ed not more often than every 4 hours; a dose of 2 mg/hour is the recommended starting dose as an intravenous infusion. The intravenous route may also be used for patient-controlled analgesia. When given subcutaneously, the starting dose is 5 mg every 4 hours; subcutaneous infusions should be started at 7.5 mg daily in opioid-naive patients. When transferring between oral and parenteral oxycodone, UK licensed product information advises that, as a guide, 2 mg of oral oxycodone is equivalent to about 1 mg of parenteral oxycodone.

Oxycodone has been given rectally as suppositories containing 30 mg of oxycodone (as the pectinate) or 10 or 20 mg of oxycodone hydrochloride; the dose may be repeated every 6 to 8 hours.

For doses in patients with hepatic or renal impairment, see below.

Oxycodone terephthalate is also used orally.

Administration in children. Although oxycodone hydrochloride is not licensed in the UK for use in children under 18 years old, the *BNFC* suggests that it may be given for the treatment of moderate to severe pain in palliative care. Those aged from 1 month to 12 years may be given initial oral doses of 200 micrograms/kg (up to 5 mg) every 4 to 6 hours increased thereafter as necessary according to response; older children may be given the usual adult dose (see above). Oxycodone hydrochloride may also be given orally as a modified-release preparation every 12 hours to those aged 8 years and older.

Administration in hepatic or renal impairment. The plasma concentrations of oxycodone may be increased in patients with hepatic or renal impairment and consequently dosage adjustment may be necessary in such patients. In the UK, licensed product information recommends that the oral starting dose for adult patients with mild hepatic impairment or mild to moderate renal impairment should be 2.5 mg given every 6 hours; it contra-indicates the use of oxycodone in those with moderate to severe hepatic impairment or severe renal impairment. US product information permits the cautious use of oxycodone in adult patients with severe hepatic or severe renal impairment.

Pain. References.

1. Sunshine A, *et al.* Analgesic efficacy of controlled-release oxycodone in postoperative pain. *J Clin Pharmacol* 1996; **36:** 595–603.
2. Curtis GB, *et al.* Relative potency of controlled-release oxycodone and controlled-release morphine in a postoperative pain model. *Eur J Clin Pharmacol* 1999; **55:** 425–9.
3. Gimbel JS, *et al.* Controlled-release oxycodone for pain in diabetic neuropathy: a randomized controlled trial. *Neurology* 2003; **60:** 927–34.
4. Gammaitoni AR, *et al.* Randomized, double-blind, placebo-controlled comparison of the analgesic efficacy of oxycodone 10 mg/acetaminophen 325 mg versus controlled-release oxycodone 20 mg in postsurgical pain.*J Clin Pharmacol* 2003; **43:** 296–304.
5. Oldfield V, Perry CM. Oxycodone/ibuprofen combination tablet: a review of its use in the management of acute pain. *Drugs* 2005; **65:** 2337–54.
6. Kalso E. Oxycodone. *J Pain Symptom Manage* 2005; **29** (suppl): S47–S56.
7. Bercovitch M, Adunsky A. High dose controlled-release oxycodone in hospice care. *J Pain Palliat Care Pharmacother* 2006; **20:** 33–9.
8. Reid CM, *et al.* Oxycodone for cancer-related pain: meta-analysis of randomized controlled trials. *Arch Intern Med* 2006; **166:** 837–43. Correction. *ibid.*; 2387.
9. Portenoy RK, *et al.* Long-term use of controlled-release oxycodone for noncancer pain: results of a 3-year registry study. *Clin J Pain* 2007; **23:** 287–99.
10. Pan H, *et al.* Efficacy and tolerability of oxycodone hydrochloride controlled-release tablets in moderate to severe cancer pain. *Clin Drug Invest* 2007; **27:** 259–67.

