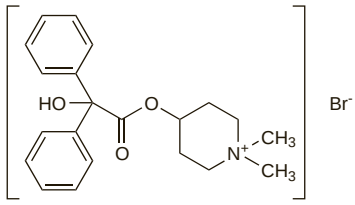
Parapenzolate Bromide *(USAN, rINN)*

Bromuro de parapenzolato; Parapenzolate, Bromure de; Parapenzolati Bromidum; Sch-3444. 4-Benziloyloxy-1,1-dimethylpiperidinium bromide.

Парапензолата Бромид

$C_{21}H_{26}BrNO_3$ = 420.3.

CAS — 5634-41-3.



Profile
Parapenzolate bromide is a quaternary ammonium antimuscarinic that has been used for the relief of visceral spasms.

Preparations
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Chile:*** Tranvagal†.

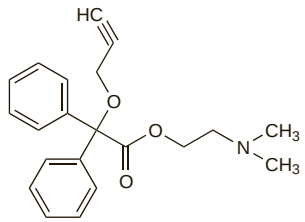
Pargeverine Hydrochloride *(rINNM)*

Pargeverina, hidrocloruro de; Pargévérine, Chlorhydrate de; Pargeverini Hydrochloridum; Propinox Hydrochloride. 2-(Dimethylamino)ethyldiphenyl(2-propynyloxy)acetate hydrochloride.

Паргеверина Гидрохлорид

$C_{21}H_{23}NO_3$,HCl = 373.9.

CAS — 13479-13-5 (pargeverine); 2765-97-1 (pargeverine hydrochloride).



(pargeverine)

Profile
Pargeverine is reported to possess antimuscarinic and smooth-muscle relaxant properties and has been used in the treatment of gastrointestinal and smooth muscle spasm.

Preparations
Proprietary Preparations (details are given in Part 3)

Arg.: Nova Paratopina; Pasmosedan†; Sertal; ***Chile:*** Bevitex; Bramedil; Pasmocalm†; Viadil; Viplan; Viproxil; ***Mex.:*** Bipasmin; Plidan; ***Port.:*** Vagopax; ***Venez.:*** Plidan.

Multi-ingredient: ***Arg.:*** Apasmo Compuesto; Binvex; Espasmo Dolex; Nova Paratropina Compositum; Pasmosedan Compuesto†; Propalgin; Sertal Compuesto; ***Chile:*** Bramedil Compuesto; Scopanil; Viadil Compuesto; Viplan Compuesto; Viproxil Compuesto; ***Mex.:*** Firac Plus; Plidan Compuesto; ***Venez.:*** Dologinex; Plidan Compuesto.

Pentaerythritol

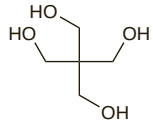
Pentaeritritol; Tetramethylolmethane. 2,2-Bis(hydroxymethyl)propane-1,3-diol.

Пентаэритритол

$C_5H_{12}O_4$ = 136.1.

CAS — 115-77-5.

ATC Vet — QA06AD14.



Profile
Pentaerythritol is an osmotic laxative used in the treatment of constipation (p.1693) in oral doses of 5 to 15 g daily.

Preparations
Proprietary Preparations (details are given in Part 3)

Fr.: Auxitrans; Hydrafuca†.

Peppermint Leaf

Black Mint; Borsosmentalevél; Hoja de Menta; Hortelã-Pimenta; Liść mięty pieprzowej; List máty peprné; Menta piperita, hoja de; Menth. Pip.; Mentha Piperita; Menthae piperitae folium; Menthe Poivrée; Menthe poivrée, feuille de; Pepparmyntblad; Peppermint; Pfefferminzblätter; Piparmintunlehti; Pipirmėčių lapai; White Mint.

Листья Мяты Перечной

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*

Ph. Eur. 6.2 (Peppermint Leaf). The whole or cut dried leaves of *Mentha* × *piperita*, containing not less than 1.2% v/w of essential oil if whole, or not less than 0.9% v/w if cut. It has a characteristic and penetrating odour and a characteristic aromatic taste. Protect from light.

USNF 26 (Peppermint). The dried leaf and flowering top of *Mentha piperita* (Labiatae). It has an aromatic, characteristic odour and a pungent taste, and produces a cooling sensation in the mouth.

