

Preparations

BP 2008: Benzydamine Cream; Benzydamine Mouthwash; Benzydamine Oromucosal Spray.

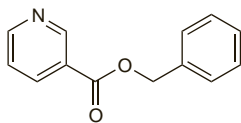
Proprietary Preparations (details are given in Part 3)

Arg.: Actifedinn; Bencifem; Emex; Sandival Desleible; **Austral.:** Diffiam; Diffiam Anti-inflammatory Throat Spray; Diffiam Solution; **Austria:** Tantum; Tantum; **Braz.:** Benflogin; Benzitrat; Ciflogex; Endiamin†; Flogin-Ped†; Flogo Rosa; Flogolab; Flogoral; Fongoral; Neoflogin; **Canad.:** Sun-Benz†; Tantum; **Cz.:** Rosalgin; Tantum; **Denn.:** Andolex; **Fr.:** Opalgine; **Ger.:** Tantum Rosa; Tantum Verde; **Gr.:** Tantum; **Hong Kong:** Dantum; Diffiam; Verax; **Hung.:** Tantum Verde; **Indon.:** Tanflex; Tantum; **Irl.:** Diffiam; **Israel:** Easy gel; **Ital.:** Afloben; Benzinn; Ginesal; Lagin†; Multum†; Saniflor Collutorio; Tantum; Verax; Xentafid; **Malaysia:** Diffiam Anti-inflammatory Lozenges; Diffiam Solution; **Mex.:** Artoben; Lonol; Vantal; **Neth.:** Tantum; **NZ:** Diffiam; **Philipp.:** Diffiam; **Pol.:** Hascosept; Tantum; **Port.:** Flogoral; Momen; Rosalgin; Tantum; Tantum Rosa; Tantum Verde; **Rus.:** Tantum Rose (Тантум Роза); Tantum Verde (Тантум Верде); **S.Afr.:** Andolex; **Singapore:** Diffiam; **Spain:** Aglona; Fulgim; Rosalgin; Tantum; Tantum Verde; **Swed.:** Andolex; **Switz.:** Bucco-Tantum; **Thai.:** Diffiam; **Turk.:** Benzidan; Tanflex; Tantum; Temex; **UK:** Diffiam; **Venez.:** Azutan; Bevi Dam; Biozendi; Flodont; Ginacol; Tantum; Tantum Verde; Zydan.

Multi-ingredient: **Arg.:** Buchex; Dresan Biotic†; Dresant; Emex Duo; Espectocural; Pentadent†; **Austral.:** Diffiam Anti-inflammatory Lozenges with Cough Suppressant; Diffiam Lozenges; Diffiam Mouth Gel; Diffiam-C; Logicin Rapid Relief; **Braz.:** Angino-Rub; **Hong Kong:** Diffiam Anti-inflammatory Lozenges; Diffiam Mouth Gel; Diffiam-C; Logicin Rapid Relief; **Hung.:** Tantum Rosa; **Ital.:** Algolisin†; Gola Action; Linea F; Medipius; **Malaysia:** Diffiam Anti-inflammatory Lozenges (with Antibacterial); Diffiam Anti-inflammatory Lozenges (with cough suppressant); Diffiam Mouth Gel; Diffiam-C; **Mex.:** Lonol Sport; **NZ:** Diffiam Cough; Diffiam Mouth Gel; Diffiam-C; **Port.:** Benoral; Gartum; Tantum Verde; **S.Afr.:** Andolex-C; **Singapore:** Diffiam Anti-inflammatory Anti-Bacterial Lozenges; Diffiam Mouth Gel; Diffiam-C; **Spain:** Bristacidina Dental; Dolosarto†; Etermol Antitusivo; Mentamida; Prosturo†; Tantum; Vinciseptil Otico; **Turk.:** Kloroben; **Venez.:** Amicets; Gencivol Compuesto; Solunovar Compuesto.

Benzyl Nicotinate

Bensylnikotināt; Bentsylinikotināatti; Benzil Nikotināt; Benzyl Nicotinas; Nicotinato de bencilo. Benzyl pyridine-3-carboxylate. $C_{13}H_{11}NO_2 = 213.2$. CAS — 94-44-0.



