole number.[8]

Number needed to treat (NNT): The number of patients that need to be treated with a specified therapy/intervention in order for one patient to benefit from treatment over a specified time.[8] The NNT is the inverse of the absolute risk reduction (1 divided by absolute risk reduction expressed as a decimal or 100 divided by the absolute risk reduction expressed as a percentage). Must be calculated with statistically significant results. Takes into account the relative risks as well as the absolute risk of no treatment. NNT = 100/(% in control group - % in intervention group). Round the NNT up to a whole number.[10]

Observational study: Patients are not randomized to intervention or treatment groups. The investigators observe patients with a disease or outcome to assess outcomes. Examples are case-control studies, cross-sectional studies, and longitudinal studies (cohort study, panel study).[5]

Odds ratio (OR): The odds of an event occurring with or without a treatment/intervention. Odds ratios and relative risk are comparable when the outcome is rare. But the odds ratio can make risk appear greater when the disease or outcome is more common. In case-control studies evaluating the risk of an adverse effect, an odds ratio of 1 indicates that exposure to the drug is equally likely in cases and controls. If the odds ratio is greater than 1, the risk of exposure is greater in cases than controls. If the odds ratio is less than 1, the risk of exposure is smaller in cases than controls.[1,2]

p-value (probability-value): The level of statistical significance (i.e., the alpha). A value of $p<0.05$ means that the probability that the result is due to chance is less than 1 in 20. The smaller the p-value, the greater the statistical significance. The p-value does not provide any information about the size of an effect. It only describes the strength of the result.[11]

Point estimate: The result of a clinical trial or meta-analysis which is used as a best estimate of what the true value is in the population that the study sample came from.[12]

Positive predictive value: Proportion of people who actually have the disease when a diagnostic test is positive. Positive predictive value = (100 x true positive)/(true positive + false positive).[8]

Power: The ability of a study to detect a significant difference between treatment groups (i.e., the probability that a study will have a statistically significant result [$p<0.05$]). Accepted study power is usually set at 0.8 (80%). Power increases as sample size increases.[2]

Prevalence: The proportion of existing cases of a disease or condition in the population at risk at a given time. Prevalence = incidence/population or people at risk.[13]

Prospective study: Studies that begin in the present and will evaluate events as they occur in the future.[8]

Randomization: Provides each patient an equal chance of being assigned to any of the groups in a study, to avoid selection bias.[2]

Randomized controlled trial (RCT): A prospective study in which patients are randomized into treatment or control groups. These groups are followed up for the variables/outcomes of interest.[2]

Relative risk: The risk of an event in individuals in an exposure group compared with the risk of that event in a non-exposed group. In a clinical trial, this is the probability of an event in the treatment group divided by the probability of that event in the placebo group.[8]

Relative risk ratio: Ratio of relative risk rates with treatment vs. control group. A relative risk ratio of 1 indicates no association between treatment and outcome. A relative risk greater than 1 indicates a positive association between treatment and outcome. A relative risk less than 1 indicates a negative association between treatment and outcome.[1]

Relative risk reduction: Relative risk subtracted from 1.[1]

Retrospective study: Observational studies that look back in time to evaluate events that occurred in the past.[8]

Sample size: Calculated prior to initiation of a study based on the number of patients required for a study to have valid results. An increased sample size is required when differences between treatment groups are small, if the power of the study is set higher (e.g., 90% power instead of the standard 80%), as statistical significance increases (as in $p<0.001$ instead of $p<0.05$), and if there is more variability in the outcome being measured. The larger the sample size, the more narrow the confidence interval.[2]

Sensitivity: The true positive rate. Measure of how many people who test positive are actually positive. Sensitivity = (100 x true positives)/(true positives + false negatives).[8]

Sensitivity analysis: A statistical method to determine how sensitive the results of a study or systematic review are to changes in the data or methodology. This is particularly important to perform in meta-analyses. Looks at the main outcome with alternative assumptions (e.g., may exclude weaker studies).[2]

Significance: Results in a study are statistically significant if the p-value is less than the predetermined value (often $p<0.05$). Statistical significance is a measure of the probability that the observed results are an actual difference and are not due to chance. Study results are clinically significant if they are important enough to implement in clinical practice.[9]

