Community pharmacy guide on medicine safety in pregnancy

Community pharmacists are a key point of contact for women seeking advice about medicines use in pregnancy. While non-pharmacological interventions and lifestyle advice should be first-line, over-the-counter (OTC) medicines may be considered if it is clear the expected benefit to the mother outweighs the potential risks to the fetus. Extra vigilance is required when dispensing medicines to pregnant women or women of childbearing potential as prescribers may not always be aware of, or consider, pregnancy.

The benefits and harms of medicines use must be carefully weighed in pregnancy

Community pharmacists are often involved in discussions about medicines with pregnant women, e.g. the safety of prescribed medicines or selecting an OTC medicine. In general, part of any clinical interaction with a woman of childbearing age is to determine whether pregnancy would affect medicine choice, and therefore whether it is appropriate to enquire about the possibility of pregnancy. The pharmacist can then determine whether pharmacy advice and OTC products are appropriate, or if referral to the woman's lead maternity carer (LMC), general practitioner or emergency medical care is indicated.

In the pharmacy setting, consider non-pharmacological interventions and lifestyle advice first-line. OTC medicines should be avoided, if possible, particularly during the first 12 weeks of pregnancy. However, this approach may not always provide adequate symptom relief. When discussing treatment options with a pregnant woman, pharmacists should consider the following:[1,2]

- Many medicines can have harmful effects on the embryo or fetus, or cause pregnancy complications at any stage of gestation. The first 12 weeks are particularly crucial in terms of fetal development and all non-essential medicines should be avoided at this stage of pregnancy.
- OTC medicines should only be considered if it is clear the expected benefit to the mother outweighs the potential risks to the fetus
- Recommend the smallest effective dose for the shortest required duration
- Only recommend medicines or products that have been widely used in pregnancy and have a good safety record; the absence of evidence does not imply safety

- If a woman has persistent or severe symptoms, or symptoms that may be indicative of an underlying condition, recommend that she discuss these with her LMC or general practitioner/nurse practitioner

Patient information about medicine use in pregnancy is available from the UK Teratology Information Service best use of medicines in pregnancy (BUMPS) leaflets: **www.medicinesinpregnancy.org**

Non-pharmacological and OTC treatment options for pregnant women[2, 3]

Pain relief

Discuss non-pharmacological strategies for pain relief, including adequate rest and hydration, hot and cold compresses, massage and back support bands (if the woman has pregnancy-related back pain).

Paracetamol may be used short-term as required, e.g. a "one-off" dose or intermittent doses for a few days only, however, products that also contain codeine* (e.g. Panadeine) should be avoided as the limited effectiveness is likely to be outweighed by potentially harmful effects. Long-term or regular paracetamol use should also be avoided.

* Regular use of codeine close to term can cause neonatal withdrawal and should therefore be avoided

NSAIDs are contraindicated from the 28th week of pregnancy. There is conflicting advice as to whether they can be used safely before this time. Some experts advise that short-term use of ibuprofen or diclofenac may be considered up until the 28th week of pregnancy if there is a clear indication and the potential risks have been considered. The NZF advises that there is a risk in the first and third trimesters, but not in the second trimester. In practice, many pharmacists and other clinicians would advise to avoid NSAIDs altogether during pregnancy. Use of small amounts of a topical NSAID for localised pain could be considered.

Head lice treatments

Head lice can be mechanically removed by regularly and thoroughly combing wet hair using a fine-toothed headlice comb. Applying hair conditioner or vegetable oil may help this process. If mechanical removal is not effective, a dimethicone head lice treatment, e.g. Hedrin, is preferable, but the parasiticide permethrin (e.g. Quellada Head Lice Treatment) may also be considered.[4]

Conjunctivitis

Bathing the eyes with cool clean water, warm compresses and using lubricating eye drops may help to reduce irritation and discomfort. Advise frequent and thorough hand washing, avoiding sharing pillows, facecloths and towels, and not wearing contact lenses or using cosmetics applied to the eye area. Chloramphenicol eyedrops may be considered for bacterial conjunctivitis if symptoms persist.

