phine hydrochloride 107.8 micrograms is equivalent to about 100 micrograms of buprenorphine.

Buprenorphine is given by all the above routes for opioid analgesia in moderate to severe **pain**.

- The dose by intramuscular or slow intravenous injection is 300 to 600 micrograms repeated every 6 to 8 hours as required
- By the sublingual route, doses of 200 to 400 micrograms may be repeated every 6 to 8 hours as required
- For opioid treatment of chronic pain in patients aged 18 years and over transdermal patches delivering varying amounts of buprenorphine are available. Doses should be individually titrated for each patient according to previous opioid usage. During transfer to treatment with buprenorphine patches previous opioid analgesic therapy should be phased out gradually in order to allow for the gradual increase in plasma-buprenorphine concentrations. Depending on dose required up to 2 patches may be applied, however, this should be done at the same time to avoid confusion. Buprenorphine patches are not appropriate for acute pain. In the UK, transdermal buprenorphine patches are available as follows:

  Transtec (*Napp, UK*) delivering buprenorphine in a range of 35 to 70 micrograms/hour. Initial dosages should not exceed 35 micrograms/hour in *opioid-naive* patients. For *patients who have been receiving a strong opioid analgesic* the initial dose should be based on the previous 24-hour opioid requirement. Use of a patch providing 35 micrograms/hour of buprenorphine is roughly equivalent to 30 to 60 mg daily of oral morphine sulfate. Patches should be replaced every 96 hours at the latest with the new patch being applied to a different site; use of the same area of the skin should be avoided for at least the next 2 applications.

  BuTrans (*Napp, UK*) delivering buprenorphine in a range of 5 to 20 micrograms/hour. Initial dosages should not exceed 5 micrograms/hour in *all* patients. Patches should be replaced every 7 days with the new patch being applied to a different site; use of the same area of the skin should be avoided for the next 3 to 4 weeks.

When used in balanced **anaesthesia** 300 micrograms may be given intramuscularly or 400 micrograms sublingually for premedication; 300 to 450 micrograms may be given intravenously as a perioperative analgesic supplement.

For the treatment of **opioid dependence** in patients aged 16 years and over, the initial dose is 0.8 to 4 mg sublingually once daily. The dose may be increased as necessary but maintenance doses should not exceed 32 mg daily. Once the patient has been stabilised, the dosage should be reduced gradually to a lower maintenance dose; treatment may eventually be stopped if appropriate. For addicts who have not undergone opioid withdrawal before starting buprenorphine, the first dose of buprenorphine should not be given until the first signs of craving appear or until at least 4 (USA) or 6 (UK) hours after the last opioid use. In those already receiving methadone replacement, the dose of methadone should be reduced to a maximum of 30 mg daily before starting buprenorphine therapy. As a deterrent to abuse, a combined sublingual preparation of buprenorphine hydrochloride and naloxone hydrochloride is available in some countries for the treatment of opioid dependence.

For details of doses in **children**, see below.

Action. Buprenorphine is generally described as a mixed agonist-antagonist acting mainly as a partial agonist at μ opioid receptors, with some antagonist activity at κ receptors. It has also been shown to bind at μ, δ, and κ opioid binding sites and to have high affinity for the μ and δ receptors and lesser affinity for the κ receptor.[1] Buprenorphine, like fentanyl, has high lipid solubility, but has a lower intrinsic activity than fentanyl. Differences between buprenorphine and pure μ opioid agonists such as fentanyl, including relatively slow onset of action, prolonged duration of action, resistance to antagonism by naloxone, and lack of correlation between plasma concentrations and analgesic effects, have been explained by differences in the way buprenorphine binds to opioid receptors. In a study *in vitro* buprenorphine had slow rates of association and dissociation from the opioid receptor when compared with fentanyl.[2]

1. Bovill JG. Which potent opioid? Important criteria for selection. *Drugs* 1987; **33:** 520–30.
2. Boas RA, Villiger JW. Clinical actions of fentanyl and buprenorphine: the significance of receptor binding. *Br J Anaesth* 1985; **57:** 192–6.

