### HYDROCODONE

Class: Opioid analgesic and antitussive.

Indications: Moderate-severe pain not relieved by non-opioid analgesics, cough.

#### Pharmacology

Hydrocodone is a  $\mu$ -opioid receptor agonist. It is several times more potent than **codeine**; postoperatively, 10mg is at least as effective as **codeine** 60mg<sup>1,2</sup> and, as an antitussive, 10mg is at least as effective as **codeine** 30mg.<sup>3</sup> It is probably less constipating than **codeine**.<sup>3</sup> Hydrocodone is more than half as potent as morphine.<sup>4</sup> However, its use is restricted by the fact that it is available only in compound preparations. Thus, in practice, hydrocodone is generally used as an alternative to **codeine**.<sup>5</sup>

Like **codeine** and **oxycodone**, hydrocodone is metabolized by cytochrome P450 to both active and inactive metabolites, including **hydromorphone**.<sup>6,7</sup> Because hydrocodone is an active drug in its own right, conversion to **hydromorphone** via CYP2D6 is not essential.<sup>6,8,9</sup> Thus, although **fluoxetine** and **paroxetine** reduce the conversion to **hydromorphone**, they do not reduce the analgesic effect of hydrocodone.<sup>8</sup> There is considerable variation in the amount of drug and the metabolite excreted by man.<sup>10</sup> Two clusters have been identified; extensive metabolizers who excrete only 6–9% of the administered dose as unchanged hydrocodone and slow metabolizers who excrete 18–20% unchanged. The former may experience a faster onset of pain relief than the latter but not a greater duration or extent of relief.<sup>9</sup>

*Bio-availability* 25% PO. <sup>11</sup> *Onset of action* 20–30min. *Plasma halflife* 4h. *Duration of action* 4–8h.

## Cautions

Compound hydrocodone and **homatropine** preparations should also be used with caution in patients with glaucoma or raised intracranial pressure.

#### Undesirable effects

For full lists, see manufacturers' PIs. In compound preparations the lists include the undesirable effects of both drugs.

*Very common* (>10%): lightheadedness, dizziness, sedation, drowsiness, weakness, tiredness, hypotension, constipation.

*Common* (<10%, >1%): hydrocodone + **ibuprofen**: seizures, respiratory depression, bronchospasm, nausea, vomiting, gastro-intestinal bleeding, diarrhea, flushing, pruritus, urticaria.

Compound hydrocodone and **homatropine**: increased intra-ocular pressure, confusion, vertigo, respiratory depression, bradycardia, tachycardia, nausea, urinary retention.

#### Dose and use

#### Pain relief

In the USA, hydrocodone is used only in combination with a non–opioid analgesic.

Compound hydrocodone and **acetaminophen**: the dose of hydrocodone is limited by the need to restrict the dose of **acetaminophen** to 4g/24h. Even so, given the available preparations, it is possible to prescribe hydrocodone 120mg/24h, equivalent to about **morphine** 80mg.

Compound hydrocodone and **ibuprofen**: only one combination is available.<sup>12,13</sup> If a patient can tolerate **ibuprofen** 2400mg/24h,<sup>14</sup> the corresponding dose of hydrocodone will be 90mg/24h, equivalent to about **morphine** 60mg.

# Cough

Compound hydrocodone and homatropine:

- start with 5mg hydrocodone (1 tablet or 5ml oral solution) b.i.d.
- if necessary, increase to 10–15mg hydrocodone (2–3 tablets or 10–15ml syrup) q4h<sup>15</sup>
- manufacturer's recommended maximum dose 6 tablets or 30ml syrup daily (= 30mg hydrocodone).

A single dose of hydrocodone is generally limited to 15mg due to the fixed combination with **homatropine**.

## Supply

Unless indicated otherwise, all preparations are Schedule III controlled substances.

Compound hydrocodone and **acetaminophen** preparations

Hydrocodone and acetaminophen 2.5/500

*Tablets* hydrocodone 2.5mg + acetaminophen 500mg, 28 days @ 2 q.i.d. = \$75 (AWP).

Hydrocodone and **acetaminophen** 5/500

*Tablets* hydrocodone 5mg + acetaminophen 500mg, 28 days @ 2 q.i.d. = \$114 (AWP).

Hydrocodone and acetaminophen 7.5/500

*Tablets* hydrocodone 7.5mg + acetaminophen 500mg, 28 days @ 2 q.i.d. = \$129 (AWP).

*Oral solution* hydrocodone 7.5mg + **acetaminophen** 500mg/15ml, 28 days @ 30ml q.i.d. = \$778.

Hydrocodone and acetaminophen 10/325

*Tablets* hydrocodone 10mg + acetaminophen 325mg, 28 days @ 2 q4h = \$120 (AWP).

Hydrocodone and **acetaminophen** 10/500 *Tablets* hydrocodone 10mg + **acetaminophen** 500mg, 28 days @ 2 q.i.d. = \$112.

Compound hydrocodone and **ibuprofen** preparations Hydrocodone/**ibuprofen** 7.5/200 (generic) **Tablets** hydrocodone 7.5mg + **ibuprofen** 200mg, 28 days @ 1 q.i.d. = \$104.

Vicoprofen® (Abbott) *Tablets* hydrocodone 7.5mg + **ibuprofen** 200mg, 28 days @ 1 q.i.d. = \$131. Compound hydrocodone and **homatropine** preparations Hycodan® (Endo)

*Tablets* hydrocodone bitartrate 5mg + homatropine methylbromide 1.5mg, 28 days @ 1 q.i.d. = \$117.

*Oral solution* hydrocodone bitartrate 5mg + homatropine methylbromide 1.5mg/5ml, 28 days @ 5ml q.i.d. = \$132.

This is not a complete list; see AHFS for more information.

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