usually occurring within the first 2 weeks of therapy, and particularly in women and in patients with seronegative rheumatoid arthritis or psoriatic arthritis. Disorders such as epidermal necrolysis, erythema multiforme, and Stevens-Johnson syndrome have also been reported. A small number of patients who develop rash may go on to develop a severe illness characterised by pulmonary eosinophilia or allergic alveolitis. Treatment with fenbufen should be stopped immediately if a rash appears.

Breast feeding. UK licensed product information advises that fenbufen should be avoided in breast-feeding mothers, because of the presence of its metabolites in breast milk.

Effects on the blood. Haemolytic anaemia[1] and aplastic anaemia[2] have been reported in patients receiving fenbufen.

1. Martland T, Stone WD. Haemolytic anaemia associated with fenbufen. *BMJ* 1988; **297:** 921.
2. Andrews R, Russell N. Aplastic anaemia associated with a non-steroidal anti-inflammatory drug: relapse after exposure to another such drug. *BMJ* 1990; **301:** 38.

Effects on the lungs. In January 1989 the UK CSM reported that it had received 7 reports of a suspected association between rash and an allergic interstitial lung disorder in patients receiving fenbufen.[1] In 5 patients, the lung disorder was diagnosed as pulmonary eosinophilia; in the 2 other patients the pulmonary component of the reaction was described as allergic alveolitis. Several of these reactions have been reported in the literature.[2,3]

1. CSM. Fenbufen, rash and pulmonary eosinophilia. *Current Problems 24* 1989. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024431&RevisionSelectionMethod=LatestReleased (accessed 01/11/07)
2. Swinburn CR. Alveolitis and haemolytic anaemia induced by azapropazone. *BMJ* 1987; **294:** 375.
3. Burton GH. Rash and pulmonary eosinophilia associated with fenbufen. *BMJ* 1990; **300:** 82–3.

Effects on the skin. In September 1988 the UK CSM reported[1] that it was still receiving large numbers of reports of adverse reactions to fenbufen when such reports were expected to have declined. Fenbufen was the most commonly reported suspect drug in 1986 and 1987. At the time of the report more than 6000 such reports had been received, 80% concerning mucocutaneous reactions and most involving a generalised florid erythematous rash, often with pruritus. There were 178 reports of erythema multiforme, 30 of Stevens-Johnson syndrome, and 2 fatalities.

1. CSM. Fenbufen and mucocutaneous reactions. *Current Problems 23* 1988. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024430&RevisionSelectionMethod=LatestReleased (accessed 01/11/07)

Hypersensitivity. See under Effects on the Lungs (above).

Interactions

For interactions associated with NSAIDs, see p.99.

Use of fenbufen with aspirin may result in decreased serum concentrations of fenbufen and its metabolites.

Pharmacokinetics

Fenbufen is absorbed from the gastrointestinal tract after oral use and peak plasma concentrations are reached in about 70 minutes. Fenbufen is over 99% bound to plasma proteins. It is metabolised in the liver to the active metabolites, biphenylacetic acid and 4-hydroxy-biphenylbutyric acid. Fenbufen and its metabolites are reported to have plasma half-lives of about 10 to 17 hours and are mainly eliminated as conjugates in the urine. Metabolites of fenbufen have been detected in breast milk in small amounts.

Uses and Administration

Fenbufen, a propionic acid derivative, is an NSAID (p.99). It is given for the relief of pain and inflammation associated with musculoskeletal and joint disorders such as rheumatoid arthritis, osteoarthritis, and ankylosing spondylitis in oral doses of 900 mg daily; the dose may be either 450 mg in the morning and evening or 300 mg in the morning with 600 mg in the evening.

Preparations

BP 2008: Fenbufen Capsules; Fenbufen Tablets.

Proprietary Preparations (details are given in Part 3)
Austria: Lederfen†; ***Indon.:*** Cybufen; ***Irl.:*** Lederfen; ***Port.:*** Basifen; Reugast†; ***Thai.:*** Cepal; Cinopal†; ***Turk.:*** Cinopal; ***UK:*** Lederfen.

