8. Guidelines for the use of methadone for cancer pain

Caution: Therapeutic Inequivalence
Methadone has both opioid and non-opioid properties, and a much longer halflife than morphine (approximately 8-80h vs 2.5h). There is therefore no single potency ratio for methadone and morphine. When switching from regular morphine, the eventual 24h dose of methadone is typically 5-10 times smaller than the previous dose of morphine, and sometimes much smaller.
Cumulation is inevitable and is the reason for the week-long intervals between adjustments in the regular dose. Unless familiar with its use, seek specialist advice.

Indications for use
Methadone is used in various situations, including:
- at some centres, as the strong opioid of choice, instead of morphine
- at some centres, as the preferred strong opioid in patients with renal failure
- neuropathic cancer pain not responding to a typical regimen of an NSAID, morphine, a tricyclic antidepressant and an anti-epileptic
- intolerable undesirable effects with morphine at any dose, e.g. sedation, hallucinations, dysphoria, delirium, myoclonus, allodynia, hyperalgesia
- intractable pain with intolerable effects when morphine increased.

Dose titration
1. When prescribing methadone as first-choice strong opioid:
   - start on methadone 5mg q12h *and* 5mg q3h p.r.n.
   - if pain relief remains minimal, consider increasing to 10mg q12h after 1–2 days (and 5mg p.r.n.), but generally do *not* increase the regular dose for one week
   - if necessary, continue to titrate the regular dose upwards by 1/3–1/2 once a week
   - with higher regular doses, consider increasing the p.r.n. dose to 1/4 of the q12h dose.

2. If the patient is already receiving morphine (or other strong opioid), use one of the methods described below. Pharmacologically, Method 1 is preferable. However, if patients and staff are not comfortable with a wholly p.r.n. regimen, Method 2 can be used (*see over*).

3. *With both methods, normal-release morphine is stopped abruptly when methadone is started*. If switching from m/r morphine, give the first dose of methadone at least 6h after the last dose of a 12h preparation, or 12h after the last dose of a 24h preparation.

Method 1: Changing from oral morphine to oral methadone, p.r.n. only (after Morley & Makin 1998)

Give q3h p.r.n. doses of methadone 1/10 of the previous 24h PO morphine dose, *up to a maximum of 30mg*.

On Day 6, the amount of methadone taken over the previous 2 days is noted and divided by 4 to give a regular q12h dose, with 1/4 of the regular q12h dose q3h p.r.n.

If ≥ 2 doses/day of p.r.n. methadone continue to be needed, the dose of regular methadone should be increased by 1/3-1/2 once a week.

Method 2: Changing from oral morphine to oral methadone, q12h & p.r.n. (after Blackburn et al 2002)

Give a loading dose of methadone *at bedtime* 1/10 of the previous 24h PO morphine dose, up to a maximum of 30mg. *If very elderly or cachectic, omit loading dose.*

Prescribe 1/2 of the loading dose as a regular q12h dose (generally starting on the same day at bedtime), and 1/4 of the regular q12h dose q3h p.r.n.

In the event of severe uncontrolled pain, despite repeated p.r.n. doses, a second loading dose can be given. This is most likely in the first 48h after the switch.

If the patient complains of pain within 3h of a regular dose, take the next regular dose early (but the one after that at the normal time).

If the patient is very drowsy, omit one dose and then continue with a reduced regular dose.

If ≥ 2 doses/day of p.r.n. methadone continue to be needed, the dose of regular methadone should be increased by 1/3-1/2 once a week.

CSCI methadone

1. CSCI infusion of methadone causes a skin reaction; this is reduced if:
   - saline 0.9% is used as diluent
   - a more dilute solution in a 20ml or 30ml syringe is used
   - the syringe is changed q12h
   - the site is changed every day.

2. When converting to CSCI methadone from:
   - PO methadone, half the total daily PO dose
   - CSCI diamorphine, start with 1/20 of the dose of diamorphine (but if diamorphine dose >1g/24h, give 1/40)
   - CSCI morphine, start with 1/10 of the dose of morphine (but if morphine dose >1g/24h, give 1/20)

3. Additional rescue doses of methadone can be given for breakthrough pain, using 1/5-1/6 of the 24h infusion dose q3h p.r.n.

4. If necessary, p.r.n. doses of morphine (or other previously used strong opioid) can be given q1h, based on previous morphine requirements.

5. If ≥ 2 doses/day of p.r.n. methadone continue to be needed, the dose of regular methadone should be increased by 1/3-1/2 once a week.