MEDICINES INFORMATION CENTRE

2024 COMMONLY USED DRUGS REQUIRING CAUTION IN PREGNANCY/BREASTFEEDING

Please note this list is not exhaustive. If a medicine is not listed this does not mean it can be safely used. This information is intended to support a discussion between a health care professional and the patient. It should guide the discussion on the risks and benefits, to both mother and foetus, when starting or continuing a particular medicine in a pregnant/breastfeeding woman **(Version 2)**

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PREGNANCY	BREASTFEEDING
BLOOD AND BLOOD-FORMING ORGANS	
WARFARIN Contraindicated by manufacturer. Foetal warfarin syndrome with 1st trimester exposure. CNS defects from exposure to any trimester. Use in late pregnancy is associated with foetal haemorrhage. **Avoid in the 1st trimester and near term, substitute heparin**. As per Standard Treatment Guidelines and EML for SA (Hospital Level, Adults 2019 Edition), for pregnant women with valvular disease and atrial fibrillation, warfarin may be used from the 2nd trimester until 36 weeks. Women of childbearing age should ensure effective contraception.	Contraindicated by manufacturer. Data suggest very little, if any, excreted in breast milk. Considered safe in normal, full-term, nursing infants.
CARDIOVASCULAR SYSTEM	
ANGIOTENSIN-CONVERTING ENZYME (ACE) INHIBITORS Contraindicated by manufacturer. Presumed to cause disturbance in foetal blood pressure regulatory mechanisms. Foetal exposure to ACE inhibitors during the 1st trimester has been reported to be associated with an increased risk of cardiac, CNS and kidney malformations. Oligohydramnios as well as hypotension, oliguria and anuria in newborns have been reported after administration of ACE inhibitors in the 2nd and 3rd trimesters. Cases of defective skull ossification have been observed. Prematurity and low birth mass may occur. Should a patient plan pregnancy or become pregnant during ACE inhibitor therapy, ACE inhibitor therapy should be stopped promptly, and safer alternative therapy should be started. Women of childbearing age should ensure effective contraception.	Contraindicated by manufacturer. Data suggests minimal quantities of **captopril, enalapril, perindopril, quinapril** found in breast milk, minor amounts ingested by infant. Adverse effects unlikely. No data for **lisinopril, ramipril, trandolapril.** Suggest safer alternative while nursing, especially for a newborn or preterm infant.
ANGIOTENSIN II RECEPTOR BLOCKERS (ARBs) Contraindicated by manufacturer. Medicines affecting the renin-angiotensin system can cause embryonal toxicity, foetal and neonatal morbidity, and mortality. Should a patient plan pregnancy or become pregnant during ARB therapy, ARB therapy should be stopped promptly, and safer alternative therapy should be started. Women of childbearing age should ensure effective contraception.	Contraindicated by manufacturer. Minimal amounts found in breast milk according to preliminary data for **candesartan.** May continue breastfeeding, however, use with caution in newborn or preterm infants. No data for **irbesartan, losartan, telmisartan, valsartan.** Suggest safer alternative while nursing, especially for a newborn or preterm infant.
HMG COA REDUCTASE INHIBITORS (STATINS) Contraindicated by manufacturer. Human data do not uniformly suggest that statins cause birth defects. However, theoretically, since statins decrease the synthesis of cholesterol, they may cause foetal harm. If a statin is used for primary prevention in women of childbearing age, effective contraception should be used. Statin therapy should be stopped 1 to 2 months before planning a pregnancy or as soon as there is an awareness of the pregnancy, and safer alternative therapy should be started. Atherosclerosis is a chronic process, and typically discontinuation of statins during pregnancy should have little impact on the long-term risk associated with primary hypercholesterolaemia. FDA recommends to limit statin use during pregnancy to high-risk patients (i.e., homozygous familial hypercholesterolaemia, secondary prevention). If it is decided to use a statin, hydrophilic statins (i.e., pravastatin, rosuvastatin) may be preferable as placental transfer may be less than the other statins.	Contraindicated by manufacturer. May disrupt lipid metabolism of infants.
