

Appendix 2 | Prescribing in Pregnancy

There are major concerns of permanent harm [teratogenesis in the 1st trimester (*see* p. 100) and effect on growth and development of foetus in the 2nd and 3rd trimester] to the baby whenever any drug is administered to pregnant women. Maternal medication can also increase the incidence of abortion, foetal death, premature or delayed labour, or create perinatal problems. Moreover, there are pronounced and progressive physiological changes during pregnancy which can affect drug disposition (*see* p. 75). As such, prescribing for the pregnant woman requires consideration of several factors and application of restraint. Possible harm to the foetus by the administered drug has to be weighed against harm to both mother and the baby due to untreated disease. There is paucity of data about safety of majority of drugs during pregnancy; largely because prospective drug trials in pregnant women are fraught with ethical, legal, emotional and practical difficulties. Information is mostly derived from anecdotal

reports and retrospective studies. The validity of the US-FDA categorization of drugs into 5 categories (*see* p. 101) according to increasing order of risk documentation during pregnancy has become questionable, because evidence on teratogenic risk of drugs keeps accumulating, and the category of many drugs needs to be changed from time-to-time, e.g. the antiretroviral drug efavirenz is no longer contraindicated during pregnancy. The FDA is having a relook on this grading system.

While insufficient data are available to make definitive recommendations regarding choice of drugs for treating common problems likely to be encountered during pregnancy, the table on the succeeding pages attempts to delineate the relatively/probably safer alternatives. The list is not exhaustive and manufacturers literature/package inserts or other authoritative texts should be consulted. Drugs marked (X) are contraindicated during pregnancy.

Principles of prescribing during pregnancy

- Where possible use nondrug therapy.
- Prescribe drugs only when definitely needed.
- Choose the drug having the best safety record over time.
- Avoid newer drugs, unless safety is clearly established.
- Over-the-counter drugs cannot be assumed to be safe.
- As far as possible, avoid medication in the initial 10 weeks of gestation.
- Use the lowest effective dose.
- Use drugs for the shortest period necessary.
- If possible, give drugs intermittently.

CHOICE OF DRUGS FOR COMMON PROBLEMS DURING PREGNANCY

Drug class (condition)	Safety uncertain/unsafe	Safer alternative
1. Antiemetics (morning sickness, other types of vomiting)	Domperidone (X), Ondansetron	Promethazine, Doxylamine, Dicyclomine, Prochlorperazine, Metoclopramide
2. Drugs for peptic ulcer and GERD	Cimetidine, Lansoprazole, Mosapride	Ranitidine, Famotidine, Omeprazole, Pantoprazole
3. Laxatives (constipation)	Senna, Bisacodyl, Docusates, Saline purgatives	Dietary fibre, Ispaghula, Lactulose
4. Antidiarrhoeals	Diphenoxylate-atropine, Loperamide	Oral rehydration salts
5. Analgesics (headache, bodyache, joint pain, visceral pain)	Aspirin, Metamizol, NSAIDs COX-2 inhibitors, Codeine, Morphine (X), Pethidine, Tramadol	Paracetamol, Ibuprofen (low dose)
6. Cold-cough remedies	Codeine, Dextromethorphan, Bromhexine, Expectorants	Xylometazoline } Oxymetazoline } Nasal drops Budesonide }
7. Antiallergics	Cetirizine, Loratadine, Fexofenadine	Chlorpheniramine, Promethazine
8. Antibacterials (systemic bacterial infections)	Cotrimoxazole, Fluoroquinolones (X), Tetracycline (X), Doxycycline (X), Chloramphenicol (X), Gentamicin, Streptomycin (X), Kanamycin (X), Tobramycin (X), Clarithromycin, Azithromycin, Clindamycin, Vancomycin, Nitrofurantoin	Penicillin G, Ampicillin, Amoxicillin-clavulanate, Cloxacillin, Piperacillin, Cephalosporins, Erythromycin
9. Antitubercular	Streptomycin (X)	Isoniazid, Rifampicin, Ethambutol, Pyrazinamide
10. Antiamoebic	Metronidazole, Tinidazole, Quiniodochlor	Diloxanide furoate, Paromomycin
11. Antimalarial	Artemether, Artesunate, Primaquine (X)	Chloroquine, Mefloquine, Proguanil, Quinine (only in 1st trimester), Pyrimethamine + Sulfadoxine (only single dose)
12. Anthelmintic	Albendazole (X), Mebendazole (X), Ivermectin, Pyrantel pamoate, Diethylcarbamazine (X)	Piperazine, Niclosamide, Praziquantel
13. Antifungal (superficial and deep mycosis)	Amphotericin B (X), Fluconazole, Itraconazole (X), Ketoconazole (X), Griseofulvin (X), Terbinafine	Clotrimazole } Nystatin } Topical Tolnaftate }

(X) Contraindicated during pregnancy.