Specificity: The ability of a diagnostic test to reliably rule out a disease. The proportion of patients without the target disease who have a negative test. Specificity = (100 x true negatives)/(true negatives + false positives).[8]

Subgroup analysis: Looks at outcomes in specific groups of patients within a study to determine if the observed outcome is consistent across groups. Subgroups can be by age, sex, concomitant medical conditions, or other characteristics.[2]

Superiority study: This type of study tests to see if a new treatment/intervention is better than an active treatment (e.g., standard of care) or control (e.g., placebo).[8]

Surrogate Endpoint: A surrogate endpoint is an endpoint that stands in for another endpoint. Examples include measurement of blood pressure as a surrogate for reducing cardiovascular events in patients with hypertension, or measurement of CD4 cell counts as surrogate for reducing mortality with antiretroviral therapy. Surrogate endpoints should measure an effect more quickly or easily and should be highly correlated to the clinical outcome it stands in for.[8]

Systematic review: Collection and review of all available studies addressing a particular clinical question. Pre-determined specific criteria and methods are used. A systematic review may include meta-analysis as a method of analyzing and quantifying the results.[2]

Type I error: To conclude there is a difference between treatments when there is really no difference between them; rejection of the null hypothesis when it is actually true.

Type II error: To conclude there is no difference between treatments when there really is a difference between them; accepting the null hypothesis when it is actually false. This type of error is common in clinical trials, often because they don't enroll enough patients.[2]

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Topical Medications in Pregnancy and Lactation

When pregnant or lactating women use topical medications, there is concern that the fetus or infant may be exposed. Some topical medications can be absorbed into the maternal circulation and cross the placenta or be excreted into breast milk. Nursing infants could also be exposed via direct contact with medications on the mother's skin. **Generally, avoid use of topical medications where the infant could come into contact with treated skin, or ingest the product directly (e.g., near the nipple)**.[6] Polymyxin B, nystatin, clotrimazole, miconazole, calcipotriene (calcipotriol) (without betamethasone), and low- or mid-potency corticosteroids can be applied to the nipple area, although excess cream should be removed before nursing.[6,8] Ointment could expose the child to high levels of mineral paraffins.[6] The table below lists topical medications that can be considered, or that should be avoided, during pregnancy and lactation. Each recommendation's rationale and additional clinically relevant information is given.

Drug Class, Topicals	Use in Pregnancy (rationale, additional information)	Use in Lactation (rationale, additional information)
Acne Medications	**Consider**: • Azelaic acid (minimal data; no known fetal effects; skin absorption 4% to 8%; ACOG-recommended)[8,20] • Benzoyl peroxide (low systemic absorption [5%]; ACOG-recommended)[8,20] • Clindamycin (low systemic absorption; no known association between topical use and malformations)[5,8,21] • Erythromycin (low systemic absorption; most data do not suggest risk with systemic use)[5,21] • Salicylic acid (amount absorbed less than with low-dose aspirin, which does not increase malformations or pregnancy complications; ACOG-recommended)[20,21] **Avoid**: • Retinoids (tretinoin, adapalene, tazarotene, "cosmeceutical" retinoids) (case reports of retinoid-like teratogenic effects with tretinoin; case report of ocular malformation with adapalene; tazarotene contraindicated [teratogenic in rats and rabbits]).[5,22] Check pregnancy test within two weeks before starting tazarotene, and start during normal menstrual cycle.[5] • Dapsone (better-studied options are preferred)[21]	**Consider**: • Azelaic acid (low systemic absorption [4% to 8%]; present in milk, wheat, rye, and barley naturally)[8] • Benzoyl peroxide (low systemic absorption [5%])[6,8] • Clindamycin (infant side effects unlikely; breast application could cause diarrhea)[6] • Erythromycin (infant side effects unlikely; breast application could cause diarrhea)[6] • Salicylic acid (unlikely to be significantly absorbed)[6] • Retinoids (tretinoin, adapalene, tazarotene) (tretinoin and adapalene poorly absorbed, but limit use of adapalene and tazarotene [e.g., apply tazarotene to no more than 20% of body surface area]).[6] **Avoid**: • Dapsone (case of hemolytic anemia in breastfed infant of mother taking oral dapsone; alternatives preferred).[5,6]