DERMATOLOGICALS	
FINASTERIDE Contraindicated by manufacturer. May cause abnormalities of the external genitalia of a male foetus when administered during pregnancy. Women should not handle crushed or broken finasteride tablets when they are or may be potentially pregnant because of the possibility of absorption of finasteride and the subsequent potential risk to the male foetus. Tablets are coated and will prevent contact with the active ingredient during normal handling, provided that the tablets have not been broken or crushed. In the event of such contact, wash with soap and water immediately.	Contraindicated by manufacturer. Data is limited. Suggest safer alternative in the first 6 months after birth, especially in neonates or preterm infants.
RETINOIDS (i.e., acitretin, isotretinoin) Contraindicated by manufacturer. Highly teratogenic. Women of childbearing age should ensure effective contraception for at least 1 month before therapy, during therapy and for at least 2 years **(for acitretin)**/1 month **(for isotretinoin)** following its discontinuation. Should pregnancy occur, despite these precautions, during therapy, or up to 2 years **(for acitretin)**/1 month **(for isotretinoin)** after its discontinuation, there is a high risk of severe malformation of the foetus. Treatment should not be started until the 2nd or 3rd day of the next normal menstrual period. A negative pregnancy test must be obtained within 2 weeks **(for acitretin)**/11 days **(for isotretinoin)** before starting therapy. Advisable to perform pregnancy tests monthly during therapy.	Contraindicated by manufacturer. Data is limited. Suggest safer alternative.
GENITOURINARY SYSTEM AND SEX HORMONES	
COMBINED HORMONAL CONTRACEPTIVES (CHCs) Contraindicated by manufacturer. Although there is no evidence that the CHCs currently available may cause foetal abnormalities, they should not be used during pregnancy, and should be discontinued if pregnancy is confirmed.	Contraindicated by manufacturer. CHCs should be avoided for the first 6 weeks. From 6 weeks to 6 months postpartum they should generally not be used since they may decrease the volume of milk and shorten the duration of breastfeeding. **Progestogen-only pills, implants or injections, or mechanical contraceptives are preferred.** Even if breastfeeding is not intended, oestrogen-containing pills should not be initiated until 21 days after delivery because of the risk of thromboembolism (42 days if additional risk factors for thromboembolism are present).
TESTOSTERONE Contraindicated by manufacturer. Pregnant women must also avoid contact with testosterone application sites. Testosterone may cause virilising effects on the foetus. In the event of contact, wash with soap and water immediately.	Contraindicated by manufacturer.
GENERAL ANTI-INFECTIVES FOR SYSTEMIC USE	
DOXYCYCLINE Contraindicated by manufacturer. Deposited in foetal bone and teeth, resulting in permanent discolouration. Risk of fatty infiltration of maternal liver with high doses of tetracyclines. Tetracyclines are not considered first-line antibiotics in pregnancy, avoid use if safer alternatives are available.	Contraindicated by manufacturer. Excreted in breast milk. Data suggest that harm is unlikely with short term-use, as infant exposure is low due to chelation with calcium in milk. Avoid prolonged (>21 days) or repeat courses of 21 days.
GRISEOFULVIN Contraindicated by manufacturer. Embryotoxic, teratogenic and tumorigenic in animals. Contraception (either alternate or additional means if taking an oestrogen-containing oral contraceptive) should be used during and for 1 month after therapy. Based on laboratory studies, griseofulvin may damage sperm cells. Delay fathering children until 6 months after therapy.	Safety not established by manufacturer. Unknown if excreted in breast milk. No human data. Best avoided.
NITROFURANTOIN Contraindicated at term by manufacturer. Possibility of neonatal haemolytic anaemia due to immature enzyme systems.	Contraindicated in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency or nursing mothers of infants with this deficiency, by manufacturer. Trace amounts found in breast milk. Avoid use in mothers of infants under 8 days of age if safer alternative is available, or in infants with G6PD deficiency of any age.