Administration in children. Buprenorphine is used for the relief of moderate to severe **pain** in children. In the UK, those aged from 6 months to 12 years may be given 3 to 6 micrograms/kg by *intramuscular* or slow *intravenous* injection every 6 to 8 hours; up to 9 micrograms/kg may be given if required in refractory cases. In the USA, parenteral buprenorphine is licensed in children aged 2 years and over; usual doses of 2 to 6 micrograms/kg may be given intramuscularly or intravenously every 4 to 6 hours to those up to 12 years old. The *sublingual* route is licensed in the UK in children aged from 6 to 12 years and the following doses are given every 6 to 8 hours according to body-weight: 16 to 25 kg, 100 micrograms; 25 to 37.5 kg, 100 to 200 micrograms; 37.5 to 50 kg, 200 to 300 micrograms. Older children requiring pain relief may be given the usual adult dose (see above) for all the above routes.

Buprenorphine is also used in the treatment of **opioid dependence**; adolescents aged 16 years and over may be given the usual adult dose (see above).

Opioid dependence. Buprenorphine is used in the treatment of opioid dependence (p.101). Its agonist-antagonist properties may mean that it has a lower potential for dependence and a lower risk of respiratory depression in overdose than pure agonists such as methadone. Buprenorphine can be used as substitution therapy in patients with moderate opioid dependence for acute management of withdrawal and in maintenance treatment as an alternative to or together with methadone. However, in patients dependent on high doses of opioids buprenorphine may precipitate withdrawal due to its partial antagonist properties; the daily opioid dose should be reduced gradually in such patients before beginning buprenorphine. Abuse of the preparation, as with other substitution therapies, may be a problem. A combined sublingual preparation of buprenorphine hydrochloride and naloxone hydrochloride is available in some countries as a deterrent to abuse.

References.

1. Kakko J, *et al.* 1-year retention and social function after buprenorphine-assisted relapse prevention treatment for heroin dependence in Sweden: a randomised, placebo-controlled trial. *Lancet* 2003; **361:** 662–8.
2. Fudala PJ, *et al.* Office-based treatment of opiate addiction with a sublingual-tablet formulation of buprenorphine and naloxone. *N Engl J Med* 2003; **349:** 949–58.
3. Montoya ID, *et al.* Randomized trial of buprenorphine for treatment of concurrent opiate and cocaine dependence. *Clin Pharmacol Ther* 2004; **75:** 34–48.
4. Fiellin DA, *et al.* Consensus statement on office-based treatment of opioid dependence using buprenorphine. *J Subst Abuse Treat* 2004; **27:** 153–9.
5. Donaher PA, Welsh C. Managing opioid addiction with buprenorphine. *Am Fam Physician* 2006; **73:** 1573–8.
6. Sung S, Conry JM. Role of buprenorphine in the management of heroin addiction. *Ann Pharmacother* 2006; **40:** 501–5.
7. Robinson SE. Buprenorphine-containing treatments: place in the management of opioid addiction. *CNS Drugs* 2006; **20:** 697–712.
8. Gowing L, *et al.* Buprenorphine for the management of opioid withdrawal. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 26/06/08).
9. NICE. Methadone and buprenorphine for the management of opioid dependence: Technology Appraisal Guidance 114 (issued January 2007). Available at: http://www.nice.org.uk/nicemedia/pdf/TA114Niceguidance.pdf (accessed 26/06/08)
10. Boothby LA, Doering PL. Buprenorphine for the treatment of opioid dependence. *Am J Health-Syst Pharm* 2007; **64:** 266–72.
11. Mattick RP, *et al.* Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2008 (accessed 26/06/08).
12. Sullivan LE, Fiellin DA. Narrative review: buprenorphine for opioid-dependent patients in office practice. *Ann Intern Med* 2008; **148:** 662–70.