Pharmacopoeias. In *Eur.*

Profile

Benzyl nicotinate is used in topical preparations as a rubefacient.

Preparations

Proprietary Preparations (details are given in Part 3)

Ger.: Leukona-Aktiv-Rheumabad†; Pernionin Thermo Teilbad; Pernionin Thermo Vollbad; Pykaryl T; Rubriment; Rubriment-BN.

Multi-ingredient: **Arg.:** Butidionat†; Oxa Sport; Pergalen; **Austria:** Ambenat; Derivon; Expectal-Balsam; Igitur-antirheumatische; Igitur-Rheumafluid; Menthoneurin; Mobilisin plus; Rheumex; Rubizon-Rheumagel; Rubriment; Thermo-Rheumon; Thrombophob; **Braz.:** Etrat†; Trombofob; **Chile:** Bayro-Therm†; **Cz.:** Dolo-Rubrimint†; Rheuma-Salbe†; Rubriment-N†; Thermo-Rheumon†; **Fin.:** Trombosol; **Fr.:** Lumbalgine; **Ger.:** ABC Wärme-Salbe†; Ambene N; Arthrodestal N†; Auroanalin Thermo; Camphopin; Capsamol N†; Caye Rheuma-Balsam; Cor-Select†; DoloVisano Salbe†; Emasex-N†; Forapin E†; Hot Thermo; Lomazell forte N†; Lumbion Thermo†; mikani†; Ostochont†; Pelvichthol N; Phardol Rheuma†; Phardol Wärme-Balsam†; Phlogont-Thermal; Praecordin S†; Rheubalmin Thermo†; Rheuma-Salbe N; Rheuma-Salbe†; Rheumasalbe†; Rheumasan N†; Rheumasil†; Rubriment; Rubriment-N†; Tachynerg Campher Herzsalbe; Thermo-Menthoneurin†; Thermo-Rheumon N†; Thermo-Rheumon†; Thermosenex; Togal Mobil-Gel†; Wärme-Gel†; zuk thermo†; **Gr.:** Bayolin; Ehrlich; Striafissant†; Thermo-Rioipon; **Hong Kong:** Salomethyl; **Hung.:** Bayolin†; Thermo-Rheumon†; **India:** Beparin; KS Hair Tincture†; Thrombophob; **Indon.:** Stop X; Thrombophob; Zeropain; **Ital.:** Salopas; Sloan; **Mex.:** Bayro Thermo; **Pol.:** Lumbolin; Thermo-Rheumon; **Port.:** Adrinex†; Balsamo Analgesico; Medalgina; **Rus.:** Capsicam (Капсикам); Heparin Ointment (Гепариновая Мазь); **Switz.:** Assan thermo; Demotherm Pommade contre le rhumatisme†; Dolo Demotherm; Forapin†; Histalgane; Marament-N†; Thermocutan†; **Turk.:** Thermo-Doline; Thermo-Rheumon; Thermoflex; **UK:** Salonair; **Venez.:** Ehrlich Balsamo.

Beta-aminopropionitrile

Aminopropionitrile; β-Aminopropionitrile; β-Aminopropionitri-
lo; BAPN. 3-Aminopropionitrile.

Бета-аминопропионитрил

$C_3H_6N_2 = 70.09$.

CAS — 151-18-8 (beta-aminopropionitrile); 1119-28-4 (beta-aminopropionitrile fumarate).
ATC Vet — QM01AX91.

**Profile**

Beta-aminopropionitrile, a lysyl oxidase inhibitor, is an anti-inflammatory used as the fumarate in veterinary medicine for the treatment of tenositis.

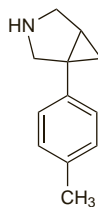
Bicifadine Hydrochloride (*USAN, rINNM*)

Bicifadina, hidrocloruro de; Bicifadine, Hydrochloride de; Bicifadini Hydrochloridum; CL-220075. (±)-1-p-Tolyl-3-azabicyclo-[3.1.0]hexane hydrochloride.