Insect bites and stings

Applying a cold compress may help to reduce swelling. If itch is intolerable, a hydrocortisone cream (0.5% or 1%) or lidocaine cream (e.g. SOOV) may be used short-term.[5] Paracetamol may be used short-term to treat pain associated with the bite or sting.

Hay fever

Allergic rhinitis may be reduced by applying ointment, e.g. Vaseline, around the nostrils to trap dust and pollen.[6] Steam inhalation or a saline nasal spray or rinse may help relieve nasal congestion. If symptoms are intolerable, an intranasal corticosteroid spray, e.g. beclomethasone, budesonide or fluticasone, may be considered. Second-line choices include oral non-sedating antihistamines, e.g. cetirizine or loratadine, cromoglicate nasal spray and eye drops. Oral sedating antihistamines may be considered third-line but should be avoided from the 28th week of pregnancy due to potential neonatal adverse effects. Oral or nasal decongestants should be avoided in pregnancy. Eucalyptus oil and menthol-containing products should be avoided.

Coughs and colds

Symptoms of an upper respiratory tract infection can be managed with adequate rest and hydration, non-medicated lozenges, lemon and honey drinks, and steam inhalation or a saline nasal spray or rinse. Paracetamol may be used short-term for pain. Cough suppressants, e.g. pholcodine or low-dose codeine, should be avoided due to limited effectiveness. Oral decongestants should be avoided in pregnancy due to potential effects on placental blood flow. Pregnant women with a temperature ≥ 38.5°C or any raised temperature lasting for three or more days should be referred to their LMC or general practitioner.[7]

"Morning sickness"

Discuss dietary and lifestyle changes to manage nausea and vomiting, e.g. eating small meals frequently, eating bland or dry foods and high protein snacks, avoiding spicy or acidic foods and triggering stimuli such as odours, heat or humidity, keeping hydrated by drinking small amounts frequently, and getting adequate rest. Early morning nausea may be helped by eating a dry biscuit or cracker or drinking herbal tea (e.g. ginger or peppermint) before getting out of bed. Some women may wish to try an acupressure wrist band. Ginger capsules (or ginger-containing foods or drinks) or low-dose vitamin B6

Consider potential safety concerns when dispensing medicines to pregnant women

There are many prescription medicines where use is cautioned or contraindicated in pregnancy. It is important that pharmacists be vigilant when dispensing medicines to women who are pregnant or who are of childbearing potential as it is possible that the prescriber may not have been aware of, or considered, a pregnancy when prescribing the medicine. Approximately 50% of pregnancies in New Zealand are unplanned, which increases the risk of unintentional fetal exposure to potentially harmful prescription medicines.[1,2]

Pregnancy-specific safety information and recommendations for prescription medicines are available from the New Zealand Formulary (NZF). If a potential safety concern is identified, ask the woman if it is possible that she could be pregnant, and for women who are pregnant, ask if her prescriber is aware of the pregnancy. For some conditions (e.g. asthma or epilepsy), poor management may have greater adverse effects on fetal outcomes than pharmacological treatment. If necessary, refer the woman to her LMC or general practitioner/primary care provider for review.

Some examples of prescription medicines where extra vigilance* is required include:[2,3]

