Antibiotic and Antifungal Use During Pregnancy and Breastfeeding

Infections such as urinary tract infection, yeast infection, or upper respiratory infection are not uncommon in pregnant or lactating women. A list of antibiotics/antifungals and their safety profiles when used during pregnancy and lactation are included in the chart below. Overall, the rule of thumb is to avoid drug use during the 1st trimester and choose an older agent with the most fetal data indicating the drug is safe and effective. Keep in mind that all drugs carry some risk during pregnancy. **It is important to weigh the risks and benefits before recommending drug use during pregnancy.** Additional fetal monitoring may be warranted if exposure to agents of uncertain teratogenic potential has occurred. When an antibiotic is used during lactation, regardless of concentration excreted into breast milk, potential problems for the nursing infant include modification of bowel flora, direct effects on the infant (e.g., allergy or sensitization), and interference with the interpretation of culture results if a fever work up is required.

### Abbreviation
- AAP=American Academy of Pediatrics; BSA=body surface area; GI=gastrointestinal; IV=intravenous.

### Drug Use in Pregnancy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Pregnancy Category</th>
<th>Use in Pregnancy</th>
<th>Use in Lactation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>D</td>
<td>• See aminoglycosides.</td>
<td>• See aminoglycosides</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Studies in patients undergoing elective abortions in the 1st and 2nd trimesters indicate that amikacin distributes to most fetal tissues except the brain and cerebrospinal fluid.</td>
<td>• Amikacin is excreted into breast milk in low concentrations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• There are no known reports linking the use of amikacin to congenital defects.</td>
<td>• Ototoxicity not expected in infant since oral absorption of amikacin is low.</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>D</td>
<td>• In a large database review, a total of 38 cases and 42 controls were treated with aminoglycosides. The investigators concluded that there was no detectable teratogenic risk for structural defects for any of the aminoglycoside antibiotics.</td>
<td>• U.S./Canadian product labeling recommend against use during breastfeeding.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• There is a theoretical risk of vestibular and auditory dysfunction associated with aminoglycoside use. However, ototoxicity or nephrotoxicity have not been reported (see exceptions below) as an effect of <em>in utero</em> exposure.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Eighth cranial nerve toxicity in the human fetus is well known after exposure to certain aminoglycosides (see kanamycin and streptomycin), and all aminoglycosides could potentially cause this.</td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>B</td>
<td>• See penicillin derivatives.</td>
<td>• Excreted into breast milk in low concentrations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Amoxicillin has been used as a single 3 g dose for treatment of bacteriuria in pregnancy without causing fetal harm.</td>
<td>• AAP classifies amoxicillin as compatible with breastfeeding.</td>
</tr>
<tr>
<td>Amphotericin B (Abelcet, etc)</td>
<td>B</td>
<td>• There are no reports linking the use of amphotericin B with congenital defects.</td>
<td>• No human data.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Amphotericin B crosses the placenta to the fetus.</td>
<td>• U.S./Canadian product labeling recommends against use of drug while breastfeeding.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• In a large database review, none of the nine 1st trimester exposures to amphotericin B showed evidence of adverse fetal effects.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Amphotericin can be used during pregnancy in patients who will clearly benefit from the drug.</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Evaluate neonate for renal dysfunction &amp; hypokalemia if mother on chronic amphotericin B at delivery.</td>
<td></td>
</tr>
<tr>
<td>Ampicillin</td>
<td>B</td>
<td>• See penicillin derivatives.</td>
<td>• Excreted into breast milk in low concentrations.</td>
</tr>
<tr>
<td>Antifungal</td>
<td>Risk Level</td>
<td>Notes</td>
<td></td>
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<td>------------</td>
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</tbody>
</table>
| **Anidulafungin** *(Eraxis)* | C | - No human data; animal data suggest low risk.  
- It is best to avoid anidulafungin in pregnancy since there are no human pregnancy data. However, if the woman's condition requires it, the benefit probably outweighs the unknown risk.  
- If the decision is made to use anidulafungin, the lowest effective dose should be used.  
- Per IDSA, use with caution during pregnancy.  
Use not recommended per CDC.  
- The effects on a nursing infant are unknown, but dose-related histamine-mediated symptoms (rash, urticaria, flushing, pruritus, dyspnea, and hypotension) have been observed in adults receiving IV anidulafungin.  |
| **Azithromycin** *(Zithromax [U.S.]; generics [Canada])* | B | - Limited human data; animal data suggest low risk.  
- Animal studies using mice and rats treated with doses up to maternal toxic levels showed no impairment of fertility or harm to the fetus.  |
| **Azole antifungals** *(Topical)* | Refer to individual agents | - Prospective and observational studies involving the use of topical antifungals did not show an increased risk of major malformations with exposure during pregnancy anytime.  
(No human data for topical ketoconazole).  
- Topical (vaginal) use of azole antifungals (e.g., clotrimazole, miconazole, terconazole, etc) are considered therapy of choice to treat vaginal yeast infection during pregnancy.  
- Topical (vaginal) azole therapy should be recommended for 7 days instead of a shorter duration for vaginal yeast infections because of improved treatment success.  
- See individual agents. |
| **Aztreonam** *(Azactam)* *(U.S. only)* | B | - No human data; animal data suggest low risk.  
- Animal studies with pregnant rats and rabbits administered high IV doses at 15 times the maximum recommended human dose and five times the maximum recommended human dose, respectively, did not produce embryotoxic, fetotoxic, or teratogenic effects.  
- Limited human data.  
- Excreted into breast milk.  
- The AAP classifies aztreonam as compatible with breastfeeding.  
- Product labeling recommends not breastfeeding during treatment. |
| **Capreomycin** *(Capastat)* *(U.S. only)* | C | - No human data.  
- Similar toxicity concerns as that of aminoglycosides (e.g., cranial nerve VIII and renal).  
- Two sources state that capreomycin should be avoided during pregnancy due to potential of ototoxicity and deafness. Neither source cited pregnancy data involving capreomycin.  
(Black Box Warning indicates safety in pregnancy unknown.)  |
| **Caspofungin** *(Cancidas)* | C | - No human data; animal data suggest risk especially if exposure is during 1st trimester.  
- If indicated, maternal treatment should avoid the 1st trimester if possible.  
- Per IDSA, use with caution during pregnancy.  
- The risk of harm from exposure to caspofungin appears to be low.  
- Monitor infants for signs and symptoms of histamine release (e.g.,
<table>
<thead>
<tr>
<th>Drug</th>
<th>Classification</th>
<th>Notes</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Cefadroxil (Duricef [U.S.]; generics[Canada]) | B              | • See cephalosporins.  
• In a large database review of the 722 exposures to cefadroxil during the 1st trimester, a total of 27 major birth defects were observed (30 expected). However, these data do not support an association between the drug and congenital defects.  
• Excreted into breast milk in low concentrations.  
• AAP classifies cefadroxil as compatible with breastfeeding.  |
| Cephalosporins       | B              | • Cephalosporins as a class do not appear to cause fetal toxicity and are usually considered safe to use during pregnancy.  
• See individual drugs for more information.  |
| Cefazolin (Ancef [U.S.], Kefzol [U.S.]; generics [Canada]) | B              | • See cephalosporins  
• Cefazolin 2 g IV every 8 hours has been used in the treatment of pyelonephritis occurring in the second half of pregnancy. No adverse fetal outcomes attributable to cefazolin was observed.  
• Excreted into breast milk in low concentrations.  
• The AAP classifies cefazolin as compatible with breastfeeding.  |
| Cefdinir (Omnicef) (U.S. only) | B              | • See cephalosporins.  
• No human data.  
• In pregnant rats, oral doses up to 11 times the human dose based on body surface area were not teratogenic, but decreased fetal weight occurred at doses ≥ 1.1 times the human dose.  
• Cefdinir is expected to be excreted into breast milk due to its low molecular weight. However, it was not detected in breast milk after a single 600 mg oral dose.  
• The AAP classifies other cephalosporins as compatible with breastfeeding.  |
| Cefditoren (Spectracef) (U.S. only) | B              | • See cephalosporins.  
• No human data.  
• In pregnant rats and rabbits, doses up to about 24 and 4 times, respectively, the human dose of 200 mg twice daily based on BSA were not teratogenic.  
• No human data.  
• Cefditoren excretion in breast milk should be expected.  
• In most cases, the effects of this exposure will be insignificant.  
• The AAP classifies other cephalosporins as compatible with breastfeeding.  |
| Cefepime (Maxipime)  | B              | • See cephalosporins.  
• No adverse effects on fertility or reproduction, including embryo toxicity and teratogenicity, were observed in mice, rats, and rabbits dosed at 1 to 4 times the recommended maximum human daily dose based on BSA.  
• Cefepime is excreted in human milk in very low concentrations.  
• The AAP classifies other cephalosporin antibiotics as compatible with breastfeeding.  |
| Cefixime (Suprax)    | B              | • See cephalosporins.  
• In an observational cohort study, cefixime was taken during the 1st trimester in 11 pregnancies. The outcomes of these pregnancies included 2 spontaneous abortions, 1 elective abortion, 7 normal newborns (1 premature), and 1 unknown outcome.  
• No human data.  
• Cefixime excretion in breast milk should be expected.  
• The AAP classifies other cephalosporin antibiotics as compatible with breastfeeding.  |
<table>
<thead>
<tr>
<th>Drug Name (Brand Name)</th>
<th>B</th>
<th>Summary</th>
</tr>
</thead>
</table>
| Cefotaxime (Claforan)   | B | • See cephalosporins.  
• No detectable teratogenic risk with cefotaxime and other cephalosporin antibiotics was found in a large 2001 population-based, case-control study of pregnant women.  
• Cefotaxime is excreted into breast milk in low concentrations.  
• The AAP classifies cefotaxime as compatible with breastfeeding. |
| Cefotetan (Cefotan) (U.S. only) | B | • See cephalosporins.  
• Reproduction studies in rats and monkeys found no evidence of impaired fertility or fetal harm at doses up to 20 times the human dose.  
• Cefotetan is excreted into breast milk in low concentrations.  
• The AAP classifies other cephalosporin antibiotics as compatible with breastfeeding. |
| Cefoxitin (Mefoxin [U.S.]; generics [Canada]) | B | • See cephalosporins.  
• There were no apparent adverse effects noted in newborns exposed to cefoxitin via the transplacental route.  
• Cefoxitin is excreted into breast milk in low concentrations.  
• The AAP classifies cefoxitin as compatible with breastfeeding. |
| Cefpodoxime (Vantin) (U.S. only) | B | • See cephalosporins.  
• No human data.  
• Based on animal reproduction studies, there is no evidence of impaired fertility or reproductive performance (in rats) or embryo toxicity or teratogenicity (in rats and rabbits) at doses up to 2 times the human dose based on BSA.  
• Cefpodoxime is excreted into breast milk in low concentrations.  
• The AAP classifies other cephalosporin antibiotics as compatible with breastfeeding.  
• U.S./Canadian product labeling recommends against use of drug while breastfeeding. |
| Cefprozil (Cefzil [U.S.]; generics [Canada]) | B | • See cephalosporins.  
• No human data.  
• Reproduction studies found no evidence in animals of impaired fertility or fetal harm at doses of 8.5, 18.5, and 0.8 times, respectively, the maximum human daily dose based on BSA.  
• Cefprozil is excreted into breast milk in low concentrations.  
• The AAP classifies cefprozil as compatible with breastfeeding. |
| Ceftazidime (Fortaz) | B | • See cephalosporins.  
• Reproduction studies in mice and rats found no evidence of impaired fertility or fetal harm at doses up to 40 times the human dose.  
• Ceftazidime is excreted into breast milk in low concentrations.  
• The AAP classifies ceftazidime as compatible with breastfeeding. |
| Ceftibuten (Cedax) (U.S. only) | B | • See cephalosporins.  
• No detectable teratogenic risk with ceftibuten and other cephalosporin antibiotics was found in a large 2001 population-based, case-control study of pregnant women.  
• No human data, but presence of ceftibuten in milk should be expected.  
• The AAP classifies other cephalosporin antibiotics as compatible with breastfeeding. |
| Ceftriaxone (Rocephin [U.S.]; generics [Canada]) | B | • See cephalosporins.  
• In a large database review, of the 60 1st trimester exposures to ceftriaxone, 4 (6.7%) major birth defects were observed (3 expected), including 3 cardiovascular defects (1 expected). A possible association between ceftriaxone and cardiovascular defects is suggested, but other factors, such as the mother's disease, concurrent drug use, and chance, may be involved. Other  
• Ceftriaxone is excreted into breast milk in low concentrations.  
• The AAP classifies ceftriaxone as compatible with breastfeeding. |
Cefuroxime (Ceftin [U.S.]; generics [Canada])