Fenoprofen Calcium *(BANM, USAN, rINNM)*

Calcii Fenoprofenum; Fénoprofène Calcique; Fenoprofeno cálcico; Lilly-69323; Lilly-53858 (fenoprofen); Lilly-61169 (fenoprofen sodium). Calcium (±)-2-(3-phenoxyphenyl)propionate dihydrate.

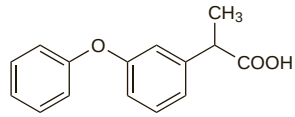
Кальций Фенопрофен

$(C_{15}H_{13}O_3)_2Ca,2H_2O$ = 558.6.

CAS — 31879-05-7 (fenoprofen); 34597-40-5 (anhydrous fenoprofen calcium); 53746-45-5 (fenoprofen calcium dihydrate).

ATC — M01AE04.

ATC Vet — QM01AE04.



(fenoprofen)

Pharmacopoeias. In *Br.*, *Chin.*, and *US.*
BP 2008 (Fenoprofen Calcium). A white or almost white odourless or almost odourless crystalline powder. Slightly soluble in water and in chloroform; soluble in alcohol.
USP 31 (Fenoprofen Calcium). A white crystalline powder. Slightly soluble in water, in methyl alcohol, and in n-hexanol; practically insoluble in chloroform. Store in airtight containers.

Adverse Effects, Treatment, and Precautions

As for NSAIDs in general, p.96.

Dysuria, cystitis, haematuria, interstitial nephritis, and acute renal insufficiency have been reported with fenoprofen. Nephrotic syndrome, which may be preceded by fever, rash, arthralgia, oliguria, azotaemia, and anuria, has also occurred. Upper respiratory-tract infection and nasopharyngitis have been reported. There have been reports of severe hepatic reactions, including jaundice and fatal hepatitis.

Breast feeding. Fenoprofen is distributed into breast milk although the amount is considered by the *BNF* to be too small to be harmful to a breast-fed infant. In contrast, licensed product information does not recommend its use since safety has not been established.

Effects on the blood. Haematological adverse effects including agranulocytosis,[1] aplastic anaemia,[2] and thrombocytopenia[3,4] have been reported in patients taking fenoprofen; licensed product information also reports haemolytic anaemia.

1. Simon SD, Kosmin M. Fenoprofen and agranulocytosis. *N Engl J Med* 1978; **299:** 490.
2. Ashraf M, *et al.* Aplastic anaemia associated with fenoprofen. *BMJ* 1982; 284: 1301–2.
3. Simpson RE, *et al.* Acute thrombocytopenia associated with fenoprofen. *N Engl J Med* 1978; **298:** 629–30.
4. Katz ME, Wang P. Fenoprofen-associated thrombocytopenia. *Ann Intern Med* 1980; **92:** 262.

Effects on the liver. Cholestatic jaundice and hepatitis developed in a 68-year-old woman after receiving fenoprofen 600 mg four times daily for 7 weeks. Subsequent use of naproxen and indometacin did not result in hepatotoxicity.[1] However, there has been a report of cross-hepatotoxicity between fenoprofen and naproxen.[2]

1. Stennett DJ, *et al.* Fenoprofen-induced hepatotoxicity. *Am J Hosp Pharm* 1978; **35:** 901.
2. Andrejak M, *et al.* Cross hepatotoxicity between non-steroidal anti-inflammatory drugs. *BMJ* 1987; **295:** 180–1.

Effects on the skin. Toxic epidermal necrolysis was associated with fenoprofen in 2 patients.[1]

1. Stotts JS, *et al.* Fenoprofen-induced toxic epidermal necrolysis. *J Am Acad Dermatol* 1988; **18:** 755–7.

Overdosage. A report of coma, respiratory depression, hypotension, and metabolic acidosis in a patient who had ingested between 24 and 36 g of fenoprofen.[1] The patient responded to gastric lavage and activated charcoal and intensive supportive care.