Бицифадина Гидрохлорид

$C_{12}H_{15}N.HCl = 209.7$.

CAS — 71195-57-8 (bicifadine); 66504-75-4 (bicifadine hydrochloride).



(bicifadine)

Profile

Bicifadine hydrochloride is a novel analgesic under investigation for the treatment of painful conditions including postoperative dental pain.

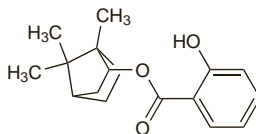
Bornyl Salicylate

Borneol Salicylate; Salicilato de bornilo. 2-Hydroxybenzoic acid 1,7,7-trimethylbicyclo[2.2.1]hept-2-yl ester.

Борнилсалицилат

$C_{17}H_{22}O_3 = 274.4$.

CAS — 560-88-3.

**Profile**

Bornyl salicylate is a salicylic acid derivative that has been used topically in rubefacient preparations similar to methyl salicylate (p.85) for the relief of pain in musculoskeletal and joint disorders.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Ger.:** Forapin E†; **Switz.:** Forapin†; Hygiodemil.

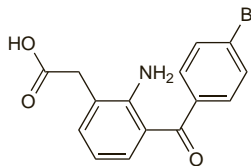
Bromfenac Sodium (*USAN, rINNM*)

AHR-10282; AHR-10282B; Bromfénac Sodique; Bromfenaco sódico; Natrii Bromfenacum. Sodium [2-amino-3-(p-bromobenzo-
zoyl)phenyl]acetate sesquihydrate.

Натрий Бромфенак

$C_{15}H_{11}BrNNaO_3 \cdot 1.5H_2O = 383.2$.

CAS — 91714-94-2 (bromfenac); 91714-93-1 (bromfenac sodium); 120638-55-3 (bromfenac sodium).



(bromfenac)

Profile

Bromfenac sodium, a phenylacetic acid derivative related to diclofenac (p.44), is an NSAID (p.96). It is instilled twice daily as 0.1% eye drops for ocular pain and inflammation including postoperative inflammation in patients who have undergone cataract extraction. When used postoperatively, it may be started 24 hours after surgery and continued for the next 14 days.

It was formerly given orally in the management of acute pain but was withdrawn from the market after reports of severe and sometimes fatal hepatic failure.

Effects on the eyes. Severe corneal melting (ulceration) was seen in 3 patients after topical use of bromfenac sodium.¹ All patients recovered after bromfenac was withdrawn. Similar ef-

fects have been reported with other ophthalmic NSAID preparations; for further details see under Adverse Effects of Diclofenac, p.45.

- Asai T, *et al.* Three cases of corneal melting after instillation of a new nonsteroidal anti-inflammatory drug. *Cornea* 2006; **25**: 224-7.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn: Bronuck; **USA:** Xibrom.

Bufexamac (*BAN, rINN*)

Bufeksamaakk; Bufeksamakas; Bufexamaco; Bufexamacum; Bufexamak†; Bufexamak. 2-(4-Butoxyphenyl)acetohydroxamic acid.

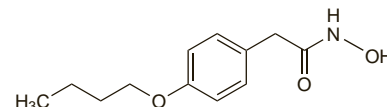
Буфексамак

$C_{12}H_{17}NO_3 = 223.3$.

CAS — 2438-72-4.

ATC — M01AB17; M02AA09.

ATC Vet — QM01AB17; QM02AA09.



Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn.*

Ph. Eur. 6.2 (Bufexamac). A white or almost white, crystalline powder. Practically insoluble in water; soluble in dimethylformamide; slightly soluble in ethyl acetate and in methyl alcohol. Protect from light.