- Antiepileptics, including sodium valproate, phenytoin, primidone, phenobarbital, topiramate and carbamazepine, due the increased risk of teratogenicity. Sodium valproate is associated with the greatest risk and must be avoided in pregnancy and in women of childbearing potential unless other treatments are ineffective or not tolerated.
- Isotretinoin is contraindicated in pregnancy and in women of childbearing potential, unless strict contraception is practised, due to the risk of teratogenicity
- Some antibiotics depending on the stage of pregnancy, e.g. nitrofurantoin should be avoided from the 36th week of pregnancy due to the risk of haemolytic anaemia in the newborn, trimethoprim should be avoided in the first 12 weeks of pregnancy due to potential teratogenicity, tetracyclines should be avoided throughout pregnancy due to potential permanent dental staining or hypoplasia of the tooth enamel in the primary teeth
- NSAIDs, e.g. ibuprofen or diclofenac, are contraindicated from the 28th week of pregnancy due to the risk of fetal ductus arteriosus closure, persistent pulmonary hypertension in the newborn, delay in labour onset and increased labour duration
- Warfarin is potentially harmful at any stage of pregnancy. If anticoagulation is indicated, specialist advice is required as warfarin exposure in the 6th to 9th weeks of pregnancy may cause a pattern of defects called fetal warfarin syndrome and exposure in the two to four weeks before delivery may lead to fetal bleeding
- Disease-modifying anti-rheumatic drugs (DMARDS): methotrexate and leflunomide are contraindicated in pregnancy due to the risk of teratogenicity, fetal toxicity and mortality; cyclophosphamide is contraindicated in the first 12 weeks of pregnancy due to the risk of teratogenicity; azathioprine and 6-mercaptopurine should be avoided from the 28th week of pregnancy, or the dose reduced, due to potential neonatal toxicity.
- Angiotensin-converting enzyme (ACE) inhibitors and angiotensin-II receptor antagonists should be avoided at all stages of pregnancy due to potential teratogenicity and developmental toxicity
- Misoprostol is contraindicated as it is an abortifacient

* There are clinical scenarios where some of these medicines may be prescribed in pregnancy. Contact the prescriber by phone if further discussion is warranted.

Further information on the use of antiepileptic medicines in women is available from: **www.bpac.org.nz/2018/antiepileptic.aspx**

(pyridoxine), e.g. 25–50 mg, two or three times daily,* may be used.[3, 8] Women with severe and ongoing vomiting are at risk for malnutrition and dehydration, and should be referred to their LMC or general practitioner.

* Long-term use of 200 mg or more daily is associated with neuropathy and should therefore be avoided.

Heartburn and reflux

Discuss lifestyle and dietary modifications such as avoiding aggravating foods, avoiding eating two to four hours before going to bed, eating smaller meals and raising the head of the bed. If these are ineffective, an antacid with or without an alginate may be used (e.g. calcium carbonate-based antacid such as Quick-Eze).[9] If the antacid does not provide adequate symptomatic relief, a short course of omeprazole may be tried.* Antacids containing aluminium may have a constipating effect and are therefore not preferred in pregnancy. Products containing magnesium hydroxide (e.g. Milk of Magnesia) should also be avoided as they may cause diarrhoea. Compound alginate preparations containing sodium bicarbonate are not recommended due to the potential for fluid retention and associated complications.

* Medicines containing ranitidine have been recalled in New Zealand as they may contain an impurity (N-nitrosodimethylamine) that has been associated with an increased cancer risk when used long term. For further information, see: **www.medsafe.govt.nz/safety/Alerts/MedicinesAndNDMA.asp**

Gastroenteritis

Advise women to keep hydrated, get plenty of rest and to try small amounts of bland foods. Oral rehydration solutions may be recommended if there are signs of dehydration, e.g. dry mouth or concentrated urine. A warm heat pack or paracetamol may be used short-term for associated abdominal pain. If symptoms are persistent or severe, recommend that the woman seeks medical advice.