1. Kolodzik JM, *et al.* Nonsteroidal anti-inflammatory drugs and coma: a case report of fenoprofen overdose. *Ann Emerg Med* 1990; **19:** 378–81.

Interactions

For interactions associated with NSAIDs, see p.99.

Aspirin is reported to reduce plasma concentrations of fenoprofen.

Antiepileptics. *Phenobarbital* might increase the rate of metabolism of fenoprofen.[1] US licensed product information suggests that dosage adjustment of fenoprofen may be required when given with phenobarbital.

1. Helleberg L, *et al.* A pharmacokinetic interaction in man between phenobarbitone and fenoprofen, a new anti-inflammatory agent. *Br J Clin Pharmacol* 1974; **1:** 371–4.

Pharmacokinetics

Fenoprofen is readily absorbed from the gastrointestinal tract; bioavailability is about 85% but food and milk may reduce the rate and extent of absorption. Peak plasma concentrations occur 1 to 2 hours after a dose. The plasma half-life is about 3 hours. Fenoprofen is 99% bound to plasma proteins. About 90% of a dose is excreted in the urine in 24 hours, chiefly as the glucuronide and the glucuronide of hydroxylated fenoprofen. Fenoprofen is distributed into breast milk.

Uses and Administration

Fenoprofen, a propionic acid derivative, is an NSAID (p.99) used in the management of mild to moderate pain and for the relief of pain and inflammation associated with disorders such as osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. It is given as the calcium salt although doses are expressed in terms of the base; fenoprofen calcium (dihydrate) 1.2 g is equivalent to about 1 g of fenoprofen. A usual oral dose is the equivalent of 300 to 600 mg of fenoprofen three or four times daily, adjusted thereafter according to response. In the USA, lower doses of 200 mg every 4 to 6 hours are recommended for mild to moderate pain. It has been recommended that the total daily dose should not exceed 3 g (UK) or 3.2 g (USA).

Preparations

BP 2008: Fenoprofen Tablets;
USP 31: Fenoprofen Calcium Capsules; Fenoprofen Calcium Tablets.

Proprietary Preparations (details are given in Part 3)
Braz.: Trandor†; ***Canad.:*** Nalfon†; ***Denm.:*** Nalfon†; ***Fr.:*** Nalgesic; ***Gr.:*** Expron†; ***Mex.:*** Nalfon†; ***S.Afr.:*** Fenopron†; ***UK:*** Fenopron; ***USA:*** Nalfon; ***Venez.:*** Fenopron†.

Fentanyl *(BAN, rINN)* ⊗

Fentanil; Fentanilis; Fentanilo; Fentanylum; Fentanyyli. *N*-(1-Phenethyl-4-piperidyl) propionanilide.

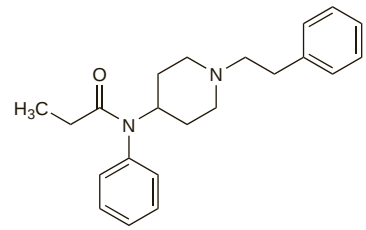
Фентанил

$C_{22}H_{28}N_2O$ = 336.5.

CAS — 437-38-7.

ATC — N01AH01; N02AB03.

ATC Vet — QN01AH01; QN02AB03.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of fentanyl:
Apache; China girl; China town; China white; Dance fever; Fentanest; Friend; Goodfellas; Great bear; He-man; Jackpot; King ivory; Murder 8; Poison; Tango & Cash; TNT; T.N.T.

Pharmacopoeias. In *Eur.* (see p.vii).
Ph. Eur. 6.2 (Fentanyl). A white or almost white polymorphic powder. Practically insoluble in water; freely soluble in alcohol and in methyl alcohol. Protect from light.