Pain. ***ACUTE PAIN.*** The *BNF* considers that buprenorphine may antagonise the analgesic effect of other opioids and is generally not recommended for the management of *postoperative* pain. Nonetheless, it can be given intramuscularly, intravenously, or sublingually for this purpose, although the intravenous route may be preferred for acute pain relief. The epidural route[1] and continuous subcutaneous infusion[2] have also been used; an intranasal formulation of buprenorphine is under investigation for the management of postoperative pain.[1] Patient-controlled analgesia with intravenous[3] and intramuscular[4] buprenorphine has been effective although its long half-life may limit such use.

Buprenorphine had no adverse cardiovascular effects when given intravenously after open-heart surgery,[5] suggesting that it was a suitable analgesic for patients with unstable circulation. Epidural analgesia with buprenorphine has also been used after cardiac surgery.[6] Buprenorphine was also considered suitable for the relief of pain in *myocardial infarction*.[7]

1. Miwa Y, *et al.* Epidural administered buprenorphine in the perioperative period. *Can J Anaesth* 1996; **43:** 907–13.
2. Kawamata T, *et al.* Pain management after lumbar spinal fusion surgery using continuous subcutaneous infusion of buprenorphine. *J Anesth* 2005; **19:** 199–203.
3. Dingus DJ, *et al.* Buprenorphine versus morphine for patient-controlled analgesia after cholecystectomy. *Surg Gynecol Obstet* 1993; **177:** 1–6.
4. Harmer M, *et al.* Intramuscular on demand analgesia: double blind controlled trial of pethidine, buprenorphine, morphine, and meptazinol. *BMJ* 1983; **286:** 680–2.
5. Rosenfeldt FL, *et al.* Haemodynamic effects of buprenorphine after heart surgery. *BMJ* 1978; **2:** 1602–3.
6. Mehta Y, *et al.* Lumbar versus thoracic epidural buprenorphine for postoperative analgesia following coronary artery bypass graft surgery. *Acta Anaesthesiol Scand* 1999; **43:** 388–93.
7. Hayes MJ, *et al.* Randomised trial comparing buprenorphine and diamorphine for chest pain in suspected myocardial infarction. *BMJ* 1979; **2:** 300–2.

CHRONIC PAIN. Transdermal buprenorphine is used for chronic intractable cancer pain.[1-4] It has also been used successfully in chronic non-cancer pain including neuropathic pain;[1,2,4-6] however, licensed product information states that this route is not suitable for the treatment of acute pain.

1. Böhme K. Buprenorphine in a transdermal therapeutic system—a new option. *Clin Rheumatol* 2002; **21** (suppl 1): S13–S16.
2. Evans HC, Easthope SE. Transdermal buprenorphine. *Drugs* 2003; **63:** 1999–2010.
3. Sittl R. Transdermal buprenorphine in cancer pain and palliative care. *Palliat Med* 2006; **20** (suppl 1): S25–S30.
4. Sittl R. Transdermal buprenorphine in the treatment of chronic pain. *Expert Rev Neurother* 2005; **5:** 315–23.
5. Bálint G. Buprenorphine treatment of patients with non-malignant musculoskeletal diseases. *Clin Rheumatol* 2002; **21** (suppl 1): S17–S18.
6. Hans G. Buprenorphine—a review of its role in neuropathic pain. *J Opioid Manag* 2007; **3:** 195–206.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Magnogen†; Temgesic†; ***Austral.:*** Norspan; Subutex; Temgesic; ***Austria:*** Subutex; Temgesic; Transtec; Tridol; ***Belg.:*** Subutex; Temgesic; Transtec; ***Braz.:*** Temgesic; ***Chile:*** Transtec; ***Cz.:*** Norspan; Suboxone; Subutex; Temgesic; Transtec; ***Denm.:*** Anorfin; Norspan; Subutex; Temgesic; Transtec; ***Fin.:*** Subutex; Temgesic; ***Fr.:*** Suboxone; Subutex; Temgesic; ***Ger.:*** Subutex; Temgesic; Transtec; ***Gr.:*** Subutex; ***Hong Kong:*** Subutex; Temgesic; ***Hung.:*** Bupren; Transtec; ***India:*** Norphin; Pentorel; Tidigesic†; ***Indon.:*** Subutex; ***Irl.:*** BuTrans; Temgesic; Transtec; ***Israel:*** Nopan; Subutex; ***Ital.:*** Subutex; Temgesic; Transtec; ***Malaysia:*** Suboxone; Subutex†; Temgesic†; ***Mex.:*** Brospina; Temgesic; Transtec; ***Neth.:*** Temgesic; ***Norw.:*** Subutex; Temgesic; ***NZ:*** Suboxone; Temgesic; ***Pol.:*** Bunondol; Transtec; ***Port.:*** Buprex; Norspan; Suboxone; Subutex; Transtec; ***Rus.:*** Nopan (Нопан)†; Transtec (Трансгек); ***S.Afr.:*** Subutex; Temgesic; ***Singapore:*** Subutex†; Temgesic†; ***Spain:*** Buprex; Prefin†; Subutex; Transtec; ***Swed.:*** Norspan; Subutex; Temgesic; ***Switz.:*** Subutex; Temgesic; Transtec; ***Thai.:*** Buprine; Temgesic†; ***UK:*** BuTrans; Suboxone; Subutex; Temgesic; Transtec; ***USA:*** Buprenex; Suboxone; Subutex.

