Administration. The elimination half-life of pethidine was prolonged and plasma clearance decreased when given perioperatively compared with postoperatively.[1]

During labour the pharmacokinetics of pethidine may depend on how it is given. In a comparison of intramuscular injection at different sites, absorption of pethidine from the gluteus muscle was impaired and the deltoid muscle was preferred.[2]

No statistically significant differences were found in pharmacokinetic parameters for deltoid and gluteal intramuscular injections in elderly postoperative patients.[3] However, substantial interpatient variability was noted for both sites, and the authors suggested that more rapid and predictable routes such as intravenous injection may be more appropriate for postoperative use in the elderly.

1. Tamsen A, *et al.* Patient-controlled analgesic therapy, part 1: pharmacokinetics of pethidine in the per- and postoperative periods. *Clin Pharmacokinet* 1982; **7:** 149–63.
2. Lazebnik N, *et al.* Intravenous, deltoid, or gluteus administration of meperidine during labor? *Am J Obstet Gynecol* 1989; **160:** 1184–9.
3. Erstad BL, *et al.* Site-specific pharmacokinetics and pharmacodynamics of intramuscular meperidine in elderly postoperative patients. *Ann Pharmacother* 1997; **31:** 23–8.

Hepatic impairment. The terminal half-life of pethidine was prolonged to about 7 hours in cirrhotic patients compared with 3 hours in healthy subjects, which was attributed to impairment of the drug-metabolising activity of the liver.[1] Another study concluded that although impaired hepatic metabolism might confer relative protection from norpethidine toxicity in patients with cirrhosis, there might be an increased risk of cumulative toxicity because of slow elimination of the metabolite.[2]

1. Klotz U, *et al.* The effect of cirrhosis on the disposition and elimination of meperidine in man. *Clin Pharmacol Ther* 1974; **16:** 667–75.
2. Pond SM, *et al.* Presystemic metabolism of meperidine to normeperidine in normal and cirrhotic subjects. *Clin Pharmacol Ther* 1981; **30:** 183–8.

Pregnancy. Some references to the pharmacokinetics of pethidine during labour are given below.

1. Tomson G, *et al.* Maternal kinetics and transplacental passage of pethidine during labour. *Br J Clin Pharmacol* 1982; **13:** 653–9.
2. Kuhnert BR, *et al.* Disposition of meperidine and normeperidine following multiple doses during labor: I mother. *Am J Obstet Gynecol* 1985; **151:** 406–9.
3. Kuhnert BR, *et al.* Disposition of meperidine and normeperidine following multiple doses during labor: II fetus and neonate. *Am J Obstet Gynecol* 1985; **151:** 410–15.

Renal impairment. Plasma protein binding of pethidine was reported to be decreased in renal disease and ranged from 58.2% in healthy subjects to 31.8% in anuric patients.[1] The same workers also reported prolonged elimination of pethidine in patients with renal dysfunction.[2]

See also under Precautions, above.

1. Chan K, *et al.* Plasma protein binding of pethidine in patients with renal disease. *J Pharm Pharmacol* 1983; **35:** 94P.
2. Chan K, *et al.* Pharmacokinetics of low-dose intravenous pethidine in patients with renal dysfunction. *J Clin Pharmacol* 1987; **27:** 516–22.

Uses and Administration

Pethidine, a phenylpiperidine derivative, is a synthetic opioid analgesic (p.104) that acts mainly as a μ opioid agonist. Pethidine is used for the relief of most types of moderate to severe acute pain including the pain of labour. It is more lipid soluble than morphine and has a less potent and shorter lasting analgesic effect; analgesia usually lasts for 2 to 4 hours. Its short duration of action and accumulation of its potentially neurotoxic metabolite norpethidine on repeated dosage make it unsuitable for the management of chronic pain. Pethidine has a weaker action on smooth muscle than morphine and its lower potential to increase biliary pressure may make it a more suitable opioid analgesic for pain associated with biliary colic and pancreatitis (but see Biliary-tract Disorders, p.103). It is also used for premedication and as an adjunct to anaesthesia. It has been given with phenothiazines such as promethazine to achieve basal narcosis. Pethidine has little effect on cough or on diarrhoea.

For the relief of **pain**, pethidine hydrochloride is given in oral doses of 50 to 150 mg every 4 hours if necessary. It may also be given by intramuscular or subcutaneous injection in doses of 25 to 100 mg and by slow intravenous injection in doses of 25 to 50 mg repeated after 4 hours. For *postoperative* pain, the *BNF* suggests that the subcutaneous or intramuscular doses may be given every 2 to 3 hours if necessary.