Profile

Bufexamac is an NSAID (p.96) that is applied topically in concentrations of 5% in various skin disorders. Stinging and burning may occur after application; hypersensitivity reactions have been reported.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Parfenac†; **Austral.:** Paraderm†; **Austria:** Bufex; Bufexan; Droxaryl; Parfenac; **Belg.:** Bufexine†; Droxaryl†; **Cz.:** Droxaryl†; **Fr.:** Parfenac; **Ger.:** Bufederm†; duradermal†; Haemo-Exhirud; Bufexamac; Jomax; Malipuray; Parfenac; VVindol; **Ital.:** Fansamac; Vafen†; **Neth.:** Droxaryl; Parfenac; **Port.:** Parfenac; **Switz.:** Parfenac.

Multi-ingredient: **Austral.:** Paraderm Plus; Resolve; **Austria:** Droxaryl; **Cz.:** Mastu S; **Ger.:** Faktu akut; Hamo-ratiopharm N; Hamoagil plus; Mastu S; **Hong Kong:** Fungo Soothing Balm; Mastu S; **Hung.:** Mastu S; **NZ:** Paraderm Plus; **Rus.:** Proctosan (Проктозан); **Thai.:** Mastu S.

Bumadizone Calcium (*rINNM*)

Bumadizone cálcica; Bumadizone Calcique; Calcii Bumadizonum. Calcium 2-(1,2-diphenylhydrazinocarbonyl)hexanoate hemihydrate.

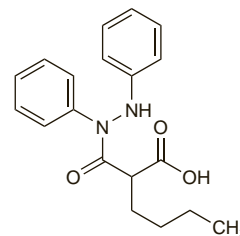
Кальций Бумадизон

$(C_{19}H_{21}N_2O_3)_2Ca \cdot H_2O = 699.8$.

CAS — 3583-64-0 (bumadizone); 34461-73-9 (bumadizone calcium).

ATC — M01AB07.

ATC Vet — QM01AB07.



(bumadizone)

Profile

Bumadizone calcium is an NSAID (p.96) that is metabolised to phenylbutazone (p.117) and oxyphenbutazone (p.107). Use has been limited by the risk of agranulocytosis and other haematological adverse effects.

Preparations

Proprietary Preparations (details are given in Part 3)

Mex.: Desilam.

Buprenorphine (BAN, rINN) ⊗

Buprenorfini; Buprenorfin; Buprenorfina; Buprenorfinas; Buprenorphine; Buprenorphinum; RX-6029-M. (6R,7R,14S)-17-Cyclopropylmethyl-7,8-dihydro-7-[(1S)-1-hydroxy-1,2,2-trimethylpropyl]-6-O-methyl-6,14-ethano-17-normorphine; (2S)-2-[(5R,6R,7R,14S)-9a-Cyclopropylmethyl-4,5-epoxy-3-hydroxy-6-methoxy-6,14-ethanomorphinan-7-yl]-3,3-dimethylbutan-2-ol.

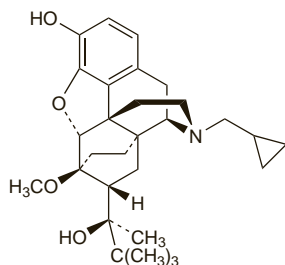
Бупренорфин

$C_{29}H_{41}NO_4 = 467.6$.

CAS — 52485-79-7.

ATC — N02AE01; N07BC01.

ATC Vet — QN02AE01; QN07BC01.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of buprenorphine: TEM; Tems.

Pharmacopoeias. In *Eur.* (see p.vii).

Ph. Eur. 6.2 (Buprenorphine). A white or almost white crystalline powder. Very slightly soluble in water; freely soluble in acetone; slightly soluble in cyclohexane; soluble in methyl alcohol. It dissolves in dilute solutions of acids. Protect from light.

Buprenorphine Hydrochloride

(BANM, USAN, rINN) ⊗

Buprenorfinihidroklorid; Buprenorfin-hidroklorid; Buprenorfinhydrochlorid; Buprenorfinhidroklorid; Buprenorfinohidroklorid; Buprenorphine, chlorhydrate de; Buprenorphini hydrochloridum; CL-112302; Hidrocloruro de buprenorfina; NIH-8805; UM-952.

Бупренорфина Гидрохлорид

$C_{29}H_{41}NO_4 \cdot HCl = 504.1$.