| B | • See cephalosporins.  
|   | • In a large database review, of the 143 1st trimester exposures to cefuroxime, there were 3 (2.1%) major birth defects observed (6 expected). These data do not support an association between the drug and congenital defects.¹ |

Cephalixin (Keflex [U.S.]; generics [Canada])

| B | • See cephalosporins.  
|   | • In a large database review, of the 3613 1st trimester exposures to cephalixin, there were 176 (4.9%) major birth defects observed (154 expected). The data for total defects, cardiovascular defects, and oral clefts suggest an association between cephalixin and congenital defects, but other factors, such as the mother's disease, concurrent drug use, and chance, may be involved.¹  
|   | • In another large database review, no teratogenic risk was found to be associated with cephalixin use during pregnancy.⁴ |

Chloramphenicol

| C | • In a large database review, there were 98 1st trimester exposures and 348 anytime exposures to chloramphenicol. There was no evidence to suggest a relationship to large categories of major or minor malformations or to individual defects in either group.  
|   | • There is one report that cardiovascular collapse (gray syndrome) developed in babies delivered from a mother treated with chloramphenicol during the final stage of pregnancy.¹  
|   | • Chloramphenicol should be used with caution at term.³ |

Ciprofloxacin (Cipro [U.S.]; generics [Canada])

| C | • See fluoroquinolones.  
|   | • In a large database review, of the 132 1st trimester exposures to ciprofloxacin, there were 3 (2.3%) major birth defects observed (6 expected). These data do not support an association between the drug and congenital defects.¹  

Clarithromycin (Biaxin [U.S.]; generics [Canada])

| C | • Clarithromycin crosses the human placenta.  
|   | • A large database review reported exposure to clarithromycin during the 1st and 2nd trimesters (n=34) for upper respiratory infections. Among the 29 known pregnancy outcomes (5 were pending), there were 8 (28%) abortions (4 spontaneous/4 voluntary), 20 (69%) normal newborns, and 1 (3%) infant with a 0.5-cm brown mark on the temple. Although follow-up of the remaining newborns had not been long  

| C | • Cefuroxime is excreted into breast milk in low concentrations.¹  
|   | • The AAP classifies other cephalosporin antibiotics as compatible with breastfeeding.³  
|   | • Consider withholding breastfeeding per U.S./Canadian product labeling. |

| B | • Cephalixin is excreted into breast milk in low concentrations.  
|   | • The AAP classifies other cephalosporin antibiotics as compatible with breastfeeding.³ |

| C | • The AAP classifies chloramphenicol as an agent whose effect on the nursing infant is unknown, but may be of concern because of the potential for idiosyncratic bone marrow suppression.¹ |

| C | • The AAP classifies ciprofloxacin as compatible with breastfeeding.³ |

| C | • See fluoroquinolones.  
|   | • Limited human data; however, the amount of ciprofloxacin in breast milk does not appear to represent a significant risk to a nursing infant.¹  
|   | • The AAP classifies ciprofloxacin as compatible with breastfeeding.³ |

| C | • No human data.  
|   | • Because other macrolides are excreted in breast milk, the passage of clarithromycin into milk should be expected.¹  
|   | • The risk of clarithromycin to the nursing infant is probably minimal, but caution should be
enough to completely exclude the presence of congenital malformations, these outcomes do not appear to be different from those expected in a nonexposed population.¹
- Toxicity has been observed in animals. Per product labeling, use only if necessary, especially during 1st three months gestation.²⁹,³⁰