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Drug class (condition)	Safety uncertain/unsafe	Safer alternative
14. Antiretroviral (HIV-AIDS)	Didanosine, Abacavir, Indinavir, Ritonavir	Zidovudine, Lamivudine, Tenofovir, Nevirapine, Nelfinavir, Saquinavir, Efavirenz
15. Antiviral (non-retroviral)	Acyclovir, Ganciclovir (X), Foscarnet (X), Amantadine (X), Vidarabine (X), α -interferon (X)	—
16. Antihypertensives	ACE inhibitors (X), Angiotensin antagonists (X), Thiazide diuretics, Furosemide, Propranolol, Nitroprusside	Methyldopa, Hydralazine, Atenolol, Metoprolol, Pindolol, Nifedipine, Prazosin, Clonidine
17. Antianaemic	—	Iron salts (oral), Iron dextran (i.m.), Folic acid, Vit B ₁₂
18. Antidiabetics	Sulfonylureas (X), Metformin (X), Pioglitazone, Repaglinide, Nateglinide, Acarbose (X)	Insulin (preferably human insulin)
19. Corticosteroids	Betamethasone, Dexamethasone (high dose and prolonged use)	Inhaled corticosteroids, Topical corticosteroids, Prednisolone oral (low dose)
20. Thyroid hormone (hypothyroidism)	—	Thyroxine
21. Antithyroid drugs (thyrotoxicosis)	Carbimazole, Radioactive iodine (X), Iodide	Propylthiouracil
22. Antipsychotic (schizophrenia)	Chlorpromazine, Fluphenazine (X), Clozapine, Olanzapine, Risperidone	Haloperidol, Trifluoperazine
23. Antimanic (bipolar illness)	Lithium carbonate, Valproate, Carbamazepine	—
24. Antidepressants	Trimipramine (X), Dothiepin (X), Sertraline, Paroxetine, Citalopram, Trazodone, Venlafaxine, Moclobemide	Amitriptyline, Imipramine, Fluoxetine
25. Anticoagulants (thromboembolism)	Warfarin (X), Acenocoumarol, Phenindione (X)	Heparin (unfractionated), Heparin (LMW)
26. Antiasthmatic	Theophylline, Ketotifen (X), Montelukast, Zafirlukast, Systemic corticosteroids	Salbutamol/Salmeterol Ipratropium bromide Beclomethasone/ Budesonide Sod. cromoglycate

} Inhaled

Appendix 3 Drugs in Breastfeeding

Administration of drugs to women who are breastfeeding may have ill effects on the suckling infant, and/or affect lactation. Estrogens (in oral contraceptives) and bromocriptine (D2 agonist) decrease milk production. Toxic effects on the infant are largely dependent on entry of the drug in milk in pharmacologically significant amounts. In the case of large number of drugs (except those acting on CNS and few others), the concentration in milk is low, and

the breastfed infant receives insufficient quantity to produce adverse effects. Maternal medication or breastfeeding should not be interfered in case of such drugs. However, currently available data are insufficient to make specific recommendations in the case of many drugs, and the list given below is not exhaustive. Manufacturer's recommendations/package inserts should be consulted.

A. Drugs whose amount in milk is too small to be harmful to the infant, or those found to be safe in ordinary doses

Acetazolamide	Ipratropium Br. (inhalation)
Albendazole	Iron dextran (i.m.)
Antacids	Iron salts (oral)
Antifungal drugs (topical)	Ketoprofen
Aspirin (low dose)	Lidocaine
Baclofen	Loperamide
Beclomethasone (Inhaled)	Mebendazole
Benzyl benzoate (topical)	Methyldopa
Bupivacaine	Naproxen
Buprenorphine	Nefopam
Cephalosporins	Niclosamide
Cloxacillin	Paracetamol
Codeine	Permethrin (topical)
Cromoglycate sod.	Piperacillin
Diclofenac	Piperazine
Digoxin	Piroxicam
Domperidone	Praziquantel
Ergometrine	Pyrantel
Erythromycin	Pyrazinamide
Ethambutol	Salbutamol (inhalation)
Folic acid	Sucralfate
Gentamicin	Terbutaline (inhalation)
Heparin	Valproate sod.
Hydralazine	Vitamins (maintenance dose)
Ibuprofen	Warfarin
Insulins	