CAS — 53152-21-9.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), and *US*.

Ph. Eur. 6.2 (Buprenorphine Hydrochloride). A white or almost white crystalline powder. Sparingly soluble in water; soluble in alcohol; practically insoluble in cyclohexane; freely soluble in methyl alcohol. Protect from light.

USP 31 (Buprenorphine Hydrochloride). pH of a 1% solution in water is between 4.0 and 6.0. Store in airtight containers. Protect from light.

Dependence and Withdrawal

As for Opioid Analgesics, p.101.

Buprenorphine may have a lower potential for producing dependence than pure agonists such as morphine. However, it has been subject to abuse (see under Precautions, below). Abrupt withdrawal of buprenorphine is said to produce only a mild abstinence syndrome, which may be delayed in onset.

Buprenorphine is used for substitution therapy in the management of opioid dependence (see under Uses and Administration, below).

Adverse Effects and Treatment

As for Opioid Analgesics in general, p.102.

Acute hepatotoxicity, including elevated liver enzyme values, hepatitis with jaundice, hepatic failure, necrosis, and encephalopathy, and hepatorenal syndrome, has been reported in opioid-dependent addicts; these reactions have also occurred after the misuse of buprenorphine, particularly after high doses or intravenous use.

Local reactions such as rash, erythema, and itching have been reported with the transdermal patches. In isolated cases delayed local allergic reactions with marked signs of inflammation have occurred; the patches should be withdrawn in such cases.

Treatment of adverse effects is similar to that for other opioid analgesics (p.102). The effects of buprenor-

phine are only partially reversed by naloxone (see Effects on the Respiratory System, below) but use of the latter is still recommended.

Incidence of adverse effects. Adverse effects reported¹ after parenteral buprenorphine in 8187 patients were nausea (8.8%), vomiting (7.4%), drowsiness (4.3%), sleeping (1.9%), dizziness (1.2%), sweating (0.98%), headache (0.55%), confusion (0.53%), lightheadedness (0.38%), blurred vision (0.28%), euphoria (0.27%), dry mouth (0.11%), depression (0.09%), and hallucinations (0.09%). Some studies^{2,3} have reported nausea, vomiting, and dizziness to be more troublesome with buprenorphine than with morphine.

In a study⁴ of sublingual buprenorphine, 50 of 141 cancer patients withdrew because of adverse effects, especially dizziness, nausea, vomiting, and drowsiness; constipation was not reported. A woman developed⁵ a painless ulcer on the upper surface of her tongue after she had put sublingual buprenorphine tablets on rather than under her tongue.

Shock occurred⁶ in 2 patients 2 hours after receiving epidural buprenorphine 300 micrograms; treatment with naloxone was unsuccessful but symptoms disappeared spontaneously after 2 to 3 hours.

In a multicentre study⁷ of transdermal buprenorphine, 252 of 1223 patients with moderate to severe cancer pain or non-cancer pain withdrew due to adverse effects. The most commonly reported were nausea (11%), vomiting (9.2%), constipation (7.8%), dizziness (7.5%), drowsiness (4.0%), retching (3.7%), generalised pruritus (2.0%), and headache (1.6%); local adverse effects included pruritus (1.4%), dermatitis (1.3%), and erythema (1.3%). Another study⁸ reported oedema, headache, nausea, palpitation, and difficulty concentrating as causes for therapy withdrawal in 4 out of 90 patients.