In *obstetric analgesia* 50 to 100 mg may be given by intramuscular or subcutaneous injection as soon as contractions occur at regular intervals. This dose may be repeated after 1 to 3 hours if necessary up to a maximum of 400 mg in 24 hours.

For **premedication** 25 to 100 mg may be given intramuscularly about 1 hour before surgery. It may also be given subcutaneously in similar doses. As an **adjunct to anaesthesia** 10 to 25 mg may be given by slow intravenous injection.

For details of doses in children, see below.

Administration. In addition to the conventional routes pethidine has been given epidurally,[1-4] intraperitoneally,[5,6] and intrathecally.[7-9] It has also been given by various routes as a patient-controlled system.[10-13] However, some consider that the use of pethidine should be avoided for patient-controlled analgesia because of the increased risk of norpethidine-induced seizures[14] (see also Incidence of Adverse Effects and Effects on the Nervous System, above).

1. Perriss BW. Epidural pethidine in labour: a study of dose requirements. *Anaesthesia* 1980; **35:** 380–2.
2. Husemeyer RP, *et al.* A study of pethidine kinetics and analgesia in women in labour following intravenous, intramuscular and epidural administration. *Br J Clin Pharmacol* 1982; **13:** 171–6.
3. Perriss BW, *et al.* Analgesia following extradural and im pethidine in post-caesarean section patients. *Br J Anaesth* 1990; **64:** 355–7.
4. Blythe JG, *et al.* Continuous postoperative epidural analgesia for gynecologic oncology patients. *Gynecol Oncol* 1990; **37:** 307–10.
5. Colbert ST, *et al.* An assessment of the value of intraperitoneal meperidine for analgesia postlaparoscopic tubal ligation. *Anesth Analg* 2000; **91:** 667–70.
6. O'Hanlon DM, *et al.* Intraperitoneal pethidine versus intramuscular pethidine for the relief of pain after laparoscopic cholecystectomy: randomized trial. *World J Surg* 2002; **26:** 1432–6.
7. Acalovschi I, *et al.* Saddle block with pethidine for perineal operations. *Br J Anaesth* 1986; **58:** 1012–16.
8. Yu SC, *et al.* Addition of meperidine to bupivacaine for spinal anaesthesia for caesarean section. *Br J Anaesth* 2002; **88:** 379–83.
9. Vranken JH, *et al.* Plasma concentrations of meperidine and normeperidine following continuous intrathecal meperidine in patients with neuropathic cancer pain. *Acta Anaesthesiol Scand* 2005; **49:** 665–70.
10. Striebel HW, *et al.* Patient-controlled intranasal analgesia (PCINA) for the management of postoperative pain: a pilot study. *J Clin Anesth* 1996; **8:** 4–8.
11. Kee N, *et al.* Comparison of patient-controlled epidural analgesia with patient-controlled intravenous analgesia using pethidine or fentanyl. *Anaesth Intensive Care* 1997; **25:** 126–32.
12. Sharma SK, *et al.* Cesarean delivery: a randomized trial of epidural versus patient-controlled meperidine analgesia during labor. *Anesthesiology* 1997; **87:** 487–94.
13. Chen PP, *et al.* Patient-controlled pethidine after major upper abdominal surgery: comparison of the epidural and intravenous routes. *Anaesthesia* 2001; **56:** 1106–12.
14. Hagmeyer KO, *et al.* Meperidine-related seizures associated with patient-controlled analgesia pumps. *Ann Pharmacother* 1993; **27:** 29–32.

Administration in children. Pethidine is used for the relief of moderate to severe acute pain and for premedication in children.

For the relief of **pain**, the *BNFC* suggests that children aged 2 months to 12 years may be given pethidine hydrochloride 0.5 to 2 mg/kg orally or by subcutaneous or intramuscular injection every 4 to 6 hours if necessary; older children up to 18 years of age may be given 50 to 100 mg orally, or 25 to 100 mg intramuscularly or subcutaneously, every 4 to 6 hours if necessary. Injection solutions may be given orally if needed, to achieve a suitable dose. Pethidine may also be given by intravenous injection in doses of 0.5 to 1 mg/kg to neonates and children up to 12 years of age, repeated every 10 to 12 hours if necessary in those up to 2 months of age and every 4 to 6 hours if necessary in older children; those aged 12 to 18 years may be given the usual adult intravenous dose (see above) repeated every 4 to 6 hours if necessary. An intravenous injection of 1 mg/kg as a loading dose followed by continuous intravenous infusion of 100 to 400 micrograms/kg per hour adjusted according to response may also be given to those aged 1 month and over.

