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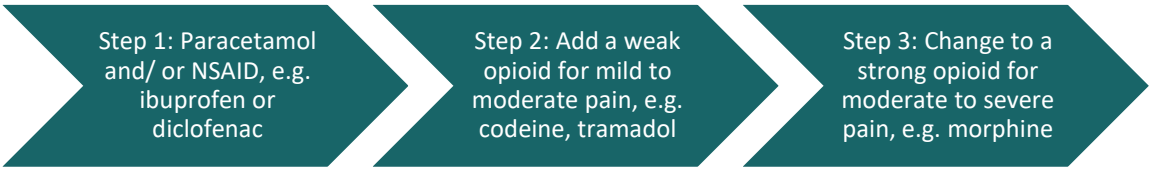
Analgesia during pregnancy or while breastfeeding

Treatment of pain in pregnant and breastfeeding women should follow the same principles as for all adults, using the analgesic ladder:



For severe acute pain the ladder may be reversed (i.e. start at Step 3 with morphine) and reduce to a weak opioid as pain resolves, then to paracetamol, ibuprofen or diclofenac[1].

All medicines may cross the placenta and be excreted into breastmilk. The benefits to the mother taking the medicine need to be weighed against possible risks to the developing foetus, or young infant.

	Pregnancy	Breastfeeding
Paracetamol	Safe to use at any stage of pregnancy.	Safe to use.
NSAIDs	Use up to week 28 of pregnancy if clinically indicated. **Avoid from week 28.**	Many NSAIDs are safe to use e.g. good safety data for ibuprofen, diclofenac, and naproxen.
Codeine[a]	Use at any stage of pregnancy when stronger pain relief than paracetamol or NSAID is required.	Codeine use in breastfeeding is controversial with some guidelines contraindicating its use. However, drug concentration data show that codeine is safe to use. Short courses (2 to 3 days) are likely to be safe[b].
Tramadol[a]	Limited and conflicting data when used in first trimester. Safe to use in 2nd or 3rd trimester.	Short courses are safe to use[b].
Morphine[a]	Use at any stage of pregnancy when maximum doses of paracetamol plus codeine or tramadol are insufficient.	Short courses safe to use when paracetamol plus tramadol are insufficient[b].

[a]Use near term may be associated with withdrawal symptoms in the neonate and respiratory depression
[b]Advise patients of the symptoms of opioid toxicity in themselves and/ or their babies. If symptoms develop discontinue opioid and seek urgent medical attention.

Paracetamol (1 g four times daily[2])

There is no clear evidence to indicate that paracetamol use in pregnancy is likely to harm the developing foetus at any stage of pregnancy[3,4,5].

Small amounts of paracetamol may be excreted into breast milk, but the quantity is too low to be a cause for concern[3,5].

Nonsteroidal Anti-Inflammatory Drugs (NSAIDs, ibuprofen 400 mg three times daily or diclofenac 75 mg twice daily[2])

Use of NSAIDs in the first and second trimesters (prior to week 28) are considered relatively safe and do not appear to be associated with an increased risk of adverse foetal outcomes. All NSAIDs are **contraindicated after week 28 of pregnancy** as they are known to cause adverse foetal effects including premature closure of the ductus arteriosus and neonatal pulmonary hypertension[2]. They are also associated with oligohydramnios with reduced foetal renal function. NSAIDs can inhibit uterine contraction, prolong the length of gestation and delay the onset of labour when given late in pregnancy. At the time of parturition, they have also been associated with excess bleeding in both the mother and the infant.

Codeine (30 mg to 60 mg up to every 4 hours when required to a maximum of 240 mg in 24 hours[6], consider limiting supply to maximum 40 × 30 mg tablets[2])

Codeine is a 'weak' opioid that is used to treat mild to moderate pain. Codeine may be used at any stage during pregnancy where the use of paracetamol or an NSAID alone provides insufficient pain relief[3].

The use of codeine near term or during labour may cause problems for the foetus and neonate. Like other opioids, codeine can cause respiratory depression in the newborn infant. Neonatal withdrawal symptoms such as tremor, jitteriness, diarrhoea and poor feeding have also been reported in infants following maternal use of large doses of codeine taken throughout pregnancy[3].

Codeine is inactive and is metabolised by cytochrome P450 (CYP) 2D6 in the liver to morphine, from which it derives its main analgesic effects. This enzyme occurs in a variety of forms, with up to 10% of the population having a form that results in ultrafast conversion of codeine to morphine and may lead to higher concentrations of morphine in breast milk and potential for toxicity to breastfed infants. The safety of taking codeine while breastfeeding remains controversial. Several papers have described toxicity in infants following maternal administration of codeine, however these papers have been refuted based on the pharmacokinetics of codeine and morphine. The reason for the apparent toxicity is unclear, but possibilities include exposure to opioid from other sources besides breastmilk. Like all opioids, patients should be advised of symptoms of opioid toxicity in themselves (nausea, vomiting, constipation, or somnolence) and their baby (increased sleepiness, difficulty breathing or breastfeeding, or limpness). If symptoms occur in either the mother or the infant discontinue the opioid and immediately seek medical attention[7].

Tramadol (50 mg to 100 mg up to four times daily when required, consider limiting supply to 20 × 50 mg immediate release capsules[2])

Tramadol is a synthetic opioid analogue with similar potency to codeine. There is limited and conflicting information on the safety of tramadol use early in pregnancy, some studies have reported a small increase in congenital malformations[3,5], while other have found no increase[8]. Tramadol, like other opioids, if used in high doses late in pregnancy has the potential to cause neonatal withdrawal symptoms[3,5]. Overall, short courses appear safe, especially in the 2nd and 3rd trimesters[3].

Small amounts of tramadol and its active metabolite are transferred to breastmilk in quantities unlikely to cause harm. Short courses are considered safe while breastfeeding[3,5,9].

Morphine (5 mg to 10 mg every 2 hours when required to a maximum of 40 mg in 24 hours, limit supply to 8 × 10 mg immediate release tablets[2])

Morphine is a 'strong' opioid used to treat moderate to severe pain when use of regular paracetamol plus codeine is ineffective. Morphine may be used at any stage during pregnancy when clinically indicated.

Use of morphine during pregnancy has not been associated with an increased risk of causing major congenital defects[3,10]. However, regular use in the third trimester or high doses near term have been associated with neonatal withdrawal symptoms and respiratory depression[3,5].

After oral administration small amounts of morphine are transferred to breastmilk[11], in quantities unlikely to cause harm. Morphine when used at the lowest effective dose for the shortest duration possible is considered safe to use while breastfeeding [3,5].

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