Effects on the liver. Fatal fulminant hepatitis occurred[1] in a 56-year-old woman who had received 600 to 1200 mg of oxaprozin daily for about 6 weeks. In another patient symptomatic hepatitis developing during oxaprozin use resolved on stopping the drug.[2]

1. Purdum PP, *et al.* Oxaprozin-induced fulminant hepatitis. *Ann Pharmacother* 1994; **28:** 1159–61.
2. Kethu SR, *et al.* Oxaprozin-induced symptomatic hepatotoxicity. *Ann Pharmacother* 1999; **33:** 942–4.

Interactions

For interactions associated with NSAIDs, see p.99.

Pharmacokinetics

Oxaprozin is slowly but extensively absorbed from the gastrointestinal tract; it is 99% bound to plasma proteins, mainly albumin. Peak plasma concentrations are reached after about 2 to 3 hours. At steady state, the biological half-life is about 44 hours. Oxaprozin is metabolised mainly in the liver by microsomal oxidation and conjugation with glucuronic acid to form inactive metabolites which are excreted in the urine (65%) and faeces (35%).

◊ References.

1. Karim A. Inverse nonlinear pharmacokinetics of total and protein unbound drug (oxaprozin): clinical and pharmacokinetic implications. *J Clin Pharmacol* 1996; **36:** 985–97.
2. Karim A, *et al.* Oxaprozin and piroxicam, nonsteroidal antiinflammatory drugs with long half-lives: effect of protein-binding differences on steady-state pharmacokinetics. *J Clin Pharmacol* 1997; **37:** 267–78.
3. Davies NM. Clinical pharmacokinetics of oxaprozin. *Clin Pharmacokinet* 1998; **35:** 425–36.

Uses and Administration

Oxaprozin, a propionic acid derivative, is an NSAID (p.99). It is used in the treatment of osteoarthritis and rheumatoid arthritis in a usual oral dose of 1.2 g given once daily, although in osteoarthritis, patients with low body-weight or mild disease should be given an initial dose of 600 mg once daily. The recommended maximum daily dose is 1.8 g or 26 mg/kg, whichever is the lower.

For doses in patients with renal impairment and in children see below.

◊ References.

1. Miller LG. Oxaprozin: a once-daily nonsteroidal anti-inflammatory drug. *Clin Pharm* 1992; **11:** 591–603.
2. Anonymous. Oxaprozin for arthritis. *Med Lett Drugs Ther* 1993; **35:** 15–16.
3. Dallegri F, *et al.* A review of the emerging profile of the anti-inflammatory drug oxaprozin. *Expert Opin Pharmacother* 2005; **6:** 777–85.

Administration in children. Oxaprozin is given orally in the treatment of juvenile idiopathic arthritis (p.10) in children aged 6 years and over. Doses are expressed in terms of body-weight and may be given once daily:

- 22 to 31 kg: 600 mg
- 32 to 54 kg: 900 mg
- 55 kg and over: 1200 mg

Administration in renal impairment. US licensed product information for oxaprozin recommends that the initial oral dose in patients with severe renal impairment or on dialysis is 600 mg once daily. The dose may be increased to 1.2 g once daily, if necessary.

Preparations

USP 31: Oxaprozin Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Zakoprosin; ***Belg.:*** Duraprox; ***Canad.:*** Daypro; ***Chile:*** Duraprox; Walix; ***Cz.:*** Dayrun; ***Ger.:*** Danoprox†; Dayrun†; ***Gr.:*** Duraprox; Misaf; Nisaid; Oxapron; Trimelot; ***Ital.:*** Walix; ***Jpn:*** Alvo; ***S.Afr.:*** Deflam; ***USA:*** Daypro.

Oxycodone *(BAN, USAN, rINN)* ⊗

Dihydrone; 14-Hydroxydihydrocodeinone; NSC-19043; Oksikodoni; Oxicodona; Oxikodon; Oxycodonum. 6-Deoxy-7,8-dihydro-14-hydroxy-3-*O*-methyl-6-oxomorphine; (–)-(5*R*,6*S*,14*S*)-4,5-Epoxy-14-hydroxy-3-methoxy-9a-methylmorphinan-6-one.

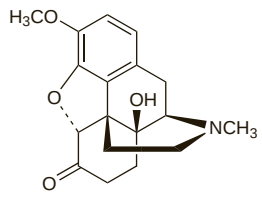
Оксикодон

$C_{18}H_{21}NO_4$ = 315.4.

CAS — 76-42-6.

ATC — N02AA05.

ATC Vet — QN02AA05.