1. Hargus AW, *et al.* Methodology of monitored release of a new preparation: buprenorphine. *BMJ* 1979; **2**: 163-5.
2. Sear JW, *et al.* Buprenorphine for postoperative analgesia. *Br J Anaesth* 1979; **51**: 71.
3. Kjaer M, *et al.* A comparative study of intramuscular buprenorphine and morphine in the treatment of chronic pain of malignant origin. *Br J Clin Pharmacol* 1982; **13**: 487-92.
4. Robbie DS. A trial of sublingual buprenorphine in cancer pain. *Br J Clin Pharmacol* 1979; **7** (suppl 3): 315S-317S.
5. Lockhart SP, Baron JH. Tongue ulceration after lingual buprenorphine. *BMJ* 1984; **288**: 1346.
6. Christensen FR, Andersen LW. Adverse reaction to extradural buprenorphine. *Br J Anaesth* 1982; **54**: 476.
7. Muriel C, *et al.* Effectiveness and tolerability of the buprenorphine transdermal system in patients with moderate to severe chronic pain: a multicentre, open-label, uncontrolled, prospective, observational clinical study. *Clin Ther* 2005; **27**: 451-62.
8. Sorge J, Sittl R. Transdermal buprenorphine in the treatment of chronic pain: results of a phase III, multicentre, randomized, double-blind, placebo-controlled study. *Clin Ther* 2004; **26**: 1808-20.

Effects on the heart. For a report of myocardial infarction associated with abuse of buprenorphine, see Abuse under Precautions, below.

Effects on mental function. Psychotomimetic effects have been relatively uncommon with buprenorphine. Hallucinations were reported¹ in only 7 of 8147 patients (0.09%) given buprenorphine by injection. There have been reports of hallucinations after sublingual² or epidural³ use.

1. Hargus AW, *et al.* Methodology of monitored release of a new preparation: buprenorphine. *BMJ* 1979; **2**: 163-5.
2. Paraskevaides EC. Near fatal auditory hallucinations after buprenorphine. *BMJ* 1988; **296**: 214.
3. MacEvilly M, O'Carroll C. Hallucinations after epidural buprenorphine. *BMJ* 1989; **298**: 928-9.

Effects on the respiratory system. There have been varying reports on the occurrence of respiratory depression with buprenorphine. It may be subject to a 'ceiling effect' in which respiratory depression does not increase further above doses of about 3 micrograms/kg.¹ However, high doses of 30 or 40 micrograms/kg given as sole intravenous analgesic in balanced anaesthesia have been associated with severe respiratory depression.²

Respiratory depression may be delayed in onset and more prolonged than with morphine and is only partially reversed by naloxone, possibly because buprenorphine is very firmly bound to opioid receptors. A study of sublingual buprenorphine for postoperative pain relief was abandoned when 3 of the first 16 patients showed signs of late-onset respiratory depression after the second dose of buprenorphine; the respiratory depression did not respond to naloxone.³ Successful reversal has been shown in healthy subjects with buprenorphine-induced respiratory depression given large doses of naloxone 5 or 10 mg, but not with 1 mg; reversal was gradual in onset and decreased the duration of the normally prolonged respiratory depression.⁴ Other studies found that lower doses of naloxone 2 to 4 mg given over 30 minutes,^{5,6} or bolus doses of 2 to 3 mg followed by a continuous infusion of 4 mg/hour,⁶ were effective in reversing buprenorphine-induced respiratory depression. The authors of both these studies suggested that a longer duration of naloxone infusion may be needed for reversal of respiratory depression caused by high doses of buprenorphine. The respiratory depressant and analgesic effects of buprenorphine were decreased by the concomitant use of naloxone.⁷ It should be noted that a combined sublingual preparation of buprenorphine hydrochloride and naloxone hydrochloride is available in some countries for the treatment of opioid dependence.

ride is available in some countries for the treatment of opioid dependence.

1. Dahan A, *et al.* Comparison of the respiratory effects of intravenous buprenorphine and fentanyl in humans and rats. *Br J Anaesth* 2005; **94**: 825-34.
2. Schmidt JF, *et al.* Postoperative pain relief with naloxone: severe respiratory depression and pain after high dose buprenorphine. *Anaesthesia* 1985; **40**: 583-6.
3. Thörn S-E, *et al.* Prolonged respiratory depression caused by sublingual buprenorphine. *Lancet* 1988; **i**: 179-80.
4. Gal TJ. Naloxone reversal of buprenorphine-induced respiratory depression. *Clin Pharmacol Ther* 1989; **45**: 66-71.
5. Dahan A. Opioid-induced respiratory effects: new data on buprenorphine. *Palliat Med* 2006; **20** (Suppl 1): s3-s8.
6. van Dorp E, *et al.* Naloxone reversal of buprenorphine-induced respiratory depression. *Anesthesiology* 2006; **105**: 51-7.
7. Lehmann KA, *et al.* Influence of naloxone on the postoperative analgesic and respiratory effects of buprenorphine. *Eur J Clin Pharmacol* 1988; **34**: 343-52.