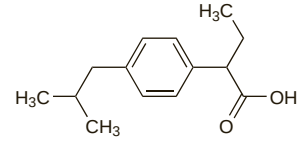
Butibufen Sodium *(rINNM)*

Butibufén sódico; Butibufène Sodique; FF-106 (butibufen); Natrii Butibufenum. Sodium 2-(4-isobutylphenyl)butyrate.

Натрий Бутибуфен

$C_{14}H_{19}NaO_2$ = 242.3.

CAS — 55837-18-8 (butibufen); 60682-24-8 (butibufen sodium).



(butibufen)

Profile

Butibufen sodium is an NSAID (p.96) that has been used orally in inflammatory and rheumatic disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Spain: Mijal†.

Butorphanol Tartrate *(BANM, USAN, rINNM)*

levo-BC-2627 (butorphanol); Butorfanolitartraatti; Butorfanoltartrat; Butorphanol, Tartrate de; Butorphanoli Tartras; Tartrato de butorfanol. (–)-17-(Cyclobutylmethyl)morphinan-3,14-diol hydrogen tartrate.

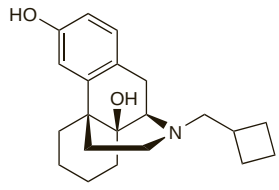
Буторфанола Тартрат

$C_{21}H_{29}NO_2.C_4H_6O_6$ = 477.5.

CAS — 42408-82-2 (butorphanol); 58786-99-5 (butorphanol tartrate).

ATC — N02AF01.

ATC Vet — QN02AF01.



(butorphanol)

Pharmacopoeias. In *US.*

USP 31 (Butorphanol Tartrate). A white powder. Its solutions are slightly acidic. Sparingly soluble in water; insoluble in alcohol, in chloroform, in ether, in ethyl acetate, and in hexane; slightly soluble in methyl alcohol; soluble in dilute acids. Store in airtight containers at a temperature of 25°, excursions permitted between 15° and 30°.

Dependence and Withdrawal

As for Opioid Analgesics, p.101.

Butorphanol 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). Abruptly stopping chronic butorphanol has produced a less severe withdrawal syndrome than with morphine.

Adverse Effects and Treatment

As for Opioid Analgesics in general, p.102, and for Pentazocine, p.112.

Headache, and feelings of floating may also occur. Hallucinations and other psychotomimetic effects are rare and have been reported less frequently than with pentazocine. In addition insomnia and nasal congestion may occur frequently when butorphanol is given intranasally.

Because butorphanol has opioid agonist and antagonist activity, naloxone is the recommended antagonist for the treatment of overdosage.