B. Drugs to be used with special precaution in breastfeeding women or drugs contraindicated

Drug	Comment/possible adverse effect on breast-fed infant
ACE inhibitors (Enalapril, Lisinopril)	: S/P amount in milk small, magnitude of risk not known, watch for hypotension
Acenocumarol	: S/P; give prophylactic vit K to infant
Acyclovir	: S/P; significant amount in milk
Alcohol	: Intoxication, reduced suckling
Allopurinol	: S/P; secreted in milk; no data on risk to infant
Amiloride	: C/I; no information on risk to infant; may reduce lactation
Aminoglycosides	: S/P; risk not known, most manufacturers advise caution
Amiodarone	: C/I; risk of hypothyroidism from released iodine
Amlodipine	: S/P; no data on risk to infant
Amphetamines	: C/I; significant amount in milk
Ampicillin/Amoxicillin	: S/P; diarrhoea, candidiasis in the infant
Androgens	: C/I; masculinization of female infant, precocious development of male infant, reduced lactation
Anthraquinones (senna, etc.)	: C/I; diarrhoea in the infant
Anticancer drugs	: C/I; anaemia, diarrhoea, immunosuppression
Anticonvulsants	: S/P; monitor infant for side effects
Antidepressants (tricyclic)	: S/P; use doses < 150 mg amitriptyline per day or equivalent; monitor infant for side effects, sedation, respiratory depression
Antihistamines (H ₁)	: S/P; significant amount in milk, watch for drowsiness, respiratory depression
Antihistamines (2nd generation)	: No data on risk to infant; manufacturers advise avoid
Antipsychotics	: S/P; drowsiness, muscle dystonia; avoid chlorpromazine, haloperidol, clozapine; amount in milk small, but long-term effect on developing nervous system not known
Aspirin	: S/P; Avoid high doses, bleeding, Reye's syndrome
Atorvastatin	: Avoid; no data on risk to infant
Atropine	: S/P; monitor for anti-muscarinic effects
Azathioprine	: C/I; immunosuppression
Azithromycin	: Avoid; no information on risk to infant
Barbiturates	: S/P; drowsiness, lethargy, withdrawal symptoms
Benzodiazepines	: S/P; compatible in single dose; avoid repeated doses; lethargy, hypotonia, reduced suckling, weight loss
Beta blockers	: S/P; amount in milk generally small; bradycardia, hypotension, cyanosis
Bromocriptine	: Suppresses lactation
Buspirone	: Avoid; no information on risk to infant
Caffeine	: Avoid regular consumption of large amounts; irritability, CNS effects
Carbamazepine	: S/P; amount in milk small but monitor infant
Carbimazole	: S/P; hypothyroidism, use lowest effective dose, or suspend breastfeeding
Carisoprodol	: S/P; concentrated in milk; avoid
Chloramphenicol	: C/I; diarrhoea, bone marrow depression
Chloroquine	: S/P; amount in milk small; haemolysis in <1 month old infant and in G-6-PD deficient
Cimetidine	: S/P; significant amount in milk, but no harmful effect reported
Ciprofloxacin	: C/I; high concentration in milk, theoretical risk of arthropathy
Clindamycin	: S/P; amount in milk small, but risk of diarrhoea, watch for blood in stools
Clofazimine	: S/P; skin discolouration
Clonidine	: S/P; sedation, hypotension