For **premedication**, UK licensed product information recommends that 1 to 2 mg/kg is given intramuscularly about 1 hour before surgery.

See also Lytic Cocktails, below.

Eclampsia and pre-eclampsia. See Lytic Cocktails under Sedation, below.

Pain. Pethidine produces prompt but short-lasting analgesia, and may be preferred to morphine when rapid control of acute pain is required. It has been widely used in obstetrics to control the pain of labour (although the *BNF* notes that morphine or other opioids are often preferred for obstetric pain), and for postoperative pain relief after caesarean section or other surgical procedures.

In a study of patients with intractable pain the minimum effective analgesic blood concentration ranged from 100 to 820 nanograms/mL (median 250 nanograms/mL) in 15 of 16; the remaining patient failed to obtain analgesia with pethidine. Additional measures were considered necessary[1] if the minimum effective concentration exceeded 400 nanograms/mL.

Pethidine has traditionally been given by intermittent intramuscular injection in the treatment of acute pain, but inconsistent pain relief can be expected because of fluctuating blood-pethidine concentrations;[2] continuous intravenous infusion might be more effective for acute pain. For reference to use by other routes see Administration, above.

1. Mather LE, Glynn CJ. The minimum effective analgesic blood concentration of pethidine in patients with intractable pain. *Br J Clin Pharmacol* 1982; **14:** 385–90.
2. Edwards DJ, *et al.* Clinical pharmacokinetics of pethidine: 1982. *Clin Pharmacokinet* 1982; **7:** 421–33.

SICKLE-CELL CRISIS. Concern has been expressed over the continued use of pethidine for analgesia in painful crises in sickle-cell disease. Control of pain may be inadequate and doses commonly used to manage crises may lead to accumulation of the neuroexcitatory metabolite of pethidine and precipitate seizures.[1,2] See also Effects on the Nervous System, above.

1. Pryle BJ, *et al.* Toxicity of norpethidine in sickle cell crisis. *BMJ* 1992; **304:** 1478–9.
2. Harrison JFM, *et al.* Pethidine in sickle cell crisis. *BMJ* 1992; **305:** 182.

Sedation. Some references to the use of pethidine for endoscopy are given below.

1. Bahal-O'Mara N, *et al.* Sedation with meperidine and midazolam in pediatric patients undergoing endoscopy. *Eur J Clin Pharmacol* 1994; **47:** 319–23.
2. Diab FH, *et al.* Efficacy and safety of combined meperidine and midazolam for EGD sedation compared with midazolam alone. *Am J Gastroenterol* 1996; **91:** 1120–5.
3. Laluna L, *et al.* The comparison of midazolam and topical lidocaine spray versus the combination of midazolam, meperidine, and topical lidocaine spray to sedate patients for upper endoscopy. *Gastrointest Endosc* 2001; **53:** 289–93.

LYTIC COCKTAILS. Lytic cocktails consisting of chlorpromazine, pethidine, and/or promethazine have been given intravenously in some countries for the management of pre-eclampsia and imminent eclampsia. However, the use of phenothiazines is generally not recommended late in pregnancy, and other treatments are preferred for hypertension (see Hypertension in Pregnancy, under Hypertension, p.1171); the management of eclampsia, which is the convulsive phase, is discussed on p.470.

Lytic cocktails have also been used for sedation and analgesia in children, by intramuscular or occasionally intravenous injection. However, there is a high rate of therapeutic failure as well as serious adverse effects with such combinations, and the American Academy of Pediatrics[1] had recommended that alternative sedatives and analgesics should be considered. Lytic cocktails are not the most appropriate means of sedation for short procedures since patients must be monitored for about 1 hour before the procedure while the drugs take effect, and for even longer during the recovery period.[2]

1. American Academy of Pediatrics Committee on Drugs. Reappraisal of Lytic cocktail/Demerol, Phenergan, and Thorazine (DPT) for the sedation of children. *Pediatrics* 1995; **95:** 598–602.
2. Barst SM, *et al.* A comparison of propofol and Demerol-Phenergan-Thorazine for brief, minor, painful procedures in a pediatric hematology-oncology clinic. *Int J Pediatr Hematol/Oncol* 1995; **1:** 587–91.