Fentanyl Citrate *(BANM, USAN, rINNM)* ⊗

Citrato de fentanilo; Fentanil-citrát; Fentanilio citratas; Fentanyl, citrate de; Fentanylcitrat; Fentanyl-citrát; Fentanyli citras; Fentanylu cytrynian; Fentanyylisitraatti; McN-JR-4263-49; Phentanyl Citrate; R-4263. *N*-(1-Phenethyl-4-piperidyl)propionanilide dihydrogen citrate.

Фентанила Цитрат

$C_{22}H_{28}N_2O,C_6H_8O_7$ = 528.6.

CAS — 990-73-8.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US*.
Ph. Eur. 6.2 (Fentanyl Citrate). White or almost white powder. Soluble in water; sparingly soluble in alcohol; freely soluble in methyl alcohol. Protect from light.
USP 31 (Fentanyl Citrate). A white crystalline powder or white glistening crystals. Sparingly soluble in water; slightly soluble in chloroform; soluble in methyl alcohol. Store at a temperature of 25°, excursions permitted between 15° and 30°. Protect from light.

Fentanyl Hydrochloride *(BANM, rINNM)* ⊗

Fentanyl, Chlorhydrate de; Fentanyli Hydrochloridum; Hidrocloruro de fentanilo.

Фентанила Гидрохлорид

$C_{22}H_{28}N_2O,HCl$ = 372.9.

CAS — 1443-54-5.

Incompatibility. Fentanyl citrate is incompatible with thiopental sodium and methohexital sodium.

A thick white precipitate formed in the intravenous tubing when fentanyl citrate with droperidol was given shortly after nafcillin sodium. There was no precipitate when fentanyl citrate alone was mixed with nafcillin sodium.[1]

Fentanyl citrate underwent rapid and extensive loss when admixed with fluorouracil in PVC containers.[2] The loss was due to sorption of fentanyl to the PVC as a result of the alkaline pH of the admixture, and presumably could occur from admixture of fentanyl citrate with any sufficiently alkaline drug.

See also Stability, below.

1. Jeglum EL, *et al.* Nafcillin sodium incompatibility with acidic solutions. *Am J Hosp Pharm* 1981; **38:** 462, 464.
2. Xu QA, *et al.* Rapid loss of fentanyl citrate admixed with fluorouracil in polyvinyl chloride containers. *Ann Pharmacother* 1997; **31:** 297–302.

Stability. In a 48-hour study fentanyl citrate in glucose 5% or sodium chloride 0.9% was stable when stored at room temperature under usual light conditions in glass or PVC containers;[1] the concentration of fentanyl delivered by a patient-controlled system was relatively constant throughout a 30-hour study period. Fentanyl citrate injection diluted to 20 micrograms/mL with sodium chloride 0.9% was stable for 30 days at 3° or 23° in PVC reservoirs for portable infusion pumps.[2] In another study[3] fentanyl citrate diluted to 50 micrograms/mL with sodium chloride 0.9% remained stable for at least 14 days when stored at room temperature in PVC reservoirs for portable patient-controlled systems.

An admixture of fentanyl citrate and bupivacaine in sodium chloride 0.9% appeared[4] compatible and stable when stored for up to 30 days at 3° or 23° in a portable infusion pump. In another study[5] the stability of solutions containing fentanyl, bupivacaine, and adrenaline, alone and in combination was studied over a period of 56 days when stored at various temperatures in the light or in the dark in PVC bags. Both fentanyl and bupivacaine were adsorbed from solution onto the PVC for the first 3 days but thereafter concentrations of these drugs remained relatively stable; freezing appeared to slow the concentration change for bupivacaine but not for fentanyl. Solutions containing adrenaline became more acidic during the study as the adrenaline progressively deteriorated but this was greatly reduced by freezing. Autoclaving produced a further reduction in the concentration of all drugs. There was no sign of precipitation from any of the solutions studied.