Drug Class, Topicals	**Use in Pregnancy (rationale, additional information)**	**Use in Lactation (rationale, additional information)**
Analgesics	**Consider**: • Lidocaine (*Lidoderm*) (systemic use compatible; low systemic absorption)[2,5] **Avoid**: • NSAIDs (constriction of ductus arteriosus reported with diclofenac)[3,4] • Salicylates (teratogenic effects and constriction of ductus arteriosus reported with methyl salicylate)[4]	**Consider**: • Diclofenac (low or undetectable levels in breast milk with systemic maternal use)[6] • Lidocaine (*Lidoderm*) (low levels in breast milk with systemic maternal administration; ingested lidocaine poorly absorbed by infant)[6] **Avoid**: Salicylates (no data)
Anesthetics	**Consider**: • Lidocaine (systemic use compatible)[5] • Dibucaine (systemic levels likely minimal)[13] • Pramoxine (not thought to be absorbed)[5] • Prilocaine (no fetal harm in rats)[13] • Benzocaine (absorption poor from intact skin, but avoid on mucous membranes or damaged skin due to paucity of data)[5]	**Consider**: • Pramoxine (not thought to be absorbed)[5] • Dibucaine (systemic levels likely minimal; unlikely to affect infant)[6,13] • Lidocaine (*Lidoderm*) (low levels in breast milk with systemic maternal administration; ingested lidocaine poorly absorbed by infant)[6] • Prilocaine (low excretion of anesthetics into breast milk)[6] • Benzocaine (absorption poor from intact skin, but avoid or limit use on mucous membranes or damaged skin)[5] **Note**: Avoid direct ingestion by infant.[6,17]
Antibiotics *Continued…*	**Consider**: • Bacitracin (data limited, but no association with malformations)[5] • Clindamycin, **topical** (low systemic absorption; conflicting first trimester data)[5,21] • Clindamycin, **vaginal** (per CDC, newer data demonstrate safety).[14] • Erythromycin, (low systemic absorption; most data do not suggest risk with systemic use)[5,21] • Metronidazole, **topical** (plasma level ~1% of peak level after a 250 mg oral dose)[6]	**Consider**: • Bacitracin (poor systemic absorption)[6] • Clindamycin, **topical** (low systemic absorption); unlikely to cause infant side effects[6,21] • Clindamycin, **vaginal** (30% absorbed, but unlikely to cause infant side effects[6]) • Erythromycin (low systemic absorption; infant side effects unlikely)[6,21] • Metronidazole (neither topical nor vaginal have been studied during breastfeeding. After vaginal administration, plasma levels are <2% of those after a

Drug Class, Topicals	**Use in Pregnancy (rationale, additional information)**	**Use in Lactation (rationale, additional information)**
Antibiotics, continued	• Metronidazole, **vaginal** for **bacterial vaginosis** (most data do not suggest significant risk).[5] • Mupirocin (low systemic absorption [<1%]; no fetal harm in rats or rabbits; quickly metabolized and eliminated)[5,6] • Neomycin (no association with malformations; risk of deafness not investigated, but expected to be small even with systemic maternal use)[5] • Polymyxin (no association with malformations)[5] **Avoid**: • Metronidazole, vaginal for **trichomoniasis** (ineffective).[14,15]	500 mg oral dose. After topical administration, blood levels are about 1% of the peak plasma levels after a 250 mg oral dose.)[6] • Mupirocin (low systemic absorption [<1%]; quickly metabolized and eliminated)[5,6] • Neomycin (clinically insignificant amounts expected in breast milk)[6] • Polymyxin (poor systemic absorption)[6]
Antifungals (topical, intravaginal) **Note**: a seven-day treatment course with a topical azole is recommended for vulvovaginal candidiasis during pregnancy.[14]	**Consider**: • Nystatin (topical antifungal of choice; no association with malformations; poorly absorbed from intact skin and mucosal membranes)[5,8] • Ciclopirox (minimal systemic absorption [1.3% with occlusion]; not teratogenic in animals)[5,9] • Clotrimazole (minimal absorption from skin and vagina; no association with malformations, but some evidence suggests vaginal use in the first trimester may be associated with pregnancy loss.)[5] See **note**. • Miconazole (small amounts absorbed from vagina; no association with malformations, but vaginal use in first trimester associated with pregnancy loss.)[5] See **note**. • Selenium disulfide/sulfide (limited data; short-term use acceptable)[8] • Terbinafine (minimal systemic absorption [<5%]; human data lacking, but not teratogenic in rats or rabbits; not a preferred option.)[5,8]	**Consider**: • Nystatin (an antifungal of choice; has the most data; poor absorption from intact skin and mucosal surfaces)[5,6,8] • Ciclopirox (minimal systemic absorption [1.3% with occlusion; likely safe])[5,6,9] • Clotrimazole (an antifungal of choice; has the most data; poor absorption from skin and vagina; likely safe)[5,6,8,9] • Miconazole (no data; poor absorption from skin and vagina; no risk expected)[5,6] • Selenium disulfide (a single case report of lactation suppression)[8,9] • Terbinafine (systemic absorption <5%; likely safe)[5,6,9]