Shivering. For reference to the use of pethidine in the management of shivering associated with anaesthesia, see under Adverse Effects of General Anaesthetics, p.1779. Pethidine has also been used to treat amphotericin B-induced shaking chills.[1]

1. Burks LC, *et al.* Meperidine for the treatment of shaking chills and fever. *Arch Intern Med* 1980; **140:** 483–4.

Preparations

BP 2008: Pethidine Injection; Pethidine Tablets;
USP 31: Meperidine Hydrochloride Injection; Meperidine Hydrochloride Syrup; Meperidine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Cluyer; Meperol; ***Austria:*** Alodan; ***Belg.:*** Dolantine; ***Braz.:*** Dolantina; Dolosal; Dornot; ***Canad.:*** Demerol; ***Chile:*** Demerol†; ***Cz.:*** Dolsin; ***Ger.:*** Dolantin; ***Hung.:*** Dolargan; ***Israel:*** Dolestine; ***Philipp.:*** Demerol; ***Pol.:*** Dolargan; Dolcontral; ***Spain:*** Dolantina; ***Turk.:*** Aldolan; ***USA:*** Demerol; ***Venez.:*** Demerol†; Dispadol†.

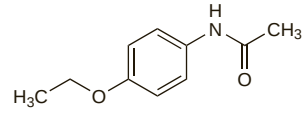
Multi-ingredient: ***Austral.:*** Marcain with Pethidine†; ***UK:*** Pamergan P100.

Phenacetin *(rINN)*

Aceto-*p*-phenetidide; Acetophenetidin; Acetylphenetidin; Fenacetin; Fenacetina; Fenasetiini; Paracetophenetidin; Phénacétine; Phenacetinum. *p*-Acetophenetidide; 4′-Ethoxyacetanilide; *N*-(4-Ethoxyphenyl)acetamide.

Фенацетин

$C_{10}H_{13}NO_2$ = 179.2.
CAS — 62-44-2.
ATC — N02BE03.
ATC Vet — QN02BE03.



Adverse Effects and Precautions

Phenacetin may cause methaemoglobinaemia, sulfhaemoglobinaemia, and haemolytic anaemia.

Prolonged use of large doses of analgesic mixtures containing phenacetin has been associated with the development of renal papillary necrosis (see Effects on the Kidneys, p.98) and transitional-cell carcinoma of the renal pelvis.

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

Uses and Administration

Phenacetin, a para-aminophenol derivative, has analgesic and antipyretic properties. It was usually given with aspirin, caffeine, or codeine but is now little used because of adverse haematological effects and nephrotoxicity.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Cz.:*** Dinyl†; Mironal†; ***Hung.:*** Antineuralgica; Dolor.

Phenazone *(BAN, rINN)*

Analgésine; Antipyrin; Antipyrine; Azophenum; Fenatsoni; Fenazon; Fenazona; Fenazonas; Phénazone; Phenazonum; Phenyldimethylpyrazolone. 1,5-Dimethyl-2-phenyl-4-pyrazolin-3-one.

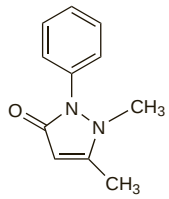
Феназон

$C_{11}H_{12}N_2O$ = 188.2.

CAS — 60-80-0.

ATC — N02BB01.

ATC Vet — QN02BB01.



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

Ph. Eur. 6.2 (Phenazone). White or almost white crystalline powder or colourless crystals. Very soluble in water, in alcohol, and in dichloromethane. Protect from light.

USP 31 (Antipyrine). Colourless crystals or white crystalline powder. Is odourless. Very soluble in water; freely soluble in alcohol and in chloroform; sparingly soluble in ether. Solutions are neutral to litmus. Store in airtight containers.

Phenazone and Caffeine Citrate

Antipyrino-Coffeinum Citricum; Fenazona y citrato de cafeína; Migrenin; Phenzone and Caffeine Citrate.

Феназон и Кофеина Цитрат

Description. Phenazone and caffeine citrate is a powder usually containing phenazone 90%, caffeine 9%, and citric acid monohydrate 1%.

Pharmacopoeias. In *Jpn*.