Constipation

Increasing dietary fibre and fluid intake are first-line for treating constipation. Bulk forming laxatives (fibre supplements such as Metamucil, Konsyl D or Normacol) may be used short-term to relieve symptoms. An osmotic laxative, such as macrogols or lactulose, can also be used. If a stimulant laxative is needed, bisacodyl, docusate or senna may be tried, however, these should only be used short-term, e.g. a few days, and patients should be advised that these stimulants can be associated with adverse effects such as abdominal pain and diarrhoea.[9]

Haemorrhoids

Dietary and lifestyle advice on avoiding constipation (see above) may prevent or lessen the effects of haemorrhoids. Advise women who have haemorrhoids to avoid sitting for long periods of time; a ring cushion may help if they are unable to take frequent breaks from sitting. A cold or warm compress or covered ice pack may help relieve symptoms including oedema. Topical products, e.g. Anusol or Proctosedyl, may be used short-term for local relief of symptoms.[9]

Threadworms

Discuss hygiene measures to clear the infection, e.g. thorough handwashing, cutting fingernails, avoiding scratching around the anus, showering or bathing each morning to remove eggs on the skin, changing underwear daily and frequently changing bedding. If these measures are ineffective, mebendazole (e.g. Vermox) may be used, but should be avoided in the first 12 weeks of pregnancy.

Vaginal thrush

Vulvovaginal candidiasis can be treated using topical (vaginal) clotrimazole or miconazole. Oral anti-fungal treatment should be avoided during pregnancy.

Urinary tract infection (UTI)

All pregnant women presenting with symptoms of a UTI should be referred to their LMC or general practitioner/nurse practitioner for diagnosis and treatment. If untreated, UTIs increase risk of pre-term delivery and low birth weight.

Complementary and alternative medicines (CAMS)

There is limited good quality evidence about the safety and effectiveness of most CAMS and a lack of regulation of the quality or contents. Products may be contaminated with heavy metals, toxic plants, microbes and pharmaceutical impurities. CAMS should be avoided in pregnancy, unless their safety is stated on the product label or packaging, e.g. fish oil supplements* and probiotics. A balanced diet should be sufficient for most pregnant women to meet nutritional requirements.† Women who are at risk of a vitamin or mineral deficiency should be referred to their LMC or general practitioner for review. Particular supplements that should be avoided in pregnancy include: vitamin A, vitamin D, black cohosh, dong quai, butterbur, cat's claw, fenugreek, flaxseed and flaxseed oil, goldenseal and liquorice root.[10, 11]

Iron: Women who are concerned about iron deficiency should be referred to their LMC or general practitioner for assessment and if appropriate, investigation and monitoring of levels. Iron supplements can be used to treat deficiency. Multi-ingredient vitamin preparations are not justified.

* Products containing fish liver oils, e.g. cod liver oil, should be avoided due to high vitamin A content.

† With the exception of folic acid and iodine, which should be supplemented. Some women may choose to purchase these as OTC prenatal supplements rather than on prescription. Check that women

are taking the recommended dose: 150 micrograms iodine, daily, and 0.8 mg folic acid, daily, or 5 mg daily if at high risk of conceiving a child with neural tube defects. For risk factors, see: "The role of the primary healthcare team in pregnancy care": **www.bpac.org.nz/2019/pregnancy-care.aspx**

Further information for pharmacists and other health professionals is available from:

- The NZF prescribing considerations in pregnancy (**www.nzf.org.nz/nzf_70762**) and the individual monographs for prescribing recommendations for specific medicines. For information on the way the NZF presents pregnancy and breastfeeding advice, see: **www.bpac.org.nz/2018/nzf-pregnancy.aspx**
- "Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk" by G. Briggs, R. Freeman, C. Towers and A. Forinash
- Hospital medicine information centres (**www.nzf.org.nz/nzf_10140**), e.g. the Christchurch Medicines Information Service provides health professionals in community or hospital settings with independent information on medicine safety – **www.medicinesinformation.co.nz**
- The United Kingdom Teratology Information Service (**www.uktis.org**)

Acknowledgement: Thank you to **Ann Roslyn (Roz) Hutton**, Medicines Information Pharmacist, Christchurch Medicines Information Service, Canterbury DHB for expert review of this article.

N.B. Expert reviewers are not responsible for the final content of the article.

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This article is available online at:
www.bpac.org.nz/2019/otc.aspx