5. Kvale PA, *et al.* American College of Chest Physicians. Lung cancer: palliative care. *Chest* 2003; **123** (suppl): 284S–311S. Also available at: http://www.chestjournal.org/cgi/reprint/123/1_suppl/284S.pdf (accessed 26/06/08)
6. Qaseem A, *et al.* Clinical Efficacy Assessment Subcommittee of the American College of Physicians. Evidence-based interventions to improve the palliative care of pain, dyspnea, and depression at the end of life: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2008; **148:** 141–6. Also available at: http://www.annals.org/cgi/reprint/148/2/141.pdf (accessed 28/08/08)
7. Lorenz KA, *et al.* Evidence for improving palliative care at the end of life: a systematic review. *Ann Intern Med* 2008; **148:** 147–59.
8. Chandler S. Nebulized opioids to treat dyspnea. *Am J Hosp Palliat Care* 1999; **16:** 418–22.
9. Foral PA, *et al.* Nebulized opioids use in COPD. *Chest* 2004; **125:** 691–4.
10. Brown SJ, *et al.* Nebulized morphine for relief of dyspnea due to chronic lung disease. *Ann Pharmacother* 2005; **39:** 1088–92.
11. Kallet RH. The role of inhaled opioids and furosemide for the treatment of dyspnea. *Respir Care* 2007; **52:** 900–10.

Pain. Opioid analgesics are used for the relief of acute and chronic pain (see Choice of Analgesic, p.2). Not every type of pain responds; neuropathic pain, for example, may not be alleviated by opioid therapy. For further discussion of specific pain states and the role of opioid analgesics in their treatment see p.5 onwards.

There has also been interest in the local analgesic effects of opioids themselves.[1,2]

The use of opioid analgesics in opioid-dependent patients receiving maintenance treatment with an opioid is the subject of much debate; however, some consider such use to be appropriate in the management of acute pain in these patients and recommendations have been issued.[3]

1. Thompson DF, Pierce DR. Local analgesia with opioid drugs. *Ann Pharmacother* 1995; **29:** 189–90.
2. Stein C. The control of pain in peripheral tissue by opioids. *N Engl J Med* 1995; **332:** 1685–90.
3. Alford DP, *et al.* Acute pain management for patients receiving maintenance methadone or buprenorphine therapy. *Ann Intern Med* 2006; **144:** 127–34.

HEADACHE. Opioid analgesics such as codeine are sometimes included in oral compound analgesic preparations used in the initial treatment of migraine (see p.616) or tension-type headache (see p.617), but are best avoided, especially in patients who experience frequent attacks.

Restless legs syndrome. Some opioids may be beneficial in the treatment of restless legs syndrome (see Sleep-associated Movement Disorders, p.958), although evidence is scanty.

Sedation. In addition to their analgesic action opioids have been used for their sedative properties. Mention of this use of opioids can be found in the discussions of anaesthesia (p.1780), endoscopy (p.956), and intensive care (p.957).

Tetanus. Opioid analgesics can be used to provide analgesia and additional sedation in patients undergoing treatment for tetanus (p.196 and p.1901). Opioids such as fentanyl, morphine, and sufentanil have also been given to control the sympathetic overactivity in such patients.[1-3]

1. Rocke DA, *et al.* Morphine in tetanus—the management of sympathetic nervous system overactivity. *S Afr Med J* 1986; **70:** 666–8.
2. Moughabghab AV, *et al.* Management of autonomic dysfunction in severe tetanus: the use of fentanyl. *Can J Anaesth* 1995; **42:** 955.
3. Bhagwanjee S, *et al.* Management of sympathetic overactivity in tetanus with epidural bupivacaine and sufentanil: experience with 11 patients. *Crit Care Med* 1999; **27:** 1721–5.

Opium

Gum Opium; Nyers ópium; Opijus, žaliavinis; Opio; Opium brut; Opium crudum; Opium surové; Raakaopiumi; Råopium; Raw Opium.

Опиум

ATC — A07DA02; N02AA02.
ATC Vet — QA07DA02; QN02AA02.

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of opium:
Ah-pen-yen; Aunti; Aunti Emma; Big O; Black; Black pill; Black shit; Black stuff; Black tar opium; Block; Boulette; Chandoo; Chandu; China; Chinese molasses; Chinese tobacco; Chocolate; Cruz; Dopium; Dover's deck; Dover's powder; Dream gum; Dream gun; Dream stick; Dreams; Dutch courage; Easing powder; Fi-do-nie; Gee; God's medicine; Goma; Gondola; Gong; Goric; Great tobacco; Gum; Guma; Hard stuff; Hocus; Hop; Hops; Incense; Indonesian bud; Joy plant; Midnight oil; Mira; Mud; O; O.P.; Ope; O-Rock DC; Pen yan; Pin gon; Pin yen; Pox; Skee; Tar; Toxy; Toys; When-shee; Ze; Zero.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.
Chin., *Eur.*, and *US* include a monograph for prepared or powdered opium. *Eur.* also contains monographs for standardised opium dry extract or standardised opium tincture. *Jpn* includes prepared opium and a diluted opium powder containing 1% of anhydrous morphine.
Ph. Eur. 6.2 (Opium, Raw; Opium BP 2008). The air-dried latex obtained by incision from the unripe capsules of *Papaver somniferum* L. It has a characteristic odour and a blackish-brown colour. It should contain not less than 10% of anhydrous morphine, not less than 2% of anhydrous codeine, and not more than 3% of anhydrous thebaine. Protect from light.
Ph. Eur. 6.2 (Opium, Prepared; Opii Pulvis Normatus). Raw opium powdered and dried at a temperature not exceeding 70°. It is a yellowish-brown or dark brown powder and contains 9.8 to 10.2% of morphine and not less than 1.0% of codeine, calculated with reference to the dried drug. The content may be adjusted by adding a suitable excipient or raw opium powder.
USP 31 (Opium). The air-dried milky exudate obtained by incising the unripe capsules of *Papaver somniferum* (Papaveraceae). Externally it is pale olive-brown or olive-grey; internally it is reddish-brown. It has a very characteristic odour and a very bitter taste. It yields not less than 9.5% of anhydrous morphine.
USP 31 (Powdered Opium). Opium dried at a temperature not exceeding 70°, and reduced to a very fine light brown or moderately yellowish-brown powder that yields not less than 10% and not more than 10.5% of anhydrous morphine. It may contain any of the permitted diluents with the exception of starch.

Profile

Opium is the air-dried latex obtained by incision from the unripe capsules of *Papaver somniferum* (Papaveraceae). It contains morphine, codeine, and thebaine and a variable mixture of other alkaloids including noscapine and papaverine. The exuded latex is dried and manipulated to form cakes of uniform composition, variously shaped according to the country of origin, and known in commerce as Turkish, Indian, or European opium.

Opium has the properties of opioid analgesics (p.101). Its analgesic and sedative actions are due mainly to its content of morphine (p.89). It acts less rapidly than morphine since opium appears to be more slowly absorbed; the relaxing action of the papaverine and noscapine on intestinal muscle makes it more constipating than morphine.

Opium is intended only as the starting material for the manufacture of galenical preparations and is not dispensed as such. It is used as Prepared Opium (Ph. Eur. 6.2), as Powdered Opium (USP 31), as Opium Tincture (BP 2008 or USP 31), or as Camphorated Opium Tincture (BP 2008) or Paregoric (USP 31) in various oral preparations. These have included Opiate Squill Linctus (BP 2008) (Gee's linctus) for cough.

Paregoric (USP 31) has been advocated in the USA for the treatment of neonatal abstinence syndrome.

Abuse. Reports of squill-associated cardiac toxicity resulting from the abuse of opiate squill linctus (Gee's linctus).[1,2]

1. Thurston D, Taylor K. Gee's linctus. *Pharm J* 1984; **233:** 63.
2. Smith W, *et al.* Wenckebach's phenomenon induced by cough linctus. *BMJ* 1986; **292:** 868.

Preparations

BP 2008: Camphorated Opium Tincture; Concentrated Camphorated Opium Tincture; Opium Tincture;
Ph. Eur.: Opium Dry Extract, Standardised; Opium Tincture, Standardised;
USP 31: Opium Tincture; Paregoric.

Proprietary Preparations (details are given in Part 3)
Braz.: Elixir Paregorico.

Multi-ingredient: ***Braz.:*** Camomila; Elixir de Marinheiro†; ***Denm.:*** Pectyl; ***Fin.:*** Tannopon; ***Fr.:*** Colchimax; Lamaline; Paregorique; ***Hong Kong:*** Brown Mixture; ***Israel:*** Davilla; Doveri; ***Mex.:*** Reglosedyl†; ***S.Afr.:*** Paragoriese-Elikser; Tandpyndruppels; ***Spain:*** Digestovital†; Tanagel; ***Switz.:*** Bromocod N; Pectocalmine; ***USA:*** B & O Supprettes No. 15A; B & O Supprettes No. 16A; ***Venez.:*** Atrobel.

Hydrochlorides of Mixed Opium Alkaloids

Alkaloidosum Opii Hydrochloridum; Extractum Concentratum Opii; Mezclas de hidrocloruros de alcaloides del opio; Omnoponum; Opialum; Opium Concentratum.

Гидрохлориды Смешанных Алкалоидов Опия

Pharmacopoeias. Preparations of the hydrochlorides of mixed opium alkaloids are included in *Jpn.*

Papaveretum *(BAN)*

A mixture of 253 parts of morphine hydrochloride, 23 parts of papaverine hydrochloride, and 20 parts of codeine hydrochloride.

Папаверетум

CAS — 8002-76-4.
ATC — N02AA10.
ATC Vet — QN02AA10.

NOTE. Do not confuse papaveretum with papaverine (p.2191).