Drug Class, Topicals	**Use in Pregnancy (rationale, additional information)**	**Use in Lactation (rationale, additional information)**
Antivirals	**Consider**: • Acyclovir (not associated with malformations)[5] **Avoid:** • Imiquimod (limited human data)[5]	**Consider**: • Acyclovir (even with the highest maternal systemic doses, the amount in breast milk is only about 1% of the typical infant dose)[6] • Imiquimod (poor systemic absorption; amount in breast milk probably clinically insignificant)[5,6]
Corticosteroids (ointments and creams)	**Consider**: • Low- to mid-potency agent (e.g., hydrocortisone) (not associated with malformations)[8] **Avoid**: • High-potency agents (e.g., clobetasol) (possible association with low birth weight)[8,10] See our chart, *Comparison of Topical Corticosteroids*, for help identifying low, medium, or high-potency agents (US)(Canada).	**Consider**: • Any (minimal risk of infant exposure, but prudent to use least potent agent necessary on smallest area necessary)[6,9] **Avoid:** • High-potency agent on nipples (case report of hypertension in infant)[9,10]
Hemorrhoid Products	**Consider** (for **external** application only[19])**:** • Anesthetics (see above) • Hydrocortisone[23] (see "Corticosteroids, above, for details) • Witch hazel[16,23] **Avoid:** • Phenylephrine (may reduce uterine blood flow; risk of minor malformations, inguinal hernia, and clubfoot with 1st trimester use of nasal spray)[5,23]	**Consider:** • Hydrocortisone (rectal cream or suppository poses very little risk to infant)[6] • Pramoxine (thought not to be absorbed)[5] • Phenylephrine (no human data; probably compatible, but could theoretically reduce milk supply)[5,6] • Witch hazel (insufficient evidence, but recommended in pregnancy)[16,23,24]

Drug Class, Topicals	**Use in Pregnancy (rationale, additional information)**	**Use in Lactation (rationale, additional information)**
Lice and Scabies Treatments	**Consider**: • Permethrin (≤2% absorbed; neither animal nor limited human data suggest risk to embryo or fetus; a preferred option for scabies or lice)[5,8] • Pyrethrins with piperonyl butoxide (poor absorption; a preferred option for lice)[5,8] • Crotamiton (<1% absorbed; considered safe)[8] • Ivermectin (no data for topical product; systemic administration teratogenic in animals at maternally toxic dose, but no evidence of teratogenicity in humans)[5] • Spinosad (*Natroba* [US]) (spinosad not systemically absorbed; also contains benzyl alcohol, but significant embryo/fetal exposure unlikely)[5] • Malathion (<10% absorbed; not teratogenic in rats or rabbits)[18] **Note**: CDC guidelines recommend permethrin or pyrethrin/piperonyl butoxide for public lice, and permethrin for scabies, in pregnant women.[14]	**Consider**: • Permethrin (minimal absorption [≤2%]; rapid metabolism; used in infants)[5,6] • Pyrethrins with piperonyl butoxide (poorly absorbed)[5] • Crotamiton (<1% absorbed; minimal data; likely safe)[8] • Ivermectin; no data for topical product, but poorly excreted into breast milk after oral administration)[6] • Spinosad (*Natroba* [US]) (spinosad not systemically absorbed; also contains benzyl alcohol, but significant infant exposure unlikely)[5] **Avoid**: • Malathion (<10% absorbed; limited data; may cause respiratory depression)[6,9] **Note**: CDC guidelines recommend permethrin or pyrethrin/piperonyl butoxide for public lice, or permethrin for scabies, in lactation.[14]
Nasal Sprays (cold, allergy)	**Consider**: • Saline nasal spray[12] • Beclomethasone (no association with malformations)[5,11] • Budesonide (extensive human safety data; ~20% absorbed; agent of choice)[5,7,11,12] • Ciclesonide (no human data; likely only minimal amounts cross the placenta)[5,11] • Flunisolide (limited human data (inhaled route); 50% of dose reaches systemic circulation, and amount reaching embryo/fetus may be even less)[5]	**Consider**: • Saline nasal spray[12] • Corticosteroid nasal sprays (amounts in breast milk probably too small to cause harm)[6] • Phenylephrine (less likely to reduce milk production than oral agent)[6] • Oxymetazoline (little expected to reach infant. Recommended over oral decongestants.)[6]

Drug Class, Topicals	Use in Pregnancy (rationale, additional information)	Use in Lactation (rationale, additional information)
	• Fluticasone (no risk identified with inhaled or nasal use; significant embryo/fetal exposure unlikely; considered safe)[5,11,12] • Mometasone (no human data; systemic absorption virtually undetectable; considered safe)[5.11] **Avoid**: • Phenylephrine (risk of minor malformations, inguinal hernia, and clubfoot with 1st trimester use; could reduce uterine blood flow)[5] • Oxymetazoline (potential risk of renal malformations with 2nd trimester use, and pyloric stenosis with 1st trimester use; could reduce uterine blood flow)[1,5] • Triamcinolone (association with respiratory tract defects)[5,11] • Xylometazoline (risk of pyloric stenosis with 1st trimester use; could reduce uterine blood flow)[1,5]	
Psoriasis Medications Continued…	**Consider**: • Moisturizer (considered safe)[10] • Low- to mid-potency topical corticosteroid (e.g., hydrocortisone) (not associated with malformations)[8,10] **Avoid**: • High-potency corticosteroid (e.g., clobetasol) (possible association with low birth weight)[8,10] • Calcipotriene/calcipotriol (fetal skeletal abnormalities in animals; could use small amount if no alternative)[8,10] • Calcineurin inhibitors (tacrolimus, pimecrolimus; little topical safety data available; oral tacrolimus associated with prematurity and low birth weight)[8,10] • Coal tar (mutagenic/carcinogenic)[8]	**Consider**: • Moisturizer (considered safe)[10] • Corticosteroids, any (minimal risk of infant exposure, but prudent to use least potent agent necessary on smallest area necessary)[6,9] • Tacrolimus (low systemic absorption)[5,6] • Pimecrolimus (low systemic absorption; high plasma protein binding [i.e., minimal passage into breast milk])[5,6] • Calcipotriene/calcipotriol (poor systemic absorption; vitamin D analogue; probably low risk)[5,6] **Avoid**: • Coal tar (mutagenic/carcinogenic; if absolutely needed, use on smallest area possible)[6]

Drug Class, Topicals	**Use in Pregnancy (rationale, additional information)**	**Use in Lactation (rationale, additional information)**
Psoriasis Medications, continued	See our chart, *Comparison of Topical Corticosteroids*, for help identifying low, medium, or high-potency agents (US)(Canada).	

Abbreviations: ACOG = American College of Obstetricians and Gynecologists

Users of this resource are cautioned to use their own professional judgment and consult any other necessary or appropriate sources prior to making clinical judgments based on the content of this document. Our editors have researched the information with input from experts, government agencies, and national organizations. Information and internet links in this article were current as of the date of publication.

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