Effects on the respiratory system. Butorphanol 2 mg produces a similar degree of respiratory depression to morphine 10 mg, but a ceiling effect is apparent with higher doses of butorphanol.[1] It has been reported to be a less potent respiratory depressant than fentanyl,[2] but more potent than nalbuphine.[3]

1. Nagashima H, *et al.* Respiratory and circulatory effects of intravenous butorphanol and morphine. *Clin Pharmacol Ther* 1976; **19:** 738–45.
2. Dryden GE. Voluntary respiratory effects of butorphanol and fentanyl following barbiturate induction: a double-blind study. *J Clin Pharmacol* 1986; **26:** 203–7.
3. Zucker JR, *et al.* Respiratory effects of nalbuphine and butorphanol in anesthetized patients. *Anesth Analg* 1987; **66:** 879–81.

Precautions

As for Opioid Analgesics in general, p.103.

Although cardiovascular effects may be less than with pentazocine, butorphanol should generally be avoided after myocardial infarction.

Butorphanol may precipitate withdrawal symptoms if given to patients physically dependent on opioids. The dosage regimen of butorphanol may need to be adjusted in the elderly and in patients with hepatic or renal impairment.

Abuse. A WHO expert committee considered in 2006 that the likelihood of butorphanol abuse was low and was not great enough to warrant international control.[1] Abuse had been reported infrequently and only in a few countries. The committee also commented that, pharmacologically, intranasal preparations of butorphanol do not appear to differ in their abuse potential from parenteral preparations; however, other factors such as availability and usage patterns may affect the likelihood of abuse. Indeed, US licensed product information states that there have been more reports of abuse with intranasal preparations than with injectable ones.

Cases of butorphanol abuse have been published[2,3] including a report of fibrous myopathy associated with chronic intramuscular abuse.

1. WHO. WHO expert committee on drug dependence: thirty-fourth report. *WHO Tech Rep Ser 942* 2006. Also available at: http://libdoc.who.int/trs/WHO_TRS_942_eng.pdf (accessed 26/06/08)
2. Wagner JM, Cohen S. Fibrous myopathy from butorphanol injections. *J Rheumatol* 1991; **18:** 1934–5.
3. Loder E. Post-marketing experience with an opioid nasal spray for migraine: lessons for the future. *Cephalalgia* 2006; **26:** 89–97.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were given butorphanol, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding.

In a study[2] of 12 women, butorphanol was detected in breast milk after both intramuscular and oral doses. However, the milk-to-plasma ratio after a 2-mg intramuscular dose (0.7) was significantly less than that after an 8-mg oral dose (1.9). Although the mothers were not breast feeding at the time of the study, the authors concluded that the potential for any adverse effects on nursing infants after maternal butorphanol use would be minimal.

1. American Academy of Pediatrics The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 26/06/08)
2. Pittman KA, *et al.* Human perinatal distribution of butorphanol. *Am J Obstet Gynecol* 1980; **138:** 797–800.

Pregnancy. Two instances of sinusoidal fetal heart rate pattern were noted out of 188 consecutive cases of butorphanol use in active-phase labour.[1] Visual hallucinations and paranoid delusions developed in a woman on receiving a 1-mg intravenous injection of butorphanol early in labour; the psychosis had resolved 40 hours after the injection and was not noted on follow-up 2 weeks later.[2]

1. Welt SI. Sinusoidal fetal heart rate and butorphanol administration. *Am J Obstet Gynecol* 1985; **152:** 362–3.
2. Davis A, *et al.* Acute psychosis associated with butorphanol. *J Neuropsychiatr Clin Neurosci* 1998; **10:** 236–7.

Interactions

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

Antimigraine drugs. No pharmacokinetic interactions were reported when butorphanol nasal spray and subcutaneous *sumatriptan* were used together within a minute of each other in healthy subjects.[1] However, another study[2] in healthy subjects found that the AUC and maximum plasma concentration of intranasal butorphanol were reduced by about 29% and 38%, respectively when given 1 minute after intranasal sumatriptan. No such effect was noted when administration was separated by 30 minutes. It was suggested that sumatriptan may reduce butorphanol absorption by inducing transient nasal vasoconstriction.