Pharmacopoeias. In *Br.*
BP 2008 (Papaveretum). It contains 80.0 to 88.4% of anhydrous morphine hydrochloride, 8.3 to 9.2% of papaverine hydrochloride, and 6.6 to 7.4% of anhydrous codeine hydrochloride. A white or almost white crystalline powder. Soluble in water, sparingly soluble in alcohol. A 1.5% solution in water has a pH of 3.7 to 4.7. Protect from light.

Profile

The opium alkaloids are the prototypical opioid analgesics (p.101). Mixtures of opium alkaloids such as papaveretum have the analgesic and sedative properties of morphine (p.89) and are used in the treatment of moderate to severe pain including postoperative and severe chronic pain. They may also be used for pre-operative sedation and as an adjunct to anaesthesia. Papaveretum (BP 2008) 15.4 mg contains the equivalent of about 10 mg of the major component, anhydrous morphine.

- In the UK, papaveretum formerly contained the hydrochlorides of morphine, codeine, noscapine, and papaverine. However, because of concern over the potential genotoxicity of noscapine (p.1566) UK preparations containing papaveretum were reformulated to exclude the noscapine component and the name papaveretum was redefined in the BP 1993 to reflect this change of formulation. It is possible that in other countries the term papaveretum is still being used to describe a mixture containing noscapine.

Doses. Papaveretum is generally given by subcutaneous or intramuscular injection in doses of 7.7 to 15.4 mg every 4 hours if necessary. The initial dose in the elderly or debilitated patients should not exceed 7.7 mg.

In the treatment of pain and as an adjunct in anaesthesia, papaveretum may also be given intravenously in doses of one-quarter to one-half the corresponding subcutaneous or intramuscular dose. For pre-operative medication papaveretum is given intramuscularly or subcutaneously sometimes with hyoscine hydrobromide.

For details of doses in children, see below.

Oral preparations containing papaveretum with aspirin have been given for the management of moderate to severe pain.

◊ Papaveretum has been confused with papaverine (p.2191) and in one such case[1] a patient became unconscious after self-injection of papaveretum in mistake for papaverine.

1. Robinson LQ, Stephenson TP. Self injection treatment for impotence. *BMJ* 1989; **299:** 1568.

Administration in children. Papaveretum may be given to children in the treatment of moderate to severe pain including postoperative and severe chronic pain. It is also used for pre-operative sedation and as an adjunct to anaesthesia. Papaveretum is generally given by subcutaneous or intramuscular injection every 4 hours if necessary, according to age as follows:

- neonates: 115 micrograms/kg
- 1 to 12 months: 154 micrograms/kg
- 1 to 6 years: 1.93 to 3.85 mg
- 6 to 12 years: 3.85 to 7.7 mg

Older children may be given the usual adult dose (see above).

In the treatment of pain and as an adjunct to anaesthesia papaveretum may also be given intravenously in doses of one-quarter to one-half the corresponding subcutaneous or intramuscular dose.

Preparations

BP 2008: Papaveretum Injection.

Proprietary Preparations (details are given in Part 3)
S.Afr.: Omnopon.

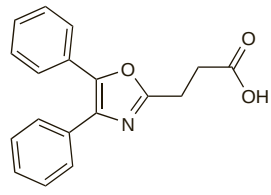
Multi-ingredient: ***UK:*** Aspav.

Oxaprozin *(BAN, USAN, rINN)*

Oksaprotsiini; Oxaprozina; Oxaprozine; Oxaprozinum; Wy-21743. 3-(4,5-Diphenyloxazol-2-yl)propionic acid.

Оксапрозин

$C_{18}H_{15}NO_3$ = 293.3.
CAS — 21256-18-8.
ATC — M01AE12.
ATC Vet — QM01AE12.



Pharmacopoeias. In *Chin.*, *Jpn.*, and *US*.
USP 31 (Oxaprozin). A white to yellowish-white, crystalline powder. Store in airtight containers at a temperature of 20° to 25°. Protect from light.

Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

Diagnosis and testing. False-positive results for testing of benzodiazepines in urine have been reported in patients taking oxaprozin.[1] The manufacturer[2] has commented that the interaction occurs with some immunoassay tests and that thin-layer chromatography can successfully discriminate between benzodiazepines and oxaprozin. False-positive results for a fluorescence polarisation immunoassay for phenytoin have also been reported in patients receiving oxaprozin.[3]

1. Pulini M. False-positive benzodiazepine urine test due to oxaprozin. *JAMA* 1995; **273:** 1905.
2. Raphan H, Adams MH. False-positive benzodiazepine urine test due to oxaprozin. *JAMA* 1995; **273:** 1905–6.
3. Patel T, *et al.* Assay interaction between oxaprozin and phenytoin. *Ann Pharmacother* 1997; **31:** 254.

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.

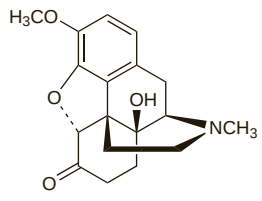
Оксикодон

$C_{18}H_{21}NO_4$ = 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-