RIBAVIRIN Contraindicated in women who are pregnant, or who intend to become pregnant and in men whose female partners are pregnant, by the manufacturer. Animal data show significant teratogenic and/or embryocidal effects. A negative pregnancy test must be obtained immediately before starting therapy. Avoid pregnancy during therapy and for 6 months after the end of therapy in females and in female partners of men who are taking ribavirin. Women of childbearing potential and their partners must use at least 2 reliable forms of contraception during therapy and for 6 months after the end of therapy (advisable to perform pregnancy tests monthly during this time).	Not recommended by manufacturer. Unknown if excreted in breast milk. Potential for adverse effects. Best avoided.
ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS	
ANTINEOPLASTIC AGENTS (i.e., antimetabolites, alkylating agents) Many cytotoxic drugs are teratogenic, and therefore patients should be counselled about effective contraception prior to commencing therapy. Ethical considerations and the risks versus benefits should be considered against the timing of chemotherapy exposure. Data suggest: The embryo remains undifferentiated during the first 4 weeks of gestation. Exposure to chemotherapy during this period may result in loss of pregnancy or pregnancy may continue seemingly unaffected by adverse effects. From weeks 5 to 10 of gestation, organogenesis takes place. Chemotherapy, particularly with antimetabolites and alkylating agents, at this point may result in foetal malformations. Chemotherapy exposure during the 1st trimester of pregnancy carries a greater and more permanent risk of foetal malformations than during the 2nd and 3rd trimesters. Myelosuppression in the neonate or a complicated delivery may occur if the mother is exposed to chemotherapy within 21 days of childbirth or after 35 weeks of pregnancy. The adverse effects on bone marrow reserves can result in complications such as bleeding, sepsis, and death.	Breastfeeding is generally contraindicated during chemotherapy, as supported by WHO, as large amounts of the drug may be present in breast milk. Nursing during chemotherapy may cause immunosuppression, impaired growth, or may be associated with carcinogenesis.
MUSCULOSKELETAL SYSTEM	
ASPIRIN Contraindicated from 20 weeks gestation or later in pregnancy by manufacturer. FDA recommends limited prescribing of NSAIDs between 20 and 30 weeks of pregnancy and to avoid prescribing them after 30 weeks of pregnancy. If treatment is determined necessary, limit use to the lowest effective dose and shortest duration possible. The above recommendations do not apply to low-dose 81 mg aspirin prescribed for certain conditions in pregnancy. As per Standard Treatment Guidelines and EML for SA (Hospital Level, Adults 2019 Edition) for women at high risk of pre-eclampsia, aspirin use may be considered from 6 weeks gestation onwards, preferably before 16 weeks gestation.	Contraindicated by manufacturer. Excreted in breast milk. Data suggests aspirin is found in breast milk, however, is considered safe when used for antiplatelet therapy at a low daily dose. Suggest safer alternative where high doses are required continuously. Infant should be monitored for bruising and bleeding if used while nursing.
METHOTREXATE Contraindicated by manufacturer in pregnant patients with rheumatoid arthritis or psoriasis and should not be used in the treatment of neoplastic diseases, unless the potential benefit outweighs the risk to the foetus. May cause foetal death, embryotoxicity, abortion or teratogenic effects. **Females:** Women of childbearing potential should not be started on methotrexate until pregnancy is excluded and should be fully counselled on the serious risk to the foetus should they become pregnant while undergoing therapy. Effective contraception must be used during therapy and for at least 6 months after stopping therapy. **Males:** Animal data suggest risk of genotoxic effects on sperm cells. Limited human data do not suggest an increased risk of malformations or miscarriage after male exposure to low-dose methotrexate (less than 30 mg/week), although it may cause a transient effect on sperm quality which reverses within 3 months after stopping therapy. For higher doses, there is inadequate data to estimate the risks of malformations or miscarriage after male exposure. As a precautionary measure, sexually active male patients or their female partners are recommended to use reliable contraception during therapy of the male patient and for at least 3 to 6 months after stopping therapy.	Contraindicated by manufacturer. Detected in breast milk. The highest breast milk-to-plasma concentration ratio measured was 0.08:1.
NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs) Contraindicated by manufacturer, however references state that NSAID use during the first 20 weeks of pregnancy is appropriate when needed. FDA recommends limited prescribing of NSAIDs between 20 and 30 weeks of pregnancy and to avoid prescribing them after 30 weeks of pregnancy. If treatment is determined necessary, limit use to the lowest effective dose and shortest duration possible. Avoid NSAIDs altogether from 30 weeks gestation, as use may cause premature closure of the foetal ductus arteriosus. NSAID use at the end of pregnancy may expose the mother and neonate to prolongation of bleeding time and inhibition of uterine contractions, resulting in delayed or prolonged labour.	Celecoxib and ibuprofen not recommended by manufacturer. Data suggest: Small amounts of **celecoxib** found in breast milk. May continue nursing as minimal quantities are ingested by the infant with no expected adverse effects. For **ibuprofen,** considered safe due to short $T_{1/2}$ and small amounts excreted in breast milk. **It is the recommended analgesic or anti-inflammatory while nursing.** Diclofenac, ketorolac and naproxen contraindicated by manufacturer. Data suggest: **Diclofenac** considered safe due to short $T_{1/2}$ and minimal glucuronide metabolite formation. For **ketorolac,** safer alternative recommended when larger quantities of breast milk are produced after the first 24 to 72 hours, particularly when breastfeeding a newborn or preterm infant. For **naproxen,** safer alternative recommended while breastfeeding a newborn or preterm infant due to long $T_{1/2}$ and reported serious adverse reactions in neonates while nursing.
CENTRAL NERVOUS SYSTEM	
ERGOTAMINE Contraindicated by manufacturer. May cause prolonged constriction of the uterine vessels and/or increased myometrial tone, resulting in decreased placental blood flow. Animal data suggest potential for foetal growth retardation. Limited human data suggest potential for congenital malformations.	Contraindicated by manufacturer. Limited data. May decrease milk supply and cause adverse effects in the infant (i.e., vomiting, diarrhoea, weak pulse and unstable blood pressure).
ANTI-EPILEPTICS (i.e., valproic acid, topiramate) **Valproic acid:** Contraindicated by manufacturer in the treatment of epilepsy unless there is no suitable alternative and contraindicated in the treatment of other indications. **Topiramate:** Contraindicated by manufacturer. Based on recent data, the European Medicines Agency (EMA) has recommended not to use as for valproic acid. **Females (for valproic acid and topiramate):** Prenatal exposure to either drug has been associated with an increased risk of congenital anomalies and adverse neurodevelopment, including autism spectrum disorder and impaired cognitive function (2– to 4– fold), and attention deficit/hyperactivity disorder. These risks increase with higher doses. Prenatal topiramate exposure may also cause foetal growth restriction. Due to its poor safety profile in pregnancy, valproic acid or topiramate is indicated for epilepsy only in women of childbearing age who are intolerant of or unresponsive to other antiepileptic treatments and who are compliant with an effective pregnancy prevention programme. If used during pregnancy, the lowest effective dose possible is advised. Folic acid supplementation is also advised. Women exposed to either drug during early pregnancy should be offered detailed anomaly scans. **Males (for valproic acid only):** Recent retrospective data suggest male valproic acid exposure in the 3 months prior to conception may be associated with an increased risk of adverse neurodevelopment. As a precautionary measure, EMA has recommended that there should be a discussion of these potential risks and the need for reliable contraception for male patients and their female partners during therapy of the male patient and for 3 months after stopping therapy.	**Valproic acid**: Contraindicated by manufacturer. Cases of haematological changes and somnolence have been reported in infants. Data suggest, levels in breast milk are low and infant serum levels range from undetectable to low. If valproic acid is required by the mother, it is not a reason to discontinue breastfeeding. Observe the infant for jaundice and unusual bruising or bleeding. **Topiramate**: Contraindicated by manufacturer. Diarrhoea and somnolence have been reported in infants. Data suggest, maternal doses of up to 200 mg/d produce relatively low levels in infant serum. Occasional reports of sedation and diarrhoea, but most infants tolerate the drug in milk well. Observe the infant for diarrhoea, irritability, and lethargy, especially in younger, exclusively breastfed infants.

BILL & MELINDA GATES foundation **NEED HELP?** University of Cape Town · Yunivesithi yaseKapa · Universiteit van Kaapstad

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