C/I=Contraindicated or suspend breastfeeding

S/P = Use with special precaution while breastfeeding; and monitor infant

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Drug	Comment/possible adverse effect on breast-fed infant
Corticosteroids	: S/P; compatible in single doses; pituitary-adrenal suppression possible with >10 mg prednisolone daily to mother, impaired growth
Cotrimoxazole	: S/P; folate deficiency, risk of kernicterus, haemolysis in G-6-PD deficient; safe for healthy older infants
Cyclosporine	: C/I; significant amount in milk
Dapsone	: S/P; haemolytic anaemia, jaundice
Depot medroxyprogesteron acetate (i.m.)	: Compatible with breastfeeding from 6 weeks postpartum
Diltiazem	: S/P; significant amount in milk
Disopyramide	: S/P; small amount in milk, antimuscarinic effects
Doxepin	: S/P; sedation, respiratory depression
Ergotamine	: C/I; ergotism in the infant; may suppress lactation
Estrogens	: C/I; gynaecomastia in male infant, may suppress lactation
Famotidine	: S/P; present in milk, but harm to infant not known
Fluconazole	: C/I; secreted in milk, but harm to infant not known
Fluoxetine	: S/P; small amount in milk, but can accumulate in infant; avoid if possible
Furosemide	: S/P; small amount in milk, electrolyte disturbances in the infant
Gemfibrozil	: Avoid; no information on risk to infant
Indomethacin	: C/I; CNS effects, convulsions
Iodine/Iodides	: C/I; concentrated in milk, hypothyroidism and goiter in the infant
Iodine radioactive	: C/I; suspend breastfeeding for 24 hr after diagnostic dose and for long-term after therapeutic dose
Isoniazid	: S/P; neuropathy, convulsions, jaundice, give prophylactic pyridoxine
Itraconazole	: Avoid unless essential; amount in milk small
Ketoconazole	: C/I; secreted in milk but harm to infant not known.
Ketorolac	: Avoid as no data on safety
Lansoprazole	: Avoid unless essential; no data on safety
Levodopa/Carbidopa	: S/P; no data on safety
Lithium carbonate	: C/I; intoxication in the infant, cardiac arrhythmias
Losartan	: S/P; magnitude of risk not known; avoid if possible
Mefloquine	: S/P; secreted in milk, but harm to infant unlikely
Metformin	: C/I; secreted in milk; hypoglycaemia, lactic acidosis
Mesalazine	: S/P; amount in milk small; watch for diarrhoea
Methotrexate	: C/I; toxicity in infant
Metoclopramide	: S/P; watch for diarrhoea, dystonia in infant
Metronidazole	: Significant amount in milk: avoid high doses; suspend breastfeeding for 12 hr after single dose therapy
Montelukast	: Avoid; no data on risk to infant
Morphine (and other opioids)	: S/P; usual doses unlikely to affect infant; lethargy, poor growth, withdrawal symptoms in infants of dependent mothers
Neostigmine	: S/P; small amount in milk but monitor infant
Nifedipine	: S/P; small amount in milk but monitor infant
Nitrofurantoin	: S/P; small amount in milk, haemolysis in G-6-PD deficient infant
Norfloxacin	: Avoid; no information on risk to infant
Omeprazole	: Not known to be harmful, manufacturer advises 'avoid'
Oral contraceptives	: Avoid until 6 month after birth, see estrogens
Penicillins	: Toxicity unlikely but risk of allergy
Phenytoin	: S/P; small amount in milk, but monitor infant
Progestins	: Low doses safe, may suppress lactation at high doses
Propylthiouracil	: S/P; hypothyroidism with high doses only
Pyrimethamine-sulfadoxine	: S/P; significant amount in milk; appears safe if infant is older

Contd...

Drug	Comment/possible adverse effect on breast-fed infant
Quinidine	: S/P; significant amount in milk but harm to infant not known
Ranitidine	: S/P; significant amount in milk but harm to infant not known
Rifampin	: S/P; amount in milk small, but monitor infant for jaundice
Sertraline	: S/P; present in milk but no harm reported in short-term
Spironolactone	: S/P; drowsiness, hirsutism, gynaecomastia
Streptomycin	: Compatible with breastfeeding; monitor infant for diarrhoea and thrush
Sulfonamides	: S/P; rashes, small risk of kernicterus in neonate, haemolysis in G-6-PD deficient; safer for older infants
Sulfonylureas	: S/P; no adverse effect reported, but watch for hypoglycaemia
Tetracyclines	: C/I; growth retardation, candidiasis, tooth discolouration
Theophylline	: S/P; irritability, CNS effects
Thiazide diuretics	: S/P; amount in milk small; may reduce lactation
Thyroxine	: S/P; monitor for hyperthyroidism
Tinidazole	: S/P; present in milk; suspend breastfeeding till 3 days after stopping
Vancomycin	: S/P; present in milk, but absorption from infant's gut unlikely
Verapamil	: S/P; small amount in milk, but monitor infant
Vigabatrin	: C/I; present in milk, no data on risk to infant
Vitamin A and D	: Avoid high doses, risk of hypervitaminosis
Zolpidem	: Avoid unless essential; amount in milk small, but watch for sedation in infant