What dose of methadone should I use?

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SPC dose rates for Comfortan®

- dogs: 0.5-1.0 mg/kg SC, IM or IV
- cats: 0.3-0.6 mg/kg IM only
What dose should I use?

What am I aiming to achieve?

- premedication
  - sedation / pre-emptive analgesia

- analgesia
What dose should I use?

- being a full opioid agonist, methadone has an almost linear dose-response curve
analgesic efficacy

full agonist

partial agonist

dose
‘Standard’ premedication doses of methadone

- 0.2-0.3 mg/kg IM (in combination with a sedative / tranquillizer)
- SPC dose 0.5-1.0 mg/kg

- 0.2-0.3 mg/kg IM (in combination with a sedative / tranquillizer)
- SPC dose 0.3-0.6 mg/kg
What might alter these doses?

Many factors influence the most appropriate dose to administer:

• temperament
  – quiet animals likely to require lower doses than aggressive animals for sedation

• health status
  – sick animals require less than healthy animals

• age
  – geriatric animals likely to have more exaggerated effect and of greater duration
Example protocols – healthy dogs

• ACP 0.03 mg/kg + methadone 0.3 mg/kg IM
• medetomidine 2-5 μg/kg + methadone 0.2 mg/kg IM
• dexmedetomidine 2-3 μg/kg + methadone 0.2 mg/kg IM
Example protocols – healthy cats

- ACP 0.05 mg/kg + methadone 0.3 mg/kg IM
- medetomidine 5-10 µg/kg + methadone 0.2 mg/kg IM
- dexmedetomidine 5 µg/kg + methadone 0.2 mg/kg IM
Example protocols – aggressive dogs

- medetomidine 5 μg/kg + methadone 0.5 mg/kg IM
- medetomidine 5 μg/kg + methadone 0.5 mg/kg + ketamine 0.5 mg/kg IM
- medetomidine 10 μg/kg + methadone 0.5 mg/kg ± ketamine 0.5-1 mg/kg IM

- or dexmedetomidine at half the above medetomidine doses

ketamine is off-licence when used in these protocols
Example protocols – aggressive cats

- medetomidine 20 µg/kg + methadone 0.5 mg/kg IM
- medetomidine 20 µg/kg + methadone 0.5 mg/kg + ketamine 2-3 mg/kg IM
- or dexmedetomidine at half the above medetomidine doses
Route of administration

• IV administration (dogs) will lead to faster and higher peak plasma concentrations
  – increased sedation and analgesia
  – increased likelihood of side-effects
• SC administration is likely to produce more variable onset and lower plasma concentrations
SPC dose rates for Comfortan®

- **dogs:** 0.5-1.0 mg/kg SC, IM or IV
- **cats:** 0.3-0.6 mg/kg IM only

The upper end of these dose ranges should not be the primary starting point.

i.e. the higher doses should only be reached following upwards titration from a lower dose.
Methadone duration - dogs and cats

- averages 4 hours
- each animal is an individual
- do not be afraid to top-up sooner if the animal needs it
  - animals in pain are very difficult to overdose with opioids if titrated to effect
Re-dosing with methadone - dogs

If you require to ‘top-up’ with methadone:

• 0.1 mg/kg diluted in 0.9% NaCl to at least 1ml and administered slowly IV over approx. 2 min
• if insufficient effect, repeat above at 10 min intervals

 or

• 0.2 mg/kg IM repeated at 20 min intervals, to effect

N.B. these doses are lower than those recommended on the Comfortan® SPC for analgesia
How quickly does methadone work?

- IV route → 10 min
- IM route → 15 min
- SC route → more variable
Re-dosing with methadone - dogs

- if you have reached a total cumulative dose of 0.6 mg/kg (IM or IV) and still have insufficient analgesia:
  - don’t forget to be multimodal!
  - consider dysphoria

...before continuing with additional increments
Re-dosing with methadone - cats

- Comfortan® is only licensed IM in cats
- lower dose range than dogs (0.3-0.6 mg/kg)
- increment with 0.1-0.2 mg/kg IM (depending on initial dose) every 20 min to achieve desired effect
Can methadone be given IV to cats?

- off licence
- lower doses should be used than those on the Comfortan® SPC
  - maximum of 0.2 mg/kg initial dose
  - can increment with 0.1 mg/kg slow IV every 10 min if required (up to total of 0.5 mg/kg)
Re-dosing with methadone – dogs and cats

- these incremental doses are suggestions only
- greater care (smaller increments) will be required if you’ve started with a relatively high dose
‘Topping-up’ during anaesthesia

• take care with the IV route, especially if the animal is anaesthetised (only licensed in dogs for this)
  – apnoea
  – severe bradycardia

• avoid these effects by using low doses IV in anaesthetised patients and titrating slowly
  – 0.1 mg/kg diluted in 0.9% NaCl to at least 1 ml and administered slowly IV over 5 min

• or give IM during anaesthesia
‘Topping-up’ during anaesthesia

• if administered IV to anaesthetised animals:
  – bradycardia → atropine 20 μg/kg IV
  – apnoea → IPPV until spontaneous ventilation resumes (turn down vaporiser)
  – avoid it in the first place!
How long can I continue methadone for?

• as long as the animal requires it!
• tolerance
  – increasing dose required over time to achieve the same effect
  – occurs rapidly with morphine
  – does not seem to occur with methadone
• dependence
  – common in humans (variable time to occur)
  – not recognised in animals
How long can I continue methadone for?

• as long as the animal requires it!

• long elimination half-life in humans → drug cumulation with repeated doses

• ? in dogs and cats
  – may need to reduce dose / increase dose interval if maintaining for > 24-48 hrs
Methadone doses - summary

A variety of factors will dictate the dose:

• degree of pain (already present or likely to occur)
• temperament
• health status
• route of administration

but...

being a full opioid agonist, methadone allows us to titrate dosing to achieve the desired effect
Methadone doses - summary