Phenazone Salicylate

Antipyrin Salicylate; Fenatsonisalisylaatti; Fenazona salicilato; Fenazonsalicylat; Phenazoni Salicylas; Salipyrin.

Феназона Салицилат

$C_{11}H_{12}N_2O,C_7H_6O_3$ = 326.3.

CAS — 520-07-0.

Pharmacopoeias. In *Fr.*

Adverse Effects and Precautions

Phenazone is liable to give rise to skin eruptions and in susceptible individuals even small doses may have this effect. Hypersensitivity reactions and nephrotoxicity have been reported. Large oral doses may cause nausea, drowsiness, coma, and convulsions.

Effects on the blood. Phenazone can cause haemolytic anaemia in certain individuals with a deficiency of G6PD.[1] Episodes of agranulocytosis were reported[2] in 6 women using a cream containing phenazone; all recovered on withdrawal.

1. Prankerd TAJ. Hemolytic effects of drugs and chemical agents. *Clin Pharmacol Ther* 1963; **4:** 334–50.
2. Delannoy A, Schmit J-C. Agranulocytosis after cutaneous contact with phenazone. *Eur J Haematol* 1993; **50:** 124.

Effects on the kidneys. Phenazone is considered nephrotoxic but only limited clinical information on phenazone is available because it has been mainly used with phenacetin.[1]

1. Prescott LF. Analgesic nephropathy: a reassessment of the role of phenacetin and other analgesics. *Drugs* 1982; **23:** 75–149.

Effects on the skin. In a summary[1] of 77 cases of fixed drug eruption phenazone derivatives were considered to be the causative agent in 9 of the 14 cases that were severe generalised reactions.

1. Stubb S, *et al*. Fixed drug eruptions: 77 cases from 1981 to 1985. *Br J Dermatol* 1989; **120:** 583.

Hypersensitivity. Immediate allergic reactions to phenazone have been reported.[1,2] In one patient leucopenia was detected 8 weeks later.[1]

1. Kadar D, Kalow W. Acute and latent leukopenic reaction to antipyrine. *Clin Pharmacol Ther* 1980; **28:** 820–22.
2. McCrea JB, *et al*. Allergic reaction to antipyrine, a marker of hepatic enzyme activity. *DICP Ann Pharmacother* 1989; **23:** 38–40.

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

Interactions

Phenazone affects the metabolism of some other drugs and its own metabolism is affected by other drugs that increase or reduce the activity of liver enzymes.

Pharmacokinetics

Phenazone is absorbed from the gastrointestinal tract and peak plasma concentrations are obtained within 1 to 2 hours of ingestion. It is distributed throughout the body fluids with concentrations in the saliva and breast milk reaching about the same levels as those in plasma. Less than 10% is bound to plasma proteins and it has an elimination half-life of about 12 hours. Phenazone is metabolised in the liver to 3 major metabolites 3-hydroxymethylphenazone, 4-hydroxyphenazone, and norphenazone. Phenazone, 3-hydroxymethylphenazone, and glucuronidated metabolites are all excreted in the urine. A small portion may be eliminated via the bile.

Uses and Administration

Phenazone is an NSAID (p.99) and has been given orally; phenazone and caffeine citrate and phenazone salicylate have similarly been given orally as analgesics.

Solutions containing about 5% of phenazone have been used topically as ear drops in disorders such as acute otitis media (but see below).

Phenazone is used as a test for the activity of drug-metabolising enzymes in the liver.

Diagnosis and testing. A review[1] of normal plasma-phenazone pharmacokinetics, urinary metabolite disposition, and total body clearances of phenazone in the presence of cirrhosis, fatty liver, hepatitis, and cholestatis.

1. St Peter JV, Awni WM. Quantifying hepatic function in the presence of liver disease with phenazone (antipyrine) and its metabolites. *Clin Pharmacokinet* 1991; **20:** 50–65.

Otitis media. There appears to be no justification[1] for the inclusion of phenazone in topical preparations used in treating acute otitis media (p.182). It is presumably included in such preparations because it is believed to have a local anti-inflammatory and, therefore, analgesic action. It would, however, seem unlikely that phenazone would have any action on the skin of the intact tympanic membrane and, therefore, on the pain which is due primarily to the stretching and distention of the membrane.

1. Carlin WV. Is there any justification for using phenazone in a local application prescribed for the treatment of acute otitis media? *BMJ* 1987; **294:** 1333.

Preparations

USP 31: Antipyrine and Benzocaine Otic Solution; Antipyrine, Benzocaine, and Phenylephrine Hydrochloride Otic Solution.

Proprietary Preparations (details are given in Part 3)

Austral.: Erasol; ***Ger.:*** Aequiton-P†; Migrane-Kranit; Mono Migranin; ***Hong Kong:*** Tropex; ***Irl.:*** Tropex; ***Pol.:*** Antotalgin; ***S.Afr.:*** Aurone; Oto-Phen; ***Venez.:*** Otamina.

Multi-ingredient: ***Arg.:*** Aqua Lent Colirio; Bajumol†; Bideon; Cerosporin GS†; Clarisoft; Coliria; Cristalomicina; Irix; Kalopsis; Leroid†; Otalex G; Otocalmia Biotic; Otocerol; Otocuril; Otonorthia; Sincerum; Usualix; Vislus; ***Austral.:*** Auralgan; ***Austria:*** Asthma Efeum; Coffo Selt; Otalgan; Spalt†; ***Belg.:*** Hemorhinol; Otocalmine; Ouate Hemostatique; Tympalgine†; ***Braz.:*** Anestesiol†; Espasmalgon†; Osmotil†; Otovix†; ***Canad.:*** Auralgan; ***Cz.:*** Otipax; ***Denm.:*** Koffisal; ***Fr.:*** Brulex; HEC; Otipax; ***Ger.:*** Coffeemed N†; Migranin†; Otalgan; ***Hung.:*** Otipax; ***India:*** Tytin; ***Israel:*** Anaesthetic Ear Drops; Otidin; ***Ital.:*** Otalgan; Otomidone; Otopax; ***Neth.:*** Spalt N; ***Norw.:*** Antineuralgica; Fanalgin; ***NZ:*** Auralgan; Degest 2†; ***Philipp.:*** Auralgan; ***Port.:*** Otocalma†; Profrin-A†; ***Rus.:*** Otipax (Отипакс); ***S.Afr.:*** Auralyt; Aurasept; Aurone Forte; Covancaine; Ilvico; Otised; Oto-Phen Forte; Universal Earache Drops; ***Singapore:*** HEC†; Tropex; ***Spain:*** AB FE†; Epistaxol; Otalgan†; Otosedol; Pomada Heridas†; Quimpedor; Tabletas Quimpe; ***Swed.:*** Doleron†; Koffazon; ***Switz.:*** Otalgan; Otipax; Otosan; Otothricinol; Seranex sans codeine†; Spedralgin sans codeine†; ***Thai.:*** Auralgan†; ***USA:*** Allergen; Auralgan; Auroguard Otic; Auroto†; Cy-Gesic; Otocalm†; Tympagesic†; ***Venez.:*** Audocaina†; Otan; Otanol†; Otirilin; Otodon†; Otofrin†.

Phenazopyridine Hydrochloride

(BANM, USAN, rINNM)

Chloridrato de Fenazopiridina; Fenazopiridin Hidroklorür; Fenazopirydyny chlorowodorek; Hidrocloruro de fenazopiridina; NC-150; NSC-1879; Phénazopyridine, Chlorhydrate de; Phenazopyridini Hydrochloridum; W-1655. 3-Phenylazopyridine-2,6-diyldiamine hydrochloride.

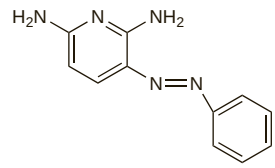
Феназопиридина Гидрохлорид

$C_{11}H_{11}N_5$,HCl = 249.7.

CAS — 94-78-0 (phenazopyridine); 136-40-3 (phenazopyridine hydrochloride).

ATC — G04BX06.

ATC Vet — QG04BX06.



(phenazopyridine)

Pharmacopoeias. In *Pol*. and *US*.

USP 31 (Phenazopyridine Hydrochloride). A light or dark red to dark violet crystalline powder. Is odourless or with a slight odour. Soluble 1 in 300 of cold water, 1 in 20 of boiling water, 1 in 59 of alcohol, 1 in 331 of chloroform, and 1 in 100 of glycerol; very slightly soluble in ether. Store in airtight containers.

Removal of stains. Phenazopyridine stains may be removed from fabric by soaking in a 0.25% solution of sodium dithionite.

Adverse Effects

Phenazopyridine hydrochloride has caused gastrointestinal adverse effects, headache, and rashes. Hepatotoxicity, haemolytic anaemia, methaemoglobinaemia, and acute renal failure have also been reported, generally associated with overdosage or with therapeutic doses in patients with renal impairment. Crystal deposits of phenazopyridine have formed in the urinary tract.

Abnormal coloration of body tissues or fluids may occur. Urine is tinged either orange or red and underclothes are apt to be stained.

Effects on the CNS. A case of aseptic meningitis, with distinct episodes of fever and confusion, was associated with the use of phenazopyridine.[1]

1. Herlihy TE. Phenazopyridine and aseptic meningitis. *Ann Intern Med* 1987; **106:** 172–3.

Overdosage. Report of a 2-year-old child who developed cyanosis and methaemoglobinaemia after ingesting at most three 200-mg tablets of phenazopyridine hydrochloride.[1]

1. Gold NA, Bithoney WG. Methemoglobinemia due to ingestion of at most three pills of pyridium in a 2-year-old: case report and review. *J Emerg Med* 2003; **25:** 143–8.

Precautions

Phenazopyridine hydrochloride is contra-indicated in patients with renal impairment or severe hepatitis and should be used with caution in those with G6PD deficiency. Treatment should be stopped if the skin or sclerae become discoloured; this may indicate accumulation as a result of impaired renal excretion. Phenazopyridine may interfere with urinalysis based on colour reactions or spectrometry.

Staining of contact lenses may occur.

Pharmacokinetics

Phenazopyridine hydrochloride is absorbed from the gastrointestinal tract. It is excreted mainly in the urine; up to 65% may be excreted as unchanged phenazopyridine and 18% as paracetamol.

Uses and Administration

Phenazopyridine is an azo dye that exerts an analgesic effect on the mucosa of the urinary tract and is used to provide symptomatic relief of pain and irritability in conditions such as cystitis and prostatitis (see p.2178 and p.2181, respectively), and urethritis (p.199). Phenazopyridine hydrochloride has been given in usual oral doses of about 200 mg three times daily after food. If given with an antibacterial for the treatment of urinary-tract infections (p.199), treatment should usually not exceed 2 days, although lower doses have been given as part of a combined preparation for at least a week.

Urinary-tract infections. There is currently no well-substantiated role for phenazopyridine in the treatment of urinary-tract infections and its adverse effects are potentially serious.[1]

1. Zelenitsky SA, Zhanel GG. Phenazopyridine in urinary tract infections. *Ann Pharmacother* 1996; **30:** 866–8.

Preparations

USP 31: Phenazopyridine Hydrochloride Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Cistalgina; ***Belg.:*** Uropyrine; ***Braz.:*** Pyridium; Pyrisept; Urologin; Urotril†; ***Canad.:*** Phenazo; Pyridium†; ***Chile:*** Nazamit; Nordox; Pyridium†; ***Hong Kong:*** CP-Pyridine; Phenadine; Pyridium; ***India:*** Pyridium; ***Indon.:*** Pyridium; Urogetix; ***Israel:*** Sedural; ***Mex.:*** Alvena; Azofur; Bioferina; Pirimir; Urezol; ***Philipp.:*** Azomir; ***Pol.:*** Nefrecil; ***S.Afr.:*** Pyridium; ***Singapore:*** Urogesic; ***Thai.:*** Ammilazo; Anazo; Phendiridine; Sumedium; ***USA:*** Azo-Standard; Baridium; Prodium; Pyridiate†; Pyridium; Re-Azo; Urogesic; ***Venez.:*** Pyridium†.

Multi-ingredient: ***Arg.:*** Bacti-Uril; Nor 2; Priper Plus; Uro-Bactrim†; Urotem Dol; ***Braz.:*** Minazol; Uro-Baxapril†; Urobiotic†; Urocrtin; Urofen†; Uropac; Uropielon; ***Chile:*** Uro-Micinovo; ***Ger.:*** Urospasmon†; ***India:*** Nephrogesic; ***Mex.:*** Azo-Uronalin; Azo-Wintomylon; Azogen; Mictasol; Nalixone; Naxilan-Plus; Pirifur; Urovec; Vodelan; ***Spain:*** Micturol Sedante; ***Turk.:*** Azo Gantrisin; Azosilin; Uriseptin; ***USA:*** Phenazopyridine Plus; Pyridium Plus; Trellium Plus; Urelief Plus; Urobiotic-250; ***Venez.:*** Azo-Mandelamine; Bacteval.