An admixture of fentanyl citrate, ketamine hydrochloride, and droperidol in sodium chloride 0.9% was stable[6] for at least 30 days when stored in glass bottles at 25°; the minor decrease in the concentrations of all 3 drugs was attributed to either hydrolytic degradation or adsorption. This admixture also appeared compatible when stored in PVC bags at 4° and 25°; the small increase in drug concentrations over 30 days may be a result of water permeation and evaporation through the bags.

Fentanyl is potentially unstable in PVC containers when admixed with alkaline drugs (see Incompatibility, above).

1. Kowalski SR, Gourlay GK. Stability of fentanyl citrate in glass and plastic containers and in a patient-controlled delivery system. *Am J Hosp Pharm* 1990; **47:** 1584–7.
2. Allen LV, *et al.* Stability of fentanyl citrate in 0.9% sodium chloride solution in portable infusion pumps. *Am J Hosp Pharm* 1990; **47:** 1572–4.
3. Chapalain-Pargade S, *et al.* Microbiological and physicochemical stability of fentanyl and sufentanil solutions for patient-controlled delivery systems. *J Pain Symptom Manage* 2006; **32:** 90–7.
4. Tu Y-H, *et al.* Stability of fentanyl citrate and bupivacaine hydrochloride in portable pump reservoirs. *Am J Hosp Pharm* 1990; **47:** 2037–40.
5. Dawson PJ, *et al.* Stability of fentanyl, bupivacaine and adrenaline solutions for extradural infusion. *Br J Anaesth* 1992; **68:** 414–17.
6. Lee DKT, *et al.* Compatibility of fentanyl citrate, ketamine hydrochloride, and droperidol in 0.9% sodium chloride injection stored in polyvinyl chloride bags. *Am J Health-Syst Pharm* 2005; **62:** 1190–2.

Dependence and Withdrawal

As for Opioid Analgesics, p.101.

Fentanyl and illicitly manufactured analogues are subject to abuse (see under Precautions, below).

◊ Plasma concentrations required to produce satisfactory sedation have been reported to increase steadily in neonates receiving continuous infusions, suggesting the development of *tolerance* to the sedating effects of fentanyl.[1]

Movement disorders, *extreme irritability*, and symptoms characteristic of *opioid abstinence syndrome* have been reported in children after withdrawal of prolonged fentanyl infusions.[2,3] Similarly, withdrawal symptoms and, in one case, myoclonus have occurred in adults when fentanyl transdermal patches have been stopped.[4,5] Acute opioid withdrawal syndrome has also been seen in cancer patients switched from modified-release oral morphine to transdermal fentanyl despite adequate analgesia being maintained.[6]

1. Arnold JH, *et al.* Changes in the pharmacodynamic response to fentanyl in neonates during continuous infusion. *J Pediatr* 1991; **119:** 639–43.
2. Lane JC, *et al.* Movement disorder after withdrawal of fentanyl infusion. *J Pediatr* 1991; **119:** 649–51.
3. Dominguez KD, *et al.* Opioid withdrawal in critically ill neonates. *Ann Pharmacother* 2003 **37:** 473–7.
4. Han PKJ, *et al.* Myoclonus secondary to withdrawal from transdermal fentanyl: case report and literature review. *J Pain Symptom Manage* 2002; **23:** 66–72.
5. Ishihara C, *et al.* Withdrawal symptom after discontinuation of transdermal fentanyl at a daily dose of 0.6 mg. *Pharm World Sci* 2005; **27:** 13–15.
6. Anonymous. Opiate withdrawal with transdermal fentanyl. *Pharm J* 1995; **255:** 680.

Adverse Effects and Treatment

As for Opioid Analgesics in general, p.102.

Respiratory depression, which occurs especially with high doses of fentanyl, responds to naloxone (see also Effects on the Respiratory System, below). Atropine may be used to block the vagal effects of fentanyl such as bradycardia. Unlike morphine, fentanyl is reported not to cause significant histamine release. Transient hypotension may follow intravenous dosage. Muscle rigidity can occur and may require neuromuscular blockers.

Local reactions such as rash, erythema, and itching have been reported with transdermal use. Gum bleeding and irritation, and taste perversion have been reported with transmucosal use.

Effects on the cardiovascular system. For a reference to the effects of fentanyl on histamine release compared with some other opioids, see under Pethidine, p.114.

Effects on mental function. Fentanyl had some dose-related effects on mental function and motor activity in healthy subjects,[1] but immediate and delayed recall were not affected. See also under Alfentanil (p.16).

Acute toxic delirium has been reported after treatment with transdermal fentanyl.[2]

1. Scamman FL, *et al.* Ventilatory and mental effects of alfentanil and fentanyl. *Acta Anaesthesiol Scand* 1984; **28:** 63–7.
2. Kuzma PJ, *et al.* Acute toxic delirium: a uncommon reaction to transdermal fentanyl. *Anesthesiology* 1995; **83:** 869–71.

Effects on the nervous system. There have been reports of seizures with low and high doses of fentanyl or sufentanil.[1] There was, however, no EEG evidence of cortical seizure activity in a patient who had seizure-like muscle movements during a fentanyl infusion;[2] the muscle movements might have been due to myoclonus produced by depression of higher CNS inhibitory centres or to a pronounced form of opioid-induced muscle rigidity.

For a report of encephalopathy associated with prolonged use of fentanyl and midazolam in infants in intensive care, see Encephalopathy under Adverse Effects of Diazepam, p.988.

1. Zaccara G, *et al.* Clinical features, pathogenesis and management of drug-induced seizures. *Drug Safety* 1990; **5:** 109–51.
2. Scott JC, Sarnquist FH. Seizure-like movements during a fentanyl infusion with absence of seizure activity in a simultaneous EEG recording. *Anesthesiology* 1985; **62:** 812–14.

Effects on the respiratory system. Fentanyl, like other opioid agonists, causes dose-related respiratory depression; it is significant with *intravenous* fentanyl doses of more than 200 micrograms and may be more prolonged than analgesia. Anaesthesia with fentanyl may result in either prolonged or delayed respiratory depression postoperatively.[1] Consequently, patients should continue to be monitored postoperatively until spontaneous breathing has been re-established. Severe respiratory depression in a 14-month-old child after intravenous sedation with fentanyl and midazolam has also highlighted the necessity for careful monitoring when giving with other respiratory depressants.[2] If present at the end of operation respiratory depression may be reversed by an opioid antagonist such as naloxone; alternatively, a respiratory stimulant such as doxapram that does not reverse analgesia has been given.

Rigidity of the respiratory muscles (chest wall rigidity) may occur during fentanyl anaesthesia. The effects can be minimised by using a slow intravenous injection but a neuromuscular blocker may be required to allow artificial ventilation; rigidity has been reversed postoperatively by naloxone. Similar muscle rigidity induced by alfentanil could be attenuated by pretreatment with a benzodiazepine whereas small doses of neuromuscular blockers appeared to be ineffective.[3]

Coughing has been associated[4] with intravenous fentanyl; incidence was decreased with a longer injection time,[5] in light cigarette smokers,[5,6] and in older patients.[6] For the use of beclometasone and lidocaine to prevent cough associated with intravenous fentanyl in anaesthesia, see p.1518 and p.1852, respectively.

The risk of respiratory depression associated with *epidural* doses of fentanyl, a highly lipid-soluble opioid, has been considered relatively small and only slight ventilatory depression was noted[7] after a dose of 50 micrograms. However, profound delayed respiratory depression has been reported in 2 women 100 minutes[8] and 80 minutes,[9] respectively after fentanyl 100 micrograms had been given epidurally for caesarean section. No adverse effects on neonatal respiration or neurobehaviour were detected in a study[10] of neonates of mothers given epidural infusions of bupivacaine and fentanyl during labour. However, a later report[11] described 2 neonates who developed respiratory depression after their mothers were given epidural fentanyl during labour; the effect was reversed by intramuscular naloxone 400 micrograms. The authors noted that the doses of fentanyl used were higher than those in the previous study.