Peppermint Oil

Borsosmentaolaj; Essence de Menthe Poivrée; Essência de Hortelã-Pimenta; Menta piperita, aceite esencial de; Menthae piperitae aetheroleum; Menthae Piperitae Etheroleum; Menthe poivrée, huile essentielle de; Nane Yağı; Ol. Menth. Pip.; Olejek miętowy; Oleum Menthae Piperitae; Pepparmyntolja; Pfefferminzöl; Piparminttuöljy; Pipirmėčių eterinis aliejus; Silice máty peprné.

Масло Мяты Перечной

CAS — 8006-90-4.

Pharmacopoeias. In *Eur.* (see p.vii). Also in *USNF.*

Ph. Eur. 6.2 (Peppermint Oil). It is obtained by steam distillation from the fresh overground parts of the flowering plant of *Mentha* × *piperita*. It contains 30.0 to 55.0% menthol, 14.0 to 32.0% menthone, and 2.8 to 10.0% menthyl acetate, 3.5 to 14.0% cineole, 1.5 to 10.0% isomenthone, 1.0 to 9.0% menthofuran, 1.0 to 5.0% limonene, not more than 4.0% pulegone, and not more than 1.0% carvone; the ratio of eucalyptol content to limonene content is greater than two.
It is a colourless, pale yellow, or pale greenish-yellow liquid with a characteristic odour and taste followed by a sensation of cold. Miscible with alcohol and with dichloromethane. Store in well-filled, airtight containers. Protect from light and heat.

USNF 26 (Peppermint Oil). The volatile oil distilled with steam from the fresh overground parts of the flowering plant *Mentha piperita* (Labiatae), rectified by distillation, and neither partially nor wholly dementholised. It yields not less than 5% of esters calculated as menthyl acetate and not less than 50% of total menthol, free and as esters.
It is a colourless or pale yellow liquid with a strong, penetrating, characteristic odour and a pungent taste, followed by a sensation of cold when air is drawn into the mouth. Soluble 1 in 3 of alcohol (70%) with not more than slight opalescence. Store in airtight containers at a temperature not exceeding 40°.

Storage. The Pharmaceutical Society of Great Britain's Department of Pharmaceutical Sciences found that PVC bottles softened and distorted fairly rapidly in the presence of peppermint oil, which should not be stored or dispensed in such bottles.[1]

1. Department of Pharmaceutical Sciences of the Pharmaceutical Society of Great Britain. Plastic medicine bottles of rigid PVC. *Pharm J* 1973; **210:** 100.

Adverse Effects and Precautions
Peppermint oil can be irritant and may rarely cause hypersensitivity reactions. Reported reactions include erythematous skin rash, headache, bradycardia, muscle tremor, and ataxia. Heartburn has also been reported.

Effects on the cardiovascular system. Idiopathic atrial fibrillation occurred in 2 patients addicted to 'peppermints'. Normal rhythm was restored when peppermint-sucking ceased.[1]

1. Thomas JG. Peppermint fibrillation. *Lancet* 1962; **i:** 222.

Hypersensitivity. Exacerbation of asthma, with wheezing and dyspnoea, was associated with the use of paste-based toothpastes containing peppermint or wintergreen as a flavouring.[1]

1. Spurlock BW, Dailey TM. Shortness of (fresh) breath—toothpaste-induced bronchospasm. *N Engl J Med* 1990; **323:** 1845–6.

Interactions
Adverse effects may be more likely if peppermint oil is taken with alcohol. Enteric-coated capsules containing peppermint oil should not be taken immediately after food or with antacids. There is some evidence that peppermint oil can inhibit the cytochrome P450 isoenzyme CYP3A4, and may affect the clearance of drugs whose metabolism is mediated by this enzyme.

◊ References.

1. Dresser GK, *et al.* Evaluation of peppermint oil and ascorbyl palmitate as inhibitors of cytochrome P4503A4 activity in vitro and in vivo. *Clin Pharmacol Ther* 2002; **72:** 247–55.