Preparations

USP 31: Oxycodone and Acetaminophen Capsules; Oxycodone and Acetaminophen Tablets; Oxycodone and Aspirin Tablets; Oxycodone Hydrochloride Extended-Release Tablets; Oxycodone Hydrochloride Oral Solution; Oxycodone Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Oxicalmans; Oxinovag; Oxycontin; ***Austral.:*** Endone; Oxycontin; Oxynorm; Proladone; ***Austria:*** Oxycontin; Oxynorm; ***Belg.:*** Oxycontin; ***Braz.:*** Oxycontin; ***Canad.:*** Oxy IR; Oxycontin; Supeudol; ***Chile:*** Oxycontin; ***Cz.:*** Oxycontin; ***Denm.:*** Oxycontin; Oxynorm; ***Fin.:*** Oxanest; Oxycontin; Oxynorm; ***Fr.:*** Eubine†; Oxycontin; Oxynorm; ***Ger.:*** Oxygesic; ***Hung.:*** Oxycontin; ***Irl.:*** Oxycontin; Oxynorm; ***Israel:*** Oxycod; Oxycontin; ***Ital.:*** Oxycontin; ***Jpn:*** Oxycontin; ***Malaysia:*** Oxycontin; ***Mex.:*** Oxycontin†; ***Neth.:*** Oxycontin; Oxynorm; ***Norw.:*** Oxycontin; Oxynorm; ***NZ:*** Oxycontin; Oxynorm; ***Philipp.:*** Oxycontin; ***Port.:*** Oxycontin; ***Singapore:*** Oxycontin; Oxynorm; ***Spain:*** Oxycontin; Oxynorm; ***Swed.:*** Oxycontin; Oxynorm; ***Switz.:*** Oxycontin; Oxynorm; ***UK:*** Oxycontin; Oxynorm; ***USA:*** Endocodone†; ETH-Oxydose; Oxycontin; Oxyfast; OxylR; Percolone†; Roxicodone; ***Venez.:*** Oxycontin.

Multi-ingredient: ***Arg.:*** Oxinovag Complex; ***Canad.:*** Endocet; Endodan; Percocet; Percodan; ratio-Oxycocet; ratio-Oxycodan; ***Israel:*** Percocet; Percodan; ***Ital.:*** Depalgos; ***USA:*** Combunox; Endocet; Magnacet; Narvox; Percocet; Percodan; Perloxx; Roxicet; Roxilox; Roxiprin†; Tylox.

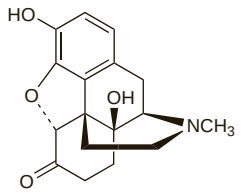
Oxymorphone Hydrochloride *(BANM, rINNM)* ⊗

7,8-Dihydro-14-hydroxymorphinone hydrochloride; Hidrocloruro de oximorfona; Oximorphone Hydrochloride; Oxymorphone, Chlorhydrate d'; Oxymorphoni Hydrochloridum. 6-Deoxy-7,8-dihydro-14-hydroxy-6-oxomorphine hydrochloride; (–)-(5*R*,6*S*,14*S*)-4,5-Epoxy-3,14-dihydroxy-9a-methylmorphinan-6-one hydrochloride.

Оксиморфона Гидрохлорид

$C_{17}H_{19}NO_4,HCl$ = 337.8.

CAS — 76-41-5 (oxymorphone); 357-07-3 (oxymorphone hydrochloride).



(oxymorphone)

Pharmacopoeias. In *US*.

USP 31 (Oxymorphone Hydrochloride). A white or slightly off-white odourless powder, darkening on exposure to light. Its aqueous solutions are slightly acidic. Soluble 1 in 4 of water, 1 in 100 of alcohol, and 1 in 25 of methyl alcohol; very slightly soluble in chloroform and in ether. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Dependence and Withdrawal

As for Opioid Analgesics in general, p.101.

Adverse Effects, Treatment, and Precautions

As for Opioid Analgesics in general, p.102.

For details on the use of oxymorphone in patients with hepatic or renal impairment see below.

Interactions

For interactions associated with opioid analgesics, see p.103.

Licensed product information for a modified-release preparation of oxymorphone hydrochloride (*Opana ER; Endo, USA*) states that patients must not ingest alcohol, including alcohol-containing medicines, at the same time due to the risk of increased plasma concentrations and a potentially fatal overdose of oxymorphone.

Pharmacokinetics

Oxymorphone hydrochloride is absorbed from the gastrointestinal tract after oral doses, but bioavailability is only about 10% because of first-pass metabolism. Absorption is increased after a high-fat meal. About 10% is bound to plasma proteins. Oxymorphone is extensively metabolised in the liver by glucuronidation and less than 1% of a dose appears in the urine and faeces as unchanged drug. With regard to its major metabolites between 33 and 38% of a dose is excreted in the urine as oxymorphone-3-glucuronide and less than 1% as 6-OH-oxymorphone. Oxymorphone crosses the placenta.

◊ References.

1. Adams MP, Ahdieh H. Pharmacokinetics and dose-proportionality of oxymorphone extended release and its metabolites: results of a randomized crossover study. *Pharmacotherapy* 2004; **24:** 468–76.
2. Adams MP, Ahdieh H. Single- and multiple-dose pharmacokinetic and dose-proportionality study of oxymorphone immediate-release tablets. *Drugs R D* 2005; **6:** 91–9.