Overdose. A small case series reported¹ acute buprenorphine intoxication in 5 children, aged from 15 to 22 months, after accidental ingestion of sublingual tablets; of these, 4 had ingested a combined preparation containing naloxone (*Suboxone*; Reckitt Benckiser, USA). Symptoms included drowsiness and miosis; decreased respiratory rates were reported in 4. All 5 children required hospital admission; 4 were treated with naloxone and 1 needed mechanical ventilation. Accidental poisoning has also been reported² in a 9-month-old infant who ingested *Suboxone*; his symptoms were reversed by naloxone. A retrospective review³ of buprenorphine overdoses in children under 6 years of age reported by US poison centres to a national surveillance system from November 2002 to December 2005 concluded that overdosage is generally well tolerated. Out of 86 reports, 54 children developed symptoms of toxicity. Such symptoms included: drowsiness or lethargy (55%), vomiting (21%), miosis (21%), respiratory depression (7%), agitation or irritability (5%), pallor (3%), and coma (2%). There were no fatalities, and significant CNS and respiratory depression occurred in 7%. *Suboxone* preparations were the most commonly ingested products. The authors considered that any child who has ingested more than 2 mg and any aged under 2 years who has had more than a lick or taste should be referred to the emergency department.

During the years 1980 to 2002, buprenorphine was mentioned in 43 cases of adult fatalities in the UK.⁴ Of these, 27 deaths were confirmed to have involved buprenorphine including 7 cases where it was taken alone. In those deaths where multiple drugs were involved sedatives or benzodiazepines were detected in 23 cases and other opioids were found in 17 cases; alcohol had also been taken in 10 cases. The authors also found an increase in buprenorphine-related fatalities since 1999 when the high-dose formulation became available.

1. Geib A-J, *et al.* Adverse effects in children after unintentional buprenorphine exposure. *Pediatrics* 2006; **118**: 1746-51.
2. Cho CS, *et al.* Exploratory buprenorphine ingestion in an infant. *Ann Emerg Med* 2006; **48**: 109.
3. Hayes BD, *et al.* Toxicity of buprenorphine overdoses in children. *Pediatrics* 2008; **121**: 807-8. Full version: <http://pediatrics.aappublications.org/cgi/reprint/121/4/e782> (accessed 22/07/08).
4. Schifano F, *et al.* Buprenorphine mortality, seizures and prescription data in the UK, 1980-2002. *Hum Psychopharmacol* 2005; **20**: 343-8.

Precautions

As for Opioid Analgesics in general, p.103.

Buprenorphine has opioid antagonist actions and may precipitate withdrawal symptoms if given to patients physically dependent on opioids.

Respiratory depression, if it occurs, is relatively slow in onset and of prolonged duration; it may be only partially reversed by naloxone.

Licensed product information states that baseline liver function levels should be established before starting buprenorphine therapy, and periodic monitoring of liver function should be performed throughout therapy in patients being treated for opioid dependence. It should be used with caution in all patients with pre-existing hepatic impairment.

Absorption of buprenorphine from transdermal patches may be increased as the temperature rises and patients should therefore avoid exposing the patch to external heat; similarly, patients with fever may require monitoring because of increased absorption. It may take up to 30 hours for plasma concentrations of buprenorphine to decrease by 50% after removal of a patch; patients who have had adverse effects should be monitored during this period.

Abuse. A 22-year-old man had chest pains on each of two occasions after he had inhaled crushed buprenorphine tablets.¹ An ECG taken after the second episode suggested that the patient had suffered a myocardial infarction. Intravenous injection of crushed sublingual tablets was associated with rhabdomyolysis and sciatic neuropathy in 2 patients.² A case series³ of 4 patients