Uses and Administration
Peppermint oil is an aromatic carminative that relaxes gastrointestinal smooth muscle and relieves flatulence and colic. Enteric-coated capsules containing peppermint oil are used for the relief of symptoms of the irritable bowel syndrome or gastrointestinal spasm secondary to other disorders. Usual oral doses in adults and adolescents from the age of 15 years are 0.2 mL three times daily, (increased to 0.4 mL three times daily if necessary) for up to 2 to 3 months. The capsules should be taken half to one hour before food and swallowed whole, not chewed.

Peppermint oil is used as a flavour and with other volatile agents in preparations for respiratory-tract disorders. It is also used in aromatherapy.

Peppermint leaf, the source of the oil, has also been used for its carminative and flavouring properties.

Gastrointestinal disorders. Menthol (p.2340), the major constituent of peppermint oil, has properties similar to those of calcium-channel blockers on smooth muscle such as that in the human gut.[1] Reviews[2,3] of the use of peppermint oil in irritable bowel syndrome (p.1699) concluded that there was some evidence of its benefit.

The relaxant effect of peppermint oil on the gastrointestinal tract has been used to reduce spasm during endoscopy by giving solubilised peppermint oil directly into the lumen, through the accessory channel of the endoscope. It has been described as effective during colonoscopy[4] and may be more effective than intramuscular hyoscine butylbromide during upper gastrointestinal endoscopy.[5] Addition of peppermint oil to barium enema has also been tried and appears to reduce spasm[6,7] and the need for intravenous antispasmodics.[6]

1. Grigoleit H-G, Grigoleit P. Pharmacology and preclinical pharmacokinetics of peppermint oil. *Phytomedicine* 2005; **12:** 612–16.
2. Pittler MH, Ernst E. Peppermint oil for irritable bowel syndrome: a critical review and metaanalysis. *Am J Gastroenterol* 1998; **93:** 1131–5.
3. Grigoleit H-G, Grigoleit P. Peppermint oil in irritable bowel syndrome. *Phytomedicine* 2005; **12:** 601–6.
4. Asao T, *et al.* An easy method for the intraluminal administration of peppermint oil before colonoscopy and its effectiveness in reducing colonic spasm. *Gastrointest Endosc* 2001; **53:** 172–7.
5. Hiki N, *et al.* Peppermint oil reduces gastric spasm during upper endoscopy: a randomized, double-blind, double-dummy controlled trial. *Gastrointest Endosc* 2003; **57:** 475–82.
6. Sparks MJW, *et al.* Does peppermint oil relieve spasm during barium enema? *Br J Radiol* 1995; **68:** 841–3.
7. Asao T, *et al.* Spasmolytic effect of peppermint oil in barium during double-contrast barium enema compared with Buscopan. *Clin Radiol* 2003; **58:** 301–5.

Preparations
BP 2008: Concentrated Peppermint Emulsion; Gastro-resistant Peppermint Oil Capsules; Peppermint Spirit;
USNF 26: Peppermint Water;
USP 31: Peppermint Spirit.

Proprietary Preparations (details are given in Part 3)

Austral.: Mintec; ***Austria:*** Colpermin; ***Cz.:*** China-Oel†; Colpermin; Gallenteе†; Ki-Min-To†; Mata Pieporna†; Matovy; Nat Maty Peprne; ***Fr.:*** Locabiotal; ***Ger.:*** Chiana†; China-Oel†; Euminz; Inspirol Heilpflanzenol; Medacalm; Mentacur†; spasmo gallo sanol N; Wildkrauterol special K; ***Gr.:*** Colpermin; ***Hong Kong:*** Colpermin; ***Irl.:*** Colpermin; ***Israel:*** China Oel; Colpermin; Po Sum On Medicated Oil; ***Ital.:*** Carmint; Mintoil; ***Mex.:*** Colpermin†; ***NZ:*** Mintec; ***Port.:*** Colomínte; ***S.Afr.:*** Pepermentdruppels; ***Singapore:*** Colpermin; ***Switz.:*** Chiana-Oel; Colpermin; ***Thai.:*** Colpermin; ***Turk.:*** China Oel; Colpermin; ***UK:*** Colpermin; Equilon Herbal; Mintec; Obbekjaers.

Multi-ingredient: numerous preparations are listed in Part 3.