### Clavulanic Acid (amoxicillin-clavulanate [Augmentin])

<table>
<thead>
<tr>
<th>Grade</th>
<th>Details</th>
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</table>
| B     | In a large database review, of the 556 1st trimester exposures to clavulanic acid, there were 24 (4.3%) major birth defects observed (24 expected).¹  
  - No adverse effects in the fetus or newborn attributable to the use of amoxicillin and potassium clavulanate were observed in several studies describing the antibiotic use in pregnant women.¹  
  - Avoid vaginal clavulanic acid in second half of pregnancy.¹  
  - There are no data on potassium clavulanate and nursing women.  
  - The effects of potassium clavulanate on the nursing infant are unknown.¹ |

### Clindamycin (Cleocin [U.S.]; generics [Canada])

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<thead>
<tr>
<th>Grade</th>
<th>Details</th>
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</table>
| B     | In a large database review, of the 647 1st trimester exposures to clindamycin, there were 31 (4.8%) major birth defects observed (28 expected). These data do not support an association between the drug and congenital defects.¹  
  - Avoid vaginal clindamycin in second half of pregnancy.¹  
  - Clindamycin is excreted into breast milk.¹  
  - The AAP classifies clindamycin as compatible with breastfeeding.³ |

### Clotrimazole (Topical/Vaginal) (Gyne-Lotrimin, etc. [U.S.]; Canesten, etc. [Canada])

<table>
<thead>
<tr>
<th>Grade</th>
<th>Details</th>
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</table>
| B     | See azole antifungals.  
  - Absorption of clotrimazole from the skin and vagina is minimal, posing little risk to the unborn baby.¹,⁸  
  - No adverse effects attributable to clotrimazole have been observed in studies.¹  
  - In a large database review, of the 2624 1st trimester exposures to clotrimazole, there were 118 (4.5%) major birth defects observed (112 expected). However, these data do not support an association between vaginal use of clotrimazole and congenital defects.¹  
  - It is doubtful that clotrimazole would appear in breast milk since its absorption through the skin and vagina is minimal.¹ |

### Cloxacillin (Cloxapen [U.S.]; generics [Canada])

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<thead>
<tr>
<th>Grade</th>
<th>Details</th>
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</table>
| B     | See penicillin derivatives.  
  - In a large database review, of the 46 trimester exposures to cloxacillin during the 1st trimester, there were 3 (6.5%) major birth defects observed (2 expected), including 2 cardiovascular defects (0.5 expected) and 1 hypospadias (none expected). Only with the former defect is there a suggestion of a possible association, but other factors, including the mother's disease, concurrent drug use, and chance, may be involved.¹  
  - No human data.  
  - Because other penicillins are excreted in breast milk in low concentrations, the presence of cloxacillin in breast milk should be expected.¹  
  - Also see ampicillin and penicillin G. |

### Dapsone

<table>
<thead>
<tr>
<th>Grade</th>
<th>Details</th>
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</table>
| C     | A number of studies have described the use of dapsone during all stages of human pregnancy. A few fetal or newborn adverse effects directly attributable to dapsone have been reported, but no congenital anomalies thought to be due to the drug have been observed.¹  
  - Neonatal hyperbilirubinemia has been reported (one case) with maternal dapsone use close to delivery.¹  
  - There is a case of hemolytic anemia in both mother and her infant. The mother was taking dapsone during the latter two-thirds of her pregnancy and during lactation.¹  
  - Although not citing the case of dapsone-induced hemolytic anemia in a mother, an infant has been reported.¹  
  - A number of reports have described the use of dapsone during all stages of pregnancy. These reports do not provide information on the effects of this exposure on the fetus and newborn.¹ |

### Clavulan Acid (amoxicillin-clavulanate [Augmentin])

<table>
<thead>
<tr>
<th>Grade</th>
<th>Details</th>
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</table>
| B     | In a large database review, of the 556 1st trimester exposures to clavulanic acid, there were 24 (4.3%) major birth defects observed (24 expected).¹  
  - No adverse effects in the fetus or newborn attributable to the use of amoxicillin and potassium clavulanate were observed in several studies describing the antibiotic use in pregnant women.¹  
  - Avoid vaginal clavulanic acid in second half of pregnancy.¹  
  - There are no data on potassium clavulanate and nursing women.  
  - The effects of potassium clavulanate on the nursing infant are unknown.¹ |
nursing infant described above, the AAP classifies dapsone as compatible with breastfeeding.¹,³
• U.S./Canadian product labeling recommends against use of drug while breastfeeding.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Rating</th>
<th>Notes</th>
</tr>
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</table>
| Daptomycin (Cubicin)        | B      | • No human data; animal data suggest low risk.¹  
• In animal studies, IV doses up to 3 (rats) and 6 (rabbits) times human dose based on BSA, no evidence of fetal harm was observed.¹  
• Vancomycin, an antibiotic with a similar spectrum and molecular weight (about 1486), is known to cross the human placenta late in the 2ⁿᵈ trimester to produce detectable concentrations in amniotic fluid.¹  
|                             |        | • No human data.  
• The high molecular weight should limit excretion into breast milk. However, vancomycin, an antibiotic with a similar spectrum and molecular weight is excreted into breast milk with concentrations nearly identical to the mother's trough serum concentration.¹  |
| Demeclocycline              | D      | • See tetracyclines.  
|                             |        | • See tetracyclines.  
|                             |        | • See tetracyclines.  
| Dicloxacillin (Dynapen, etc) | B      | • See penicillin derivatives.  
• Crosses the placenta into the fetal circulation and amniotic fluid. Levels are low compared with other penicillins due to the high degree of maternal protein binding.¹  
• In a large database review, of the 46 1ⁿᵗ trimester exposures to dicloxacillin, there was 1 (2.2%) major birth defect observed (2 expected).¹  
| (U.S. only)                 |        | • No human data.  
• Excretion of dicloxacillin into breast milk should be expected, since other penicillins are excreted into the breast milk in low concentrations.¹  |
| Doxycycline (Periostat, etc. [U.S.]; Doxycycline [Canada]) | D      | • See tetracyclines.  
|                             |        | • See tetracyclines.  
|                             |        | • See tetracyclines.  
| Ertapenem (Invanz)          | B      | • No human data.  
• No teratogenicity observed in mice and rats at 3 times the recommended human dose.¹  
• There is no evidence that any beta-lactam antibiotics cause developmental toxicity in humans at therapeutic doses. Therefore, it is probably safe to use ertapenem anytime during gestation if maternal condition requires its use.¹  
|                             |        | • Limited human data.  
• Ertapenem is excreted into breast milk based on reports of 5 nursing women treated with ertapenem.¹  
• The effects on a nursing infant are unknown, but are of doubtful clinical significance.¹  |
| Erythromycin (excluding estolate salt) | B      | • In a large database review, there were 79 1ⁿᵗ trimester exposures to erythromycin and 230 exposures for use at any time during pregnancy. There was no evidence to suggest a relationship to large categories of major and minor malformations or to individual defects.¹  
• In another large database review, of the 6972 1ⁿᵗ trimester exposure to erythromycin, there were 320 (4.6%) major birth defects observed (297 expected). However, these data do not support an association between the drug and congenital malformations.¹  
|                             |        | • Erythromycin is excreted into breast milk.¹  
• The AAP classifies erythromycin as compatible with breastfeeding.³  |
| Erythromycin estolate (generics[Canada]) | N/A    | • Approximately 10% of 161 women treated with the estolate salt of erythromycin in the 2ⁿᵈ trimester had abnormally elevated levels of  
|                             |        | • See erythromycin.  

¹AAP: American Academy of Pediatrics, B: Breastfeeding, D: Discontinue, N/A: Not Available, U.S.: United States
<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Notes</th>
</tr>
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<tbody>
<tr>
<td>Ethambutol (Myambutol [U.S.; Etibi [Canada])</td>
<td>C</td>
<td>• Ethambutol, isoniazid, and rifampin combination are considered the safest option for treatment of tuberculosis.1,22 • Ophthalmic abnormalities have occurred in infants born to women on antituberculosis therapy that included ethambutol.27 There are no reports of long-term follow-up examinations for ocular damage.1 • High doses teratogenic in animals.27,37 No evidence of teratogenicity in humans.1,37 Avoid in 1st trimester if possible.27</td>
</tr>
<tr>
<td>Ethionamide (Trecator) (U.S. only)</td>
<td>C</td>
<td>• Of the 5 human studies describing the outcome of pregnancies exposed to ethionamide, only one of the studies found an increased incidence of birth defects (2 cases of Down's syndrome from 23 exposed infants). The other reports found no association with congenital malformations.1 • Animal studies suggest teratogenic potential. Do not use in women who are pregnant or likely to become pregnant unless use is essential.18,37</td>
</tr>
<tr>
<td>Fluconazole (Diflucan [U.S.; generics [Canada])</td>
<td>C</td>
<td>• There are several reports of women treated with 400 mg to 800 mg of fluconazole orally daily throughout the 1st trimester. One of the women continued the treatment until delivery. The infants were born with grossly dysmorphic features including malformations in the head, face, and extremities.1 • In a retrospective review of 289 pregnant women treated with either a single dose of fluconazole 150 mg (n=275), multiple 50 mg doses (n=3), or multiple 150 mg doses (n=11) during or shortly before pregnancy for vaginal candidiasis, anomalies were only observed in four infants. In each of the four cases with congenital anomalies, the mother had taken fluconazole before conception for 1 to 26 weeks before the last monthly menstrual period.1 • The use of fluconazole during the 1st trimester appears to be teratogenic with continues daily doses of 400 mg/day or more according to the limited data.1 • Currently, there is no evidence of increased risk of major malformations associated with short-term use of 150 mg of fluconazole.8 • For vaginal candidiasis, only topical azoles are recommended for use in pregnancy.19,20 • Generally avoid in pregnant women per IDSA.36</td>
</tr>
<tr>
<td>Fluoroquinolones</td>
<td>C</td>
<td>• Concerns regarding the safety of fluoroquinolones originated from reports of arthropathy in animal studies; however, such</td>
</tr>
</tbody>
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1,29 It is recommended that pregnant women avoid erythromycin estolate due to potential for hepatotoxicity.1

Fluoroquinolones C

• Concerns regarding the safety of fluoroquinolones originated from reports of arthropathy in animal studies; however, such

• See individual agents.

• U.S./Canadian product labeling recommends against use of drug while breastfeeding.
reports are rare in human cases.\(^5,6\)

- In a 1993 review on the safety of fluoroquinolones, the authors concluded that fluoroquinolones should be avoided during pregnancy because of the difficulty in extrapolating animal mutagenicity results to humans and because interpretation of this toxicity is controversial. The authors were not convinced that fluoroquinolone-induced fetal cartilage damage and subsequent arthropathies were a major concern in humans.\(^7\)
- Data from a prospective follow-up study conducted by the European Network of Teratology Information Services (ENTIS), data on 549 pregnancies exposed to fluoroquinolone (levofloxacin=0; ofloxacin=93) and data on another 116 prospective and 25 retrospective pregnancy exposures to fluoroquinolones were analyzed. Of the 666 cases with known outcomes, 32 (4.8\%) of the embryos, fetuses, or newborns had congenital malformations. From previous epidemiology data, the authors concluded that the 4.8\% frequency of malformations did not exceed the background rate.\(^1\)
- Because a causal relationship with some of the birth defects cannot be excluded, fluoroquinolones should be used with caution, especially during first trimester.\(^1\)
- Some have suggested that fluoroquinolones should be considered contraindicated in pregnancy because safer alternatives are usually available.\(^1\) Both CDC and Canadian STD guidelines consider quinolones to be contraindicated during pregnancy.\(^19,20\)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosfomycin (Mono uurol)</td>
<td>B</td>
<td>Fosfomycin has been used in all trimesters of pregnancy with no apparent harm to the fetus or newborn.(^1)</td>
</tr>
</tbody>
</table>
| Gemifloxacin (Factive) (U.S. only) | C        | See fluoroquinolones.  
It is unknown if gemifloxacin crosses the human placenta.  
Animal data from mice, rats, and rabbits show growth retardation of fetus.\(^1\) |
| Gentamicin         | D        | See aminoglycosides.  
Human data suggest low risk.\(^1\)  
Crosses the placenta into the fetal circulation and amniotic fluid.\(^1,2\) |

- No human data.  
- Because of its relatively low molecular weight, excretion into milk should be expected.\(^1\)  
- U.S./Canadian product labeling recommends against use of drug while breastfeeding.  
- No human data. See fluoroquinolones.  
- The AAP classifies both ciprofloxacin and ofloxacin as compatible with breastfeeding.\(^1\)
- See aminoglycosides.  
- Small amounts of gentamicin are excreted into breast milk and poorly absorbed by the nursing infant.\(^1\) The levels were low and not likely to cause clinical effects.\(^2\)  
- The AAP classifies gentamicin as compatible
<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Note</th>
<th>Note</th>
</tr>
</thead>
<tbody>
<tr>
<td>Griseofulvin (Fulvicin, etc)</td>
<td>C</td>
<td>• Limited human data; animal data suggest risk.(^1)</td>
<td>• No human data.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Griseofulvin is tumorigenic, embryotoxic, and teratogenic in some species of animals.(^1)</td>
<td>• The use of griseofulvin during breastfeeding is not recommended due to the tumorigenicity and other toxicities in animals.(^1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• In a large database review, of the 34 1(^{st}) trimester exposures to griseofulvin, there was 1 (2.9%) major birth defect observed (1 expected). The number of exposure is too small to draw any conclusions.(^1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Per product labeling, contraindicated during pregnancy.(^3)</td>
<td>• Limited human data.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Griseofulvin is tumorigenic, embryotoxic, and teratogenic in some species of animals.(^1)</td>
<td>• Small amount, comparable to those for other beta-lactam antibiotics, is excreted into breast milk.(^1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• In a large database review, of the 34 1(^{st}) trimester exposures to griseofulvin, there was 1 (2.9%) major birth defect observed (1 expected). The number of exposure is too small to draw any conclusions.(^1)</td>
<td>• The effects, if any, on a nursing infant are unknown.(^1)</td>
</tr>
<tr>
<td>Imipenem/cilastatin (Primaxin)</td>
<td>C</td>
<td>• Limited human data; animal data suggest low risk.(^1)</td>
<td>• Limited human data.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Crosses the placenta to the fetus.(^1)</td>
<td>• Small amount, comparable to those for other beta-lactam antibiotics, is excreted into breast milk.(^1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Animal studies in pregnant rabbits and rats showed no evidence of adverse fetal effect at doses up to 2 to 30 times the maximum human dose.(^1)</td>
<td>• The effects, if any, on a nursing infant are unknown.(^1)</td>
</tr>
<tr>
<td>Isoniazid</td>
<td>C</td>
<td>• In a large database review; of the 11 1(^{st}) trimester exposures, one (0.1) major birth defect was observed (0.5 expected).(^1)</td>
<td>• Both isoniazid and its metabolite acetylisoniazid are excreted in breast milk.(^1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Association between isoniazid and hemorrhagic disease of the newborn has been suspected in two infants. However, the mothers were also treated with rifampin and ethambutol. Although other reports of this potentially serious reaction have not been found, prophylactic vitamin K is recommended at birth.(^1)</td>
<td>• The AAP classifies isoniazid as compatible with breastfeeding.(^3)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The CDC recommends a combination of isoniazid (plus pyridoxine), rifampin, and ethambutol as treatment of choice for pulmonary tuberculosis during pregnancy and breastfeeding.(^22)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• The American Thoracic Society recommends use of the drug for tuberculosis occurring during pregnancy.(^1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• INH-induced hepatotoxicity more frequent during pregnancy/postpartum. Monthly LFTs recommended.(^37)</td>
<td></td>
</tr>
<tr>
<td>Itraconazole (Sporanox)</td>
<td>C</td>
<td>• In an observational cohort study, itraconazole was taken orally during the 1(^{st}) trimester in 41 pregnancies. The outcomes of these pregnancies included 1 ectopic pregnancy, 2 spontaneous abortions, 6 elective abortions, 2 cases lost to follow-up, and 30 normal newborns (1 premature). One of the normal full-term newborns had a minor congenital anomaly (thin, prominent, and protruding left ear).(^1)</td>
<td>• Limited human data; potential toxicity.(^1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Another azole antifungal, fluconazole, has demonstrated possible dose-related association with major malformations. Therefore, is best to avoid itraconazole during organogenesis (1(^{st}) trimester).(^3)</td>
<td>• Itraconazole is excreted into breast milk.(^1)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Per IDSA, itraconazole should generally be avoided in pregnant women.(^36)</td>
<td>• The potential effects of itraconazole exposure to nursing infants have not been studied, therefore, women taking itraconazole should probably not breastfeed.(^1)</td>
</tr>
<tr>
<td>Kanamycin (U.S. only)</td>
<td>D</td>
<td>• See aminoglycosides.</td>
<td>• See aminoglycosides.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Eighth cranial nerve damage has been reported</td>
<td>• Limited human data;</td>
</tr>
<tr>
<td>Drug</td>
<td>Category</td>
<td>In Utero Exposure</td>
<td>Breastfeeding Compatibility</td>
</tr>
<tr>
<td>------</td>
<td>----------</td>
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<td>-----------------------------</td>
</tr>
</tbody>
</table>
| Kanamycin | C | In utero exposure to kanamycin. | probably compatible. | 1
| | | In a retrospective survey of 391 mothers who had received kanamycin, 50 mg/kg, for prolonged periods during pregnancy, 9 (2.3%) children were found to have hearing loss. | Kanamycin is excreted into breast milk. | 1
| | | Except for ototoxicity, no reports of congenital defects due to kanamycin have been located. | Ototoxicity not expected in infant since oral absorption of kanamycin is low. | 1
| | | The AAP classifies kanamycin as compatible with breastfeeding. | | 3
| Ketoconazole (Oral) (Nizoral, etc) | C | Ketoconazole is embryotoxic and teratogenic in rats at a dose 10 times the maximum recommended human dose based on weight. | Ketoconazole is excreted into breast milk. | 1
| | | In a large database review, of the 20 1st trimester exposures to oral ketoconazole, no major birth defects were observed (one expected). Since the study, the FDA has received 6 reports of limb defects. | The effects on the nursing infant from exposure to ketoconazole in the milk are unknown. | 1
| | | Generally avoid in pregnant women. | The AAP classifies ketoconazole as compatible with breastfeeding. | 3
| | | The molecular weight is low enough that excretion into breast milk should be expected. | U.S./Canadian product labeling recommends against use of drug while breastfeeding. | 1
| Levofloxacin (Levaquin) | C | See fluoroquinolones. | See fluoroquinolones. | 1
| | | Human data suggest low risk. | Limited human data. | 1
| | | Levofloxacin should be use with caution during pregnancy, especially during the 1st trimester. | The use of levofloxacin during lactation was not recommended when the product was first marketed due to the potential of arthropathy and other toxicity in the nursing infant. | 1
| | | U.S./Canadian product labeling still recommend against use while breastfeeding. | Photosensitivity has also been reported in nursing infants who have been exposed to levofloxacin via breastfeeding. | 1
| | | The AAP classifies both ciprofloxacin and ofloxacin as compatible with breastfeeding. | | 3
| Linezolid (Zyvox [U.S.]; Zyvoxam [Canada]) | C | No human data. | No human data. | 1
| | | No evidence of teratogenicity was observed in mice and rats at doses 4 and 1 times the expected human exposure based on AUC, respectively. However fetal toxicity (embryodeath, total litter loss, decreased fetal weight, and an increased incidence of costal cartilage fusion) were observed at this dose. | The molecular weight is low enough that excretion into breast milk should be expected. | 1
| | | It is unknown if linezolid crosses the human placenta. However, the molecular weight is low enough that transfer to the fetus should be expected. | Because myelosuppression has occurred in dogs and rats and reversible thrombocytopenia in adult humans, women taking linezolid should probably not breastfeed. | 1
| | | If no other alternatives are available and linezolid must be used, the maternal benefit | | 1

References:
<table>
<thead>
<tr>
<th>Medication</th>
<th>Category</th>
<th>Notes</th>
<th>Notes</th>
</tr>
</thead>
</table>
| Meropenem     | B        | • No human data; animal data suggest low risk.  
• Animal studies in rats and cynomolgus monkeys at doses up to 1.8 and 3.7 times, respectively, the usual human dose found no evidence of impaired fertility or fetal harm.  
• The fetal risk of use before 28 weeks of gestation is unknown. | • No human data.  
• The potential effects, if any, on nursing infants are unknown. |
| Metronidazole | B        | • In a large database review, 31 who had 1st trimester exposure to metronidazole. A possible association with malformations was found based on defects in 4 children (RR=2.02), but independent confirmation is required.  
• In another large database review, of the 2445 1st trimester exposures to metronidazole, there were 100 (4.1%) major birth defects observed (97 expected). Only with oral clefts is there a suggestion of possible association.  
• Oral metronidazole is contraindicated during the 1st trimester in patients with trichomoniasis per U.S. product labeling. (Note: Canadian product labeling and some U.S. products consider drug contraindicated during 1st trimester regardless of indication.)  
Metronidazole use during 2nd and 3rd trimester for trichomoniasis or bacterial vaginosis is acceptable.  
• For other indications, metronidazole can be used during pregnancy if there are no other alternatives.  
• Some recommend routine screening for and treatment of asymptomatic bacterial vaginosis only if patient high-risk for preterm birth.  
• Considered safe for use during pregnancy per CDC/Canadian STD guidelines.  
• Metronidazole is excreted into breast milk.  
• Unnecessary exposure to metronidazole should be avoided since the drug is mutagenic and carcinogenic in some test species.  
• If a single 2 gram oral dose of metronidazole is used for trichomoniasis, the AAP recommends discontinuing breastfeeding for 12-24 hours to allow excretion of the drug. | • Metronidazole is excreted into breast milk.  
• Unnecessary exposure to metronidazole should be avoided since the drug is mutagenic and carcinogenic in some test species.  
• If a single 2 gram oral dose of metronidazole is used for trichomoniasis, the AAP recommends discontinuing breastfeeding for 12-24 hours to allow excretion of the drug. |
| Micafungin     | C        | • No human data; animal data suggest moderate risk.  
• Per IDSA, use with caution during pregnancy.  
Use not recommended per CDC. | • No human data.  
• The high molecular weight, low lipid solubility, and very high protein binding suggests that excretion into breast milk will be limited. However, the drug is excreted into the milk of lactating rats. |
| Miconazole    | C        | • See azole antifungals.  
• Miconazole is normally used as a topical antifungal and small amounts are absorbed from the vagina.  
• Use of miconazole vaginally has not been associated with increased congenital malformations.  
• In a large database review, of the 2092 1st trimester exposures to miconazole, the estimated relative risk for birth defects from the data was 1.02 (95% CI 0.9-1.2). No association | • No data available. |
was found between miconazole use and oral clefts, spina bifida, or cardiovascular defects. However, the possibility of an association with other specific defects cannot be excluded.\(^1\)
- If possible, avoid vaginal use in 1\(^{st}\) trimester.\(^3\)

<table>
<thead>
<tr>
<th>Drug</th>
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<tbody>
<tr>
<td>Minocycline (Solodyn, etc [U.S.]; generics [Canada])</td>
<td>D</td>
<td>See tetracyclines.</td>
</tr>
</tbody>
</table>
| Moxifloxacin (Avelox) | C | See fluoroquinolones.  
- Animal data showed growth retardation and delayed fetal skeletal development in rats exposed to moxifloxacin.\(^1\)  
- U.S./Canadian product labeling recommend against use of moxifloxacin while breastfeeding. |
| Nafcillin (Unipen, etc) (U.S. only) | B | See penicillin derivatives and Penicillin G.  
- No reports linking nafcillin use with congenital defects have been located.\(^1\)  
- The AAP classifies both ciprofloxacin and ofloxacin as compatible with breastfeeding.\(^3\)  
- U.S. product labeling recommends against use of moxifloxacin while breastfeeding. |
| Nitrofurantoin (Macrobid, Macrodantin [U.S.]; generics [Canada]) | B | Data suggest risk in 3\(^{rd}\) trimester.\(^1\)  
- Case-control studies and case series involving thousands of women who received nitrofurantoin in pregnancy reported no increase of major malformations among the newborns. In addition, a meta-analysis failed to show teratogenic risk with first-trimester use of nitrofurantoin.\(^5\)  
- In a large database review, of the 1292 1\(^{st}\) trimester exposures to nitrofurantoin, there were 52 (4.0%) major birth defects observed (55 expected). However, these data do not support an association between the drug and congenital defects.\(^1\)  
- A retrospective analysis of 91 pregnancies in which nitrofurantoin was used yielded no evidence of fetal toxicity. Other studies have also supported the safety of this drug in pregnancy.\(^1\)  
- Nitrofurantoin can theoretically induce hemolytic anemia in glucose-6-phosphate dehydrogenase (G-6-PD)-deficient patients and in patients whose red blood cells are deficient in reduced glutathione; however, cases of this toxicity are rare.\(^1,5\)  
- Contraindicated in pregnant women at term (38 to 42 weeks gestation), during labor and delivery, or when onset of labor is imminent.\(^1,21\)  
- Limited human data.  
- Nitrofurantoin is excreted into breast milk.\(^1\)  
- Based on measurement of nitrofurantoin excretion in milk, investigators estimated that if a 60 kg woman was taking nitrofurantoin 100 mg twice daily, the infant dose would be 0.2 mg/kg, or about 6% of the mother's weight-adjusted dose.\(^1\)  
- Although this exposure was thought to be low, nursing infants younger than 1 month of age and those with a high frequency of G-6-PD deficiency or sensitivity to nitrofurantoin may be at risk for toxicity.\(^1\)  
- The AAP classifies nitrofurantoin as compatible with breastfeeding.\(^3\)  
- U.S. product labeling recommends against use of drug while breastfeeding (Canadian labeling advises caution). |
| Norfloxacin (Noroxin [U.S.]; generics[Canada]) | C | See fluoroquinolones.  
- The use of norfloxacin during human gestation does not appear to be associated with an increased risk of major congenital malformations. However, a causal relationship with some of the birth defects cannot be established.\(^3\)  
- U.S. product labeling recommends against use of drug while breastfeeding (Canadian labeling advises caution).  
- See fluoroquinolones.  
- No human data.  
- Although it is not known whether norfloxacin is excreted into human milk, the high concentrations of norfloxacin in maternal milk may be at risk for toxicity.\(^1\) |

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Details</th>
</tr>
</thead>
</table>
| Nystatin | C | - Nystatin is poorly absorbed after oral administration and from intact skin and mucous membranes.  
- In a large database review of the 489 1st trimester exposures, a total of 20 (4.1%) major birth defects were observed (21 expected).  
- Topical nystatin is probably a safe alternative to topical azole antifungals for the treatment of vaginal yeast infections.  
- No association with the risk of major malformations have been observed in numerous trials.  
- Nystatin is poorly absorbed, if at all.  
- Excretion into breast milk is not expected.  
- The AAP classifies nystatin as compatible with breastfeeding. |
| Ofloxacin *(Floxin [U.S.]; generics [Canada])* | C | - See fluoroquinolones.  
- Although a number of birth defects have occurred in the offspring of women who had taken ofloxacin during pregnancy, the use of ofloxacin during human gestation does not appear to be associated with an increased risk of major congenital malformations.  
- A causal relationship with some of the birth defects cannot be excluded. Because of this and the available animal data, ofloxacin should be used with caution during pregnancy, especially during the 1st trimester.  
- See fluoroquinolones.  
- Limited human data.  
- Excreted into breast milk.  
- The use of ofloxacin during lactation was not recommended when the product was first marketed due to the potential of arthropathy and other toxicity in the nursing infant.  
- Photosensitivity has also been reported in nursing infants who have been exposed to ofloxacin via breastfeeding.  
- The AAP classifies ofloxacin as compatible with breastfeeding. |
| Oxacillin *(Bactocill, etc)* (U.S. only) | B | - See penicillin derivatives.  
- Crosses the placenta in low concentrations.  
- Oxacillin is excreted in breast milk in low concentrations. |
| Oxytetracycline | D | - See tetracyclines.  
- See tetracyclines. |
| Paromomycin *(Humatin)* | C | - See aminoglycosides.  
- Limited human data.  
- No reports linking this agent with congenital malformations have been located.  
- Two women, one at 13 weeks' and the other at 23 weeks' gestation, were treated for a symptomatic intestinal infection caused by *Giardia lamblia*. Both delivered normal female infants at term.  
- No human data.  
- Paromomycin excretion in human milk is not expected because the drug is not absorbed into the systemic circulation after oral dosing. |
| Penicillin G | B | - See penicillin derivatives.  
- In a controlled study, 110 patients received one to three antibiotics during the 1st trimester for a |
total of 589 weeks. Penicillin G was given for a total of 107 weeks. The incidence of birth defects was no different than in a nontreated control group.¹

| **Penicillin V** | B | • See penicillin derivatives.  
• In a large database review, of the 4597 1st trimester exposures to penicillin V, there were 202 (4.4%) major birth defects observed (195 expected). However, these data do not support an association between the drug and congenital defects.¹  
• Excreted into breast milk in low concentrations.² |
| **Penicillin Derivatives** | B | • Penicillins transferred to the fetus and amniotic fluid reach therapeutic levels.²  
• In a large database review, of the 3546 cases of 1st trimester exposure to penicillin derivatives and 7171 cases of exposures for use anytime during pregnancy, there was no evidence found to suggest a relationship to large categories of major or minor malformations or to individual defects.¹  
• Excreted into breast milk in low concentrations.¹,²  
• See individual agents for details. |
| **Piperacillin/Tazobactam (**Zosyn [U.S.], Tazocin [Canada])** | B | • Rapidly crosses the placenta to the fetus.¹  
• No reports linking the use of piperacillin with congenital defects in humans have been located.³  
• No adverse maternal or fetal effects have been observed when used between 24 and 35 weeks' gestation in women with premature rupture of the membranes to delay delivery.¹  
• Excreted into breast milk in low concentrations.¹ |
| **Posaconazole (**Noxafil [U.S.]; Posanol [Canada])** | C | • No human data; animal data suggest risk.¹  
• See fluconazole and itraconazole for related risks.  
• Avoid posaconazole during pregnancy, especially in the 1st trimester.¹  
• If use can't be avoided, use lowest dose possible.¹  
• Per IDSA, generally avoid in pregnant women.³⁶  
• No human data.  
• Excretion to breast milk should be limited due to its molecular weight, low metabolism, long elimination half-life, and high plasma protein binding.¹  
• The effects on the nursing infant is unknown, but it's been associated with hepatic toxicity, nausea, and vomiting in adults.¹  
• U.S./Canadian product labeling recommends against use of drug while breastfeeding.  
• The relatively high molecular weights for the two components suggest that only small amounts, if any, will pass into human milk.¹  
• Quinupristin/dalfopristin is not recommended during breastfeeding due to the potential of the development of resistance to quinupristin/dalfopristin.¹ |
| **Quinupristin/Dalfopristin (**Synercid)** (U.S. only)** | B | • No human data.  
• Quinupristin/dalfopristin crosses rat placenta and is expected to cross human placenta.¹  
• There is no evidence of impaired fertility or fetal harm in pregnant mice, rats, and rabbits at approximately 0.5, 2.5, and 0.5 times the human dose, respectively.¹  
• Because the indication for the combination involves potentially life-threatening infections, the maternal benefit of therapy appears to far outweigh the unknown embryo or fetal risk.¹  
• No human data; potential toxicity.³⁰  
• The relatively high molecular weights for the two components suggest that only small amounts, if any, will pass into human milk.¹  
• Quinupristin/dalfopristin is not recommended during breastfeeding due to the potential of the development of resistance to quinupristin/dalfopristin.¹ |
<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Notes</th>
</tr>
</thead>
</table>
| **Rifabutin** *(Mycobutin)* | B        | • No human data; animal data suggest low risk.  
• Animal studies showed that doses ≤40 times recommended human daily dose were not teratogenic in rats and rabbits, but the high dose caused a decrease in fetal viability.  
• It is unknown if rifabutin or its active metabolites crosses the human placenta. However, the low molecular weight, moderate plasma protein binding, high lipid solubility, and prolonged terminal half-life suggests that passage to the fetus will occur.  
• Therapy should not be withheld if maternal benefit outweighs the unknown fetal risk. |
| **Rifampin** *(Rifadin [U.S.]; Rofact [Canada])* | C        | • Teratogenicity in rodents has been reported with oral doses 15-25 times the human dose.  
• Studies with rabbits showed no evidence of teratogenicity.  
• In a large database review, of the 201st trimester exposures to rifampin, there were no major birth defects observed (one expected).  
• Rifampin can potentially cause hemorrhagic disease in the newborn and mother when given in the last few weeks of pregnancy. Prophylactic vitamin K is recommended to prevent this serious complication.  
• The CDC recommends a combination of isoniazid (plus pyridoxine), rifampin, and ethambutol as treatment of choice for pulmonary tuberculosis during pregnancy and breastfeeding.  
• One report described 9 malformations in 204 pregnancies that went to term (incidence=4.4%, which is similar to the expected frequency of defects in a healthy nonexposed population, but much higher than other tuberculosis patients [1.8%]). |
| **Rifapentine** *(Priftin)* *(U.S. only)* | C        | • Limited human data; animal data suggest risk.  
• When taken in the last few weeks of pregnancy, rifapentine may cause hemorrhage in both the mother and newborn (similar to that observed with rifampin). Prophylactic vitamin K recommended to prevent serious complication.  
• Avoid rifapentine during 1st trimester until more human data are available. |
| **Rifaximin**             | C        | • No human data; animal data suggest risk. |

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1. No human data.
2. The molecular weight, moderate plasma protein binding, and prolonged terminal half-life suggest excretion into milk should be expected.
3. Milk may be stained a brown-orange color.
4. Potential serious toxicity to the fetus include leucopenia, neutropenia, rash, etc. (U.S./Canadian product labeling recommends against use while breastfeeding.)
5. The AAP classifies rifampin as compatible with breastfeeding.
6. U.S./Canadian product labeling recommends against use of drug while breastfeeding.
<table>
<thead>
<tr>
<th>(Xifaxan) (U.S. only)</th>
<th>• Teratogenic in rats and rabbits. The adverse effects included cleft palate, agnathia, jaw shortening, hemorrhage, partially open eye, small eyes, brachygnathia, incomplete ossification, and increased thoracolumbar vertebrae. It is not known if rifaximin crosses the human placenta, but its molecular weight is low enough for passive transfer. Although the embryo/fetal risk is suspected to be low due to minimal absorption, rifaximin should be avoided during 1st trimester until human data are available.</th>
<th>• The molecular weight (about 786) is low enough for excretion into breast milk, but only very small amounts of the antibiotic are absorbed into the systemic circulation. The effects of this exposure on a nursing infant are unknown but appear to be negligible. Product labeling recommends against use of drug while breastfeeding.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Streptomycin</td>
<td>D</td>
<td>• See aminoglycosides. Several cases of maternal use of streptomycin during pregnancy resulted in infant ototoxicity have been reported. However, in general, the risk of congenital ototoxicity, cochlear or vestibular, from streptomycin is low, especially with careful dosage calculations and the duration of fetal exposure is limited. Except for eighth cranial nerve damage, no reports of congenital defects caused by streptomycin have been located. In a large database review, there were 135 1st trimester exposures to streptomycin and 355 exposures recorded for use any time during pregnancy. There was no evidence to suggest a relationship to large categories of major or minor malformations or to individual defects in either group. Avoid use during pregnancy if possible.</td>
</tr>
<tr>
<td>Sulbactam (ampicillin/sulbactam [Unasyn]) (U.S. only)</td>
<td>B</td>
<td>• Sulbactam is always given in combination with ampicillin. It has caused no harm in animal reproduction studies, but reports of human exposure in early gestation are lacking. However, none of the penicillins has been shown to be teratogenic. Sulbactam readily crosses the human placenta to the fetus. Although no direct adverse effects of this exposure on the fetus or newborn have been reported, use of ampicillin/sulbactam combination near delivery may result in superinfection with resistant bacteria in the newborn.</td>
</tr>
<tr>
<td>Sulfamethoxazole/trimethoprim (Bactrim DS, etc [U.S.]; generics [Canada])</td>
<td>C</td>
<td>• Sulfonamides as a group do not appear to pose a serious teratogenic risk. However, trimethoprim is a folic acid antagonist and its use in 1st trimester has been associated with structural defects (e.g., neural tube and cardiovascular defects). Sulfamethoxazole can persist in neonatal circulation for several days after delivery if taken near term and there is a theoretical risk of</td>
</tr>
<tr>
<td>Drug</td>
<td>Category</td>
<td>Notes</td>
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<td>----------------------------------------------------------------------</td>
</tr>
<tr>
<td>Sulfonamides</td>
<td></td>
<td>Increasing unbound bilirubin owing to competitive protein binding.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• In most cases, TMP-SMX should be avoided during the 1st trimester.</td>
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<td></td>
<td></td>
<td>• Per product labeling, TMP-SMX contraindicated during pregnancy.</td>
</tr>
<tr>
<td>Telithromycin (Ketek)</td>
<td>C</td>
<td>No human data; animal data suggest low risk.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Telithromycin may cause severe hepatocellular hepatitis that can be fatal.</td>
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<td></td>
<td>• Avoid use of telithromycin in human pregnancy until more data are available.</td>
</tr>
<tr>
<td>Terbinafine (Lamisil [U.S.]; generics [Canada])</td>
<td>B</td>
<td>No human data.</td>
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<tr>
<td></td>
<td></td>
<td>• No evidence of fetal harm has been found in animal studies at doses up to 12 times the maximum recommended human dose based on BSA in rats 9 times the maximum recommended human dose in rabbits.</td>
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<tr>
<td></td>
<td></td>
<td>• Product labeling recommends against use during pregnancy (oral or topical).</td>
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<tr>
<td>Terconazole (Terazol, etc)</td>
<td>C</td>
<td>No human data.</td>
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<td></td>
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<td>• See azole antifungals.</td>
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<td></td>
<td></td>
<td>• Terconazole is available as either a vaginal cream or suppositories and is absorbed into the systemic circulation in humans after vaginal administration.</td>
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<td></td>
<td></td>
<td>• In a large database review, of the 1167 1st trimester exposures to terconazole a total of 34 (2.9%) major birth defects were observed (48 expected). However, these data do not support an association between terconazole and congenital defects.</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>D</td>
<td>See tetracyclines.</td>
</tr>
<tr>
<td>Tetracyclines</td>
<td>D</td>
<td>• Contraindicated in 2nd and 3rd trimesters.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• However, evidence of embryotoxicity noted in animals treated early in pregnancy.</td>
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<td>• Tetracyclines, as a class, should not be used during pregnancy unless absolutely necessary.</td>
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<td></td>
<td></td>
<td>• Problems attributable to the use of the tetracyclines during or around the gestational period include: adverse effects on fetal teeth and bones, maternal liver toxicity, congenital defects, miscellaneous effects.</td>
</tr>
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<td>• In a large database review, there were 341 1st trimester exposures to tetracycline, 14 to chlortetracycline, 90 to demeclocycline, and 119 to oxytetracycline. For use anytime in pregnancy, 1336 exposures were recorded for tetracycline, 0 for chlortetracycline, 280 for demeclocycline, and 328 for oxytetracycline.</td>
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<td></td>
<td></td>
<td>• See individual agents.</td>
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<td></td>
<td></td>
<td>• Tetracycline is excreted into breast milk in low concentrations.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Theoretically, dental staining and inhibition of bone growth could occur in breastfed infants whose mothers were taking tetracycline. However, the possibility seems remote, because tetracycline serum levels in infants exposed in such a manner were undetectable (&lt;0.05 mcg/mL).</td>
</tr>
</tbody>
</table>
|                      |          | • The AAP classifies
No evidence was found to suggest a relationship to large categories of major or minor malformations or to individual defects with chlortetracycline, demeclocycline, or oxytetracycline. However, the sample size is extremely small, and safety should not be inferred from these negative results. There was evidence to suggest a relationship to minor, but not major malformations with tetracycline.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Category</th>
<th>Notes</th>
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</thead>
</table>
| Tigecycline (Tygacil) | D        | - Tigecycline is a glyyclcycline broad-spectrum antibacterial agent, which is structurally related to the tetracycline class of antibiotics and may have similar adverse effects.  
- Similar to tetracyclines, tigecycline can permanently discolor the teeth if used in the second half of pregnancy.  
- Use in the 1\textsuperscript{st} trimester probably does not represent a major risk to the embryo or fetus, but use in later trimesters should be avoided.  
- No human data.  
- Tigecycline is expected to be excreted into the breast milk based on its molecular weight (about 586), prolonged elimination half-life, and wide distribution in tissues.  
- It is best to not to nurse if a woman is receiving this antibiotic.  

| Tinidazole (Tindamax) (U.S. only) | C        | - Limited human data.  
- Tinidazole is chemically related to metronidazole, and there is no convincing evidence of embryo or fetal harm with metronidazole.  
- Tinidazole can be used in cases where metronidazole has failed to eradicate the infection.  
- Contraindicated during 1\textsuperscript{st} trimester per product labeling.  
- The AAP classifies tinidazole as an agent whose effect on nursing infants is unknown but may be of concern.  
- Discontinue breastfeeding while being treated and for 3 days following the last dose.  

| Tobramycin            | D        | - Human data suggest low risk.  
- See aminoglycosides.  
- In a large database review, of the 81 1\textsuperscript{st} trimester exposures to tobramycin, there were 3 (3.7\%) major birth defects observed (3 expected), one of which was a cardiovascular defect (1 expected).  
- See aminoglycosides  

| Vancomycin (Vancocin [U.S.]; generics [Canada]) | C        | - There are no cases of congenital defects attributable to vancomycin and the manufacturer has received reports on the use of vancomycin in pregnancy without adverse fetal effects.  
- Vancomycin crosses the human placenta and appears in umbilical cord blood after IV maternal treatment. Amniotic fluid and umbilical cord blood concentrations during the early 3\textsuperscript{rd} trimester are comparable to maternal blood levels (fetal-maternal serum concentration ratio of 0.76).  
- Limited human data.  
- Vancomycin is excreted into breast milk.  
- Vancomycin is poorly absorbed from the normal intact gastrointestinal tract, and thus, systemic absorption would not be expected.  
- Product labeling recommends against use of drug while breastfeeding.  

| Voriconazole (Vfend)  | D        | - No human data. Teratogenic in animals.  
- A closely related antifungal, fluconazole, is a suspected teratogen. Therefore, voriconazole should be avoided during 1\textsuperscript{st} trimester.  
- Per IDSA, voriconazole contraindicated during pregnancy because of fetal abnormalities observed in animals.  
- No human data; potential toxicity.  
- Excretion to breast milk is expected with its low molecular weight.  
- There is potential for toxicity in nursing infants. Therefore, women taking voriconazole should not breastfeed while taking the drug.  
- No human data; potential toxicity.  
- Excretion to breast milk is expected with its low molecular weight.  
- There is potential for toxicity in nursing infants. Therefore, women taking voriconazole should not breastfeed while taking the drug.  

- U.S./Canadian product labeling recommends against use while breastfeeding.
a. FDA Categories for the use of medications in pregnancy:¹
   o A: adequate, well-controlled studies in pregnant women have not shown an increased risk of fetal abnormalities.
   o B: Animal studies have revealed no evidence of harm to the fetus, however, there are no adequate and well-controlled studies in pregnant women. OR Animal studies have shown an adverse effect, but adequate and well-controlled studies in pregnant women have failed to demonstrate a risk to the fetus.
   o C: Animal studies have shown an adverse effect and there are no adequate and well-controlled studies in pregnant women. OR No animal studies have been conducted and there are no adequate and well-controlled studies in pregnant women.
   o D: Studies, adequate, well-controlled or observational, in pregnant women have demonstrated a risk to the fetus. However, the benefits of therapy may outweigh the potential risk.
   o X: Studies, adequate, well-controlled or observational, in animals or pregnant women have demonstrated positive evidence of fetal abnormalities. The use of the product is contraindicated in women who are or may become pregnant.