Respiratory depression is also a risk with *topically* applied fentanyl preparations. Severe hypoventilation with some fatalities has occurred in patients given fentanyl as a transdermal patch for minor painful conditions.[12] More recently, Health Canada had received 2 reports of fatal respiratory depression associated with the use of transdermal fentanyl patches in adolescents for relatively minor conditions (chronic headache and throat pain);[13] in both cases the respiratory depression developed within 24 hours of applying the first and only patch. See also Administration, Transdermal Route, under Precautions below.

1. Bennett MRD, Adams AP. Postoperative respiratory complications of opiates. *Clin Anaesthesiol* 1983; **1:** 41–56.
2. Yaster M, *et al.* Midazolam-fentanyl intravenous sedation in children: case report of respiratory arrest. *Pediatrics* 1990; **86:** 463–7.
3. Sanford TJ, *et al.* Pretreatment with sedative-hypnotics, but not with nondepolarizing muscle relaxants, attenuates alfentanil-induced muscle rigidity. *J Clin Anesth* 1994; **6:** 473–80.
4. Tweed WA, Dakin D. Explosive coughing after bolus fentanyl injection. *Anesth Analg* 2001; **92:** 1442–3.
5. Lin J-A, *et al.* Prolonged injection time and light smoking decrease the incidence of fentanyl-induced cough. *Anesth Analg* 2005; **101:** 670–4.
6. Oshima T, *et al.* Identification of independent risk factors for fentanyl-induced cough. *Can J Anesth* 2006; **53:** 753–8.
7. Morisot P, *et al.* Ventilatory response to carbon dioxide during extradural anaesthesia with lignocaine and fentanyl. *Br J Anaesth* 1989; **63:** 97–102.
8. Brockway MS, *et al.* Profound respiratory depression after extradural fentanyl. *Br J Anaesth* 1990; **64:** 243–5.
9. Wang CY. Respiratory depression after extradural fentanyl. *Br J Anaesth* 1992; **69:** 544.
10. Porter J, *et al.* Effect of epidural fentanyl on neonatal respiration. *Anesthesiology* 1998; **89:** 79–85.
11. Kumar M, Paes B. Epidural opioid analgesia and neonatal respiratory depression. *J Perinatol* 2003; **23:** 425–7.
12. *FDC Reports Pink Sheet* 1994; January 24: 12.
13. Health Canada. Transdermal fentanyl (Duragesic): respiratory arrest in adolescents. *Can Adverse React News* 2004; **14** (4): 1–2. Also available at: http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/medeff/carn-bcei_v14n4-eng.pdf (accessed 26/06/08)

Effects on the skin. A patient developed a macular rash covering the whole body, except for the face and scalp, while using transdermal fentanyl patches.[1]

1. Stoukides CA, Stegman M. Diffuse rash associated with transdermal fentanyl. *Clin Pharm* 1992; **11:** 222.

Effects on the urinary tract. Urinary retention developed in 2 premature infants after sedation with fentanyl infusion at a dose of 3 micrograms/kg per hour.[1] In both cases catheterisation relieved symptoms.

1. Das UG, Sasidharan P. Bladder retention of urine as a result of continuous intravenous infusion of fentanyl: 2 case reports. *Pediatrics* 2001; **108:** 1012–1015.

Precautions

As for Opioid Analgesics in general, p.103.

Caution is advised in patients with myasthenia gravis; the effects of muscular rigidity on respiration may be particularly pronounced in these patients.

US licensed product information contra-indicates the use of standard transdermal fentanyl patches in opioid-naive patients because of the risk of fatal respiratory depression (see Effects on the Respiratory System, above and Administration, Transdermal Route, below). Similar contra-indications apply to fentanyl buccal tablets (see Administration, Transmucosal Route, below).