Uses and Administration

Oxymorphone hydrochloride, a phenanthrene derivative, is an opioid analgesic (p.101) with actions and uses similar to those of morphine (p.86), apart from a lack of cough suppressant activity. Oxymorphone is given orally, parenterally, or rectally for the relief of moderate to severe pain, including pain in obstetrics, and is reported to provide analgesia for 3 to 6 hours. It may also be used parenterally for premedication, as an adjunct to anaesthesia, and to relieve dyspnoea due to pulmonary oedema resulting from left ventricular failure.

A usual *oral* starting dose for opioid-naive patients is 10 to 20 mg of oxymorphone hydrochloride every 4 to 6 hours adjusted thereafter as necessary; some patients may be started on lower doses of 5 mg. For patients who have been receiving a strong opioid analgesic the initial dose of oxymorphone should be based on the daily opioid requirement; licensed product information suggests that 10 mg of oral oxymorphone is equivalent to about 30 mg of oral morphine and recommends giving half the calculated equivalent dose of oxymorphone initially. Oxymorphone hydrochloride may also be given orally as a modified-release preparation every 12 hours. Oral preparations of oxymorphone should be taken on an empty stomach.

Oxymorphone hydrochloride is given by *intramuscular* or *subcutaneous injection* in initial doses of 1 to 1.5 mg, repeated every 4 to 6 hours as necessary; 500 micrograms may be given by intravenous injection. The usual dose for analgesia during labour is 0.5 to 1 mg intramuscularly. When transferring between oral and parenteral oxymorphone, licensed product information advises that, as a guide, 10 mg of oral oxymorphone is equivalent to about 1 mg of parenteral oxymorphone.

Oxymorphone hydrochloride is also given *rectally* as a suppository in a dose of 5 mg every 4 to 6 hours.

◊ References.

1. Prommer E. Oxymorphone: a review. *Support Care Cancer* 2006; **14:** 109–15.
2. Chamberlin KW, *et al.* Oral oxymorphone for pain management. *Ann Pharmacother* 2007; **41:** 1144–52.

Administration in hepatic impairment. Advice on the use of oxymorphone in patients with hepatic impairment is conflicting. Licensed product information for one range of preparations (*Opana* and *Opana ER tablets; Endo, USA*) recommends caution in patients with mild hepatic impairment; these patients should be started on the lowest oral dose and titrated slowly thereafter. In addition, it is stated that oxymorphone is contra-indicated in those with moderate or severe impairment. However, licensed information for another oxymorphone preparation (*Numorphan injection and suppositories; Endo, USA*) only recommends caution in hepatic disease although lower doses (unspecified) are advised in those patients with severe impairment.

Administration in renal impairment. In patients with moderate to severe renal impairment, the bioavailability of oxymorphone was found to increase by over 50%; consequently, it is recommended that oxymorphone is given with caution and in reduced doses (unspecified) to those with a creatinine clearance of less than 50 mL/minute.

Preparations

USP 31: Oxymorphone Hydrochloride Injection; Oxymorphone Hydrochloride Suppositories.

Proprietary Preparations (details are given in Part 3)

Canad.: Numorphan†; ***USA:*** Numorphan; Opana.

Oxyphenbutazone *(BAN, rINN)*

G-27202; Hydroxyphenylbutazone; Oksifenbutatsoni; Oxifenbutazon; Oxifenbutazona; Oxyphenbutazonum. 4-Butyl-1-(4-hydroxyphenyl)-2-phenylpyrazolidine-3,5-dione monohydrate.

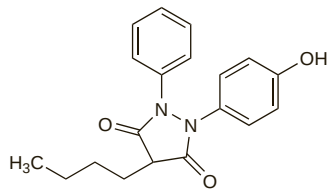
Оксифенбутазон

$C_{19}H_{20}N_2O_3,H_2O$ = 342.4.

CAS — 129-20-4 (anhydrous oxyphenbutazone); 7081-38-1 (oxyphenbutazone monohydrate).

ATC — M01AA03; M02AA04; S01BC02.

ATC Vet — QM01AA03; QM02AA04; QS01BC02.



Profile

Oxyphenbutazone, a metabolite of phenylbutazone (p.117), is an NSAID (p.96). It has been applied topically to the eye as an anti-inflammatory ointment in conditions such as episcleritis. Oxyphenbutazone was used systemically in disorders such as ankylosing spondylitis, osteoarthritis, and rheumatoid arthritis but such use is no longer considered justified because of the risk of severe haematological adverse effects (see also Effects on the Blood, under Phenylbutazone, p.117).

The piperazine salt has also been used.

Porphyria. Oxyphenbutazone has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Preparations

Proprietary Preparations (details are given in Part 3)

India: Sioril†; ***Mex.:*** Edefen†; Redolet†.

Multi-ingredient: ***Braz.:*** Algi Peralgin†; Algiflamanil; Analtrix†; Febupen; Flamanan; Reumazine†; ***Mex.:*** Dartrizon.