NOTE. Compounded preparations of oxycodone may be represented by the following names:

- Co-oxycodAPAP (*PEN*)—oxycodone and paracetamol.

The following terms have been used as 'street names' (see p.vi) or slang names for various forms of oxycodone:
40; 40-bar; 80; Blue; Cotton; Hillbilly heroin; Kicker; OC; Os; Ox; Oxy; Oxy Cotton; Oxycotton; Percs; Perks; Pills; Pink spoons; Rushbo.

Oxycodone Hydrochloride *(BANM, USAN, rINNM)* ⊗

7,8-Dihydro-14-hydroxycodeinone hydrochloride; Dihydrone Hydrochloride; Hidrocloruro de oxicodona; Oksikodonihydrokloridi; Oksikodono hidrochloridas; Oxikodonhydroklorid; Oxycodone, chlorhydrate d'; Oxycodoni hydrochloridum; Oxycone Hydrochloride; Oxykodon-hydrochlorid; Thecodine.

Оксикодона Гидрохлорид

$C_{18}H_{21}NO_4$,HCl = 351.8.

CAS — 124-90-3.

ATC — N02AA05.

ATC Vet — QN02AA05.

Pharmacopoeias. In *Eur.* (see p.vii) and *US. Jpn* includes the trihydrate.

Ph. Eur. 6.2 (Oxycodone Hydrochloride). A white or almost white, hygroscopic, powder. Freely soluble in water; sparingly soluble in dehydrated alcohol; practically insoluble in toluene. Store in airtight containers. Protect from light.

USP 31 (Oxycodone Hydrochloride). A white to off-white, odourless, hygroscopic crystals or powder. Soluble in water; slightly soluble in alcohol. Store in airtight containers.

Oxycodone Terephthalate ⊗

Oxicodona, tereftalato de. 4,5α-Epoxy-14-hydroxy-3-methoxy-17-methylmorphinan-6-one 1,4-benzenedicarboxylate (2:1) salt.

Оксикодона Терефталат

$(C_{18}H_{21}NO_4)_2,C_8H_6O_4$ = 796.9.

CAS — 64336-55-6.

Pharmacopoeias. In *US.*

USP 31 (Oxycodone Terephthalate). Store in airtight containers.

Dependence and Withdrawal

As for Opioid Analgesics in general, p.101.

Oxycodone has been subject to abuse (see under Adverse Effects, Treatment, and Precautions, below).

◊ Takotsubo-like cardiomyopathy developed in a 61-year-old woman when her dose of oxycodone was inadvertently and greatly reduced 7 days after surgery for degenerative osteoarthritis.[1] The patient had a chronic history of opioid dependence and had been treated with oxycodone (80 mg daily) and hydromorphone (4 mg every 3 hours as needed) for several months before surgery; postoperatively, her dose of oxycodone had been increased to 120 mg daily with additional doses for breakthrough pain.

1. Rivera JM, *et al.* "Broken heart syndrome" after separation (from OxyContin). *Mayo Clin Proc* 2006; **81:** 825–8.

Adverse Effects, Treatment, and Precautions

As for Opioid Analgesics in general, p.102.

UK licensed product information contra-indicates the use of oxycodone in patients with moderate to severe hepatic impairment or severe renal impairment; however, product information in the USA permits its cautious use in patients with severe hepatic or severe renal impairment although doses may need to be reduced.

Abuse. Oxycodone hydrochloride modified-release tablets have been subject to abuse.[1-3] The crushed tablets have been inhaled or injected by addicts and in some cases this has resulted in fatalities.

1. Wolf BC, *et al.* One hundred seventy two deaths involving the use of oxycodone in Palm Beach County. *J Forensic Sci* 2005; **50:** 192–5.
2. Cicero TJ, *et al.* Trends in abuse of OxyContin and other opioid analgesics in the United States: 2002-2004. *J Pain* 2005; **6:** 662–72.
3. Adlaf EM, *et al.* Use of OxyContin by adolescent students. *Can Med Assoc J* 2006; **174:** 1303.

Effects on the respiratory system. References[1,2] to respiratory depression occurring in children given oxycodone.

1. Olkkola KT, *et al.* Pharmacokinetics and ventilatory effects of intravenous oxycodone in postoperative children. *Br J Clin Pharmacol* 1994; **38:** 71–6.
2. Kalso E. Pharmacokinetics and ventilatory effects of intravenous oxycodone in postoperative children. *Br J Clin Pharmacol* 1995; **39:** 214.

Hepatic impairment. The clearance and elimination of oxycodone were prolonged in 6 women with end-stage liver cirrhosis awaiting liver transplantations.[1] Significant ventilatory depression also occurred. Pharmacokinetic values after successful transplantation were similar to those previously reported for healthy adults. It was recommended that, when giving oxycodone to patients with end-stage liver disease, the dosing frequency should be reduced and the dose lowered.

1. Tallgren M, *et al.* Pharmacokinetics and ventilatory effects of oxycodone before and after liver transplantation. *Clin Pharmacol Ther* 1997; **61:** 655–61.

Porphyria. Oxycodone is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals*.

Interactions

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

Antidepressants. For reference to possible cases of serotonin syndrome associated with use of oxycodone and *SSRIs*, see Opioid Analgesics under Interactions of Fluoxetine, p.397.

Pharmacokinetics

Oxycodone is absorbed from the gastrointestinal tract; oral bioavailability is about 60 to 87% due to lower pre-systemic and/or first-pass metabolism compared with other opioids. About 45% is bound to plasma proteins. It is metabolised to noroxycodone, via cytochrome P450 isoenzymes of the CYP3A family, and, to a lesser extent, to oxymorphone (p.107) via CYP2D6. Both metabolites undergo glucuronidation and are excreted with unchanged drug in urine. The elimination half-life of oxycodone is reported to be 2 to 4 hours. Oxycodone crosses the placenta and is distributed into breast milk.

◊ References.

1. Pöyhiä R, *et al.* The pharmacokinetics of oxycodone after intravenous injection in adults. *Br J Clin Pharmacol* 1991; **32:** 516–18.
2. Leow KP, *et al.* Single-dose and steady-state pharmacokinetics and pharmacodynamics of oxycodone in patients with cancer. *Clin Pharmacol Ther* 1992; **52:** 487–95.
3. Mandema JW, *et al.* Characterization and validation of a pharmacokinetic model for controlled-release oxycodone. *Br J Clin Pharmacol* 1996; **42:** 747–56.
4. Kaiko RF, *et al.* Pharmacokinetic-pharmacodynamic relationships of controlled-release oxycodone. *Clin Pharmacol Ther* 1996; **59:** 52–61.
5. Gammaitoni AR, Davis MW. Comparison of the pharmacokinetics of oxycodone administered in three Percocet formulations. *J Clin Pharmacol* 2002; **42:** 192–7.
6. Lalovic B, *et al.* Pharmacokinetics and pharmacodynamics of oral oxycodone in healthy human subjects: role of circulating active metabolites. *Clin Pharmacol Ther* 2006; **79:** 461–79.

Children. The pharmacokinetics of oxycodone in children have been studied[1-4] and are generally considered similar to those in adults.[2,4] However, pharmacokinetics may be more variable in infants aged from 0 to 6 months, particularly those aged 2 months and under.[5]

1. Olkkola KT, *et al.* Pharmacokinetics and ventilatory effects of intravenous oxycodone in postoperative children. *Br J Clin Pharmacol* 1994; **38:** 71–6.
2. Kokki H, *et al.* Pharmacokinetics of oxycodone after intravenous, buccal, intramuscular and gastric administration in children. *Clin Pharmacokinet* 2004; **43:** 613–22.
3. El-Tahtawy A, *et al.* Population pharmacokinetics of oxycodone in children 6 months to 7 years old. *J Clin Pharmacol* 2006; **46:** 433–42.
4. Kokki H, *et al.* Comparison of oxycodone pharmacokinetics after buccal and sublingual administration in children. *Clin Pharmacokinet* 2006; **45:** 745–54.
5. Pokela ML, *et al.* Marked variation in oxycodone pharmacokinetics in infants. *Paediatr Anaesth* 2005; **15:** 560–565.

Uses and Administration

Oxycodone, a phenanthrene derivative, is an opioid analgesic (p.104). Oxycodone hydrochloride is given orally or by subcutaneous or intravenous injection for the relief of moderate to severe pain.

A usual oral starting dose for opioid-naive patients in severe pain is 5 mg every 4 to 6 hours increased thereafter as necessary according to response. For patients who have been receiving a strong opioid analgesic the initial dose of oxycodone should be based on the daily opioid requirement; UK licensed product information suggests that 10 mg of oral oxycodone is equivalent to about 20 mg of oral morphine. Most patients do not require more than 400 mg daily. Preparations containing oxycodone hydrochloride and aspirin, ibuprofen, or paracetamol are also used. Oxycodone hydrochloride may also be given orally as a modified-release preparation every 12 hours.

For details of doses in children, see below.

Intravenous doses of oxycodone hydrochloride range from 1 to 10 mg, given over 1 to 2 minutes, and repeat-