1. Srinivas NR, *et al.* Lack of pharmacokinetic interaction between butorphanol tartrate nasal spray and sumatriptan succinate. *J Clin Pharmacol* 1995; **35:** 432–7.
2. Vachharajani NN, *et al.* A pharmacokinetic interaction study between butorphanol and sumatriptan nasal sprays in healthy subjects: importance of the timing of butorphanol administration. *Cephalalgia* 2002; **22:** 282–7.

Pharmacokinetics

Butorphanol is absorbed from the gastrointestinal tract but it undergoes extensive first-pass metabolism. Peak plasma concentrations occur 0.5 to 1 hour after intramuscular and intranasal doses and 1 to 1.5 hours after oral doses. Butorphanol has a plasma elimination half-life of about 4.5 hours. About 80% is bound to plasma proteins.

Butorphanol is extensively metabolised in the liver through hydroxylation, *N*-dealkylation, and conjugation, only 5% being excreted unchanged. Excretion is mainly in the urine; about 15% of a parenteral dose is excreted in the bile. It crosses the placenta and is distributed into breast milk.

Administration. *INTRANASAL ROUTE.* References.

1. Davis GA, *et al.* Pharmacokinetics of butorphanol tartrate administered from single-dose intranasal sprayer. *Am J Health-Syst Pharm* 2004; **61:** 261–6.
2. Davis GA, *et al.* Bioavailability of intranasal butorphanol administered from a single-dose sprayer. *Am J Health-Syst Pharm* 2005; **62:** 48–53.
3. Wermeling DP, *et al.* Pharmacokinetics, bioequivalence, and spray weight reproducibility of intranasal butorphanol after administration with 2 different nasal spray pumps. *J Clin Pharmacol* 2005; **45:** 969–73.

Uses and Administration

Butorphanol tartrate, a phenanthrene derivative, is an opioid analgesic (p.104) with opioid agonist and antagonist properties; it is pharmacologically similar to pentazocine (p.113). Butorphanol is used for the relief of moderate to severe pain, including the pain of labour, and as an adjunct to anaesthesia. Onset of analgesia occurs within 15 minutes of intramuscular injection or an intranasal dose and may last for 3 to 4 hours after parenteral doses or for 4 to 5 hours after intranasal doses.

For the relief of moderate to severe **pain**, butorphanol tartrate is given in doses of 1 to 4 mg (usually 2 mg) by intramuscular injection or in doses of 0.5 to 2 mg (usually 1 mg) by intravenous injection every 3 to 4 hours. It may also be given as a nasal spray, in usual doses of 1 mg (1 spray in 1 nostril), repeated after 60 to 90 minutes, if necessary. This sequence may be repeated after 3 to 4 hours as needed. An initial dose of 2 mg (1 spray in each nostril) may be given for severe pain, but should not be repeated until 3 to 4 hours later.

In *obstetric analgesia* 1 to 2 mg may be given by intramuscular or intravenous injection during early labour in women at term. This dose may be repeated after 4 hours if necessary but an alternative analgesic should be used if delivery is expected within 4 hours.

In **anaesthesia**, 2 mg may be given intramuscularly for premedication 60 to 90 minutes before surgery. For use in balanced anaesthesia, a usual dose is 2 mg given intravenously shortly before induction and/or 0.5 to 1 mg given intravenously in increments during anaesthesia. The total dose needed varies but most patients require 4 to 12.5 mg.

Dosage adjustment may be needed in the elderly. When given by injection the initial dose of butorphanol for pain should be half the usual initial adult dose. Subsequent doses should be determined by the patient's response; a dosage interval of at least 6 hours has been recommended. For nasal use the initial dose should be limited to 1 mg followed by 1 mg after 90 to 120 minutes if necessary; subsequent doses if required should generally be given at intervals of not less than 6 hours. Similar recommendations have also been made for patients with hepatic or renal impairment, see below.

◊ References.

1. Atkinson BD, *et al.* Double-blind comparison of intravenous butorphanol (Stadol) and fentanyl (Sublimaze) for analgesia during labor. *Am J Obstet Gynecol* 1994; **171:** 993–8.
2. Gillis JC, *et al.* Transnasal butorphanol: a review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential in acute pain management. *Drugs* 1995; **50:** 157–75.
3. Commiskey S, *et al.* Butorphanol: effects of a prototypical agonist-antagonist analgesic on κ-opioid receptors. *J Pharmacol Sci* 2005; **98:** 109–16.

Administration in hepatic or renal impairment. The dosage of butorphanol may need to be adjusted in patients with hepatic or renal impairment. When given by injection the initial dose for pain should be half the usual initial adult dose (see above). Subsequent doses should be determined by the patient's response; a dosage interval of at least 6 hours has been recommended. For nasal use the initial dose should be limited to 1 mg followed by 1 mg after 90 to 120 minutes if necessary; subsequent doses if required should generally be given at intervals of not less than 6 hours.

Headache. Butorphanol has been advocated for use as a nasal spray in the treatment of migraine, but there have been problems with abuse and dependence (see above) and its place in therapy, if any, still remains to be established. See also Antimigraine Drugs, under Interactions, above.

References.

1. Freitag FG. The acute treatment of migraine with transnasal butorphanol (TNB). *Headache Q* 1993; **4** (suppl 3): 22–8.
2. Hoffert MJ, *et al.* Transnasal butorphanol in the treatment of acute migraine. *Headache* 1995; **35:** 65–9.
3. Melanson SW, *et al.* Transnasal butorphanol in the emergency department management of migraine headache. *Am J Emerg Med* 1997; **15:** 57–61.

Pruritus. Results from a small study[1] of 6 patients with severe opioid-induced pruritus unresponsive to diphenhydramine, and from a case series of 5 patients with intractable pruritus from other causes,[2] suggest that intranasal butorphanol may be an effective treatment. Doses have ranged from 1 mg every other day to 2 mg every 4 to 6 hours.

1. Dunteman E, *et al.* Transnasal butorphanol for the treatment of opioid-induced pruritus unresponsive to antihistamines. *J Pain Symptom Manage* 1996; **12:** 255–60.
2. Dawn AG, Yosipovitch G. Butorphanol for treatment of intractable pruritus. *J Am Acad Dermatol* 2006; **54:** 527–31.

Preparations

USP 31: Butorphanol Tartrate Injection; Butorphanol Tartrate Nasal Solution.

Proprietary Preparations (details are given in Part 3)
Canad.: Stadol†; ***Chile:*** Stadol†; ***Cz.:*** Beforal†; Moradol†; ***India:*** Butrum; ***Mex.:*** Stadol; ***Philipp.:*** Stadol; ***Rus.:*** Stadol (Стадол); ***USA:*** Stadol.

Capsaicin

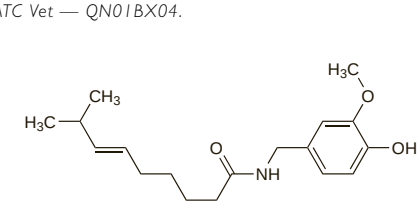
Capsaicina; Capsaicinum; Kapsaicin; Kapsaicyna; Kapsaisiini. (*E*)-8-Methyl-*N*-vanillylnon-6-enamide.

$C_{18}H_{27}NO_3$ = 305.4.

CAS — 404-86-4.

ATC — N01BX04.

ATC Vet — QN01BX04.



NOTE. Do not confuse capsaicin with capsicin, which is capsicum oleoresin (see Capsicum, p.2276).

Pharmacopoeias. In *US.*

USP 31 (Capsaicin). An off-white powder. M.p. 57° to 66°. Practically insoluble in cold water; soluble in alcohol, in chloro-