Phenamazide Hydrochloride

Fenamazida, hidrocloruro de; Phenamacide Hydrochloride. (±)-α-Aminobenzeneacetic acid 3-methylbutyl ester hydrochloride.

$C_{13}H_{19}NO_2$,HCl = 257.8.

CAS — 84580-27-8 (phenamazide); 31031-74-0 (phenamazide hydrochloride).

Profile
Phenamazide is an antimuscarinic with actions similar to those of atropine (p.1219). It has been used as the hydrochloride in the treatment of visceral spasms.

Preparations
Proprietary Preparations (details are given in Part 3)

Ger.: Aklonin†.

Phenolphthalein *(BAN, rINN)*

Dihydroxyphthalophenone; Fenolftalein; Fenolftaleína; Fenolftaleinas; Fenoliftaleiini; Fenoloftaleina; Phénolphtaléine; Phenolphtaleinum; Phenolphthaleinum. 3,3-Bis(4-hydroxyphenyl)-phthalide.

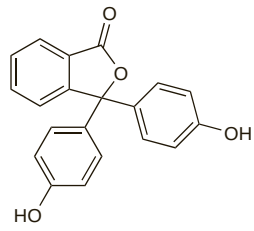
Фенолфталеин

$C_{20}H_{14}O_4$ = 318.3.

CAS — 77-09-8.

ATC — A06AB04.

ATC Vet — QA06AB04.



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

Ph. Eur. 6.2 (Phenolphthalein). A white or almost white powder. Practically insoluble in water; soluble in alcohol. Protect from light.

Adverse Effects and Precautions

As for Bisacodyl, p.1710. Hypersensitivity reactions, usually as skin rashes or eruptions, have occurred with phenolphthalein. Phenolphthalein may cause pink discoloration of alkaline urine.

Tumours have occurred in *rats* and *mice* given very high doses of phenolphthalein; there does not appear to be evidence of carcinogenicity in humans, but phenolphthalein-containing products have been withdrawn in many countries because of concerns about long-term safety.

Effects on the skin. Reports of skin reactions associated with phenolphthalein include fixed drug eruptions,[1,2] erythema multiforme reactions,[1,3] and toxic epidermal necrolysis.[4,5]

1. Baer RL, Harris H. Types of cutaneous reactions to drugs. *JAMA* 1967; **202:** 710–13.
2. Savin JA. Current causes of fixed drug eruptions. *Br J Dermatol* 1970; **83:** 546–9.
3. Shelley WB, *et al.* Demonstration of intercellular immunofluorescence and epidermal hysteresis in bullous fixed drug eruption due to phenolphthalein. *Br J Dermatol* 1972; **86:** 118–25.
4. Kar PK, *et al.* Toxic epidermal necrolysis in a patient induced by phenolphthalein. *J Indian Med Assoc* 1986; **84:** 189–93.
5. Artymowicz RJ, *et al.* Phenolphthalein-induced toxic epidermal necrolysis. *Ann Pharmacother* 1997; **31:** 1157–9.

Overdosage. The most likely consequence of phenolphthalein overdosage is excessive purgation, which may require fluid and electrolyte replacement. However, a possible association with acute pancreatitis occurred in a 34-year-old man who inadvertently ingested phenolphthalein 2 g. There was complete recovery with no sequelae from the pancreatitis.[1] Widespread organ failure with disseminated intravascular coagulation, massive liver damage, pulmonary oedema, renal failure, and myocardial damage in a second patient[2] were attributed to self-poisoning with an unknown quantity of phenolphthalein-containing laxative, although the diagnosis was problematic. The patient died despite intensive support.

1. Lambrianides AL, Rosin RD. Acute pancreatitis complicating excessive intake of phenolphthalein. *Postgrad Med J* 1984; **60:** 491–2.
2. Sidhu PS, *et al.* Fatal phenolphthalein poisoning with fulminant hepatic failure and disseminated intravascular coagulation. *Hum Toxicol* 1989; **8:** 381–4.

Pharmacokinetics

Up to 15% of phenolphthalein given orally is subsequently excreted in the urine. Enterohepatic circulation occurs and the glucuronide is excreted in the bile. Elimination may take several days.

Uses and Administration

Phenolphthalein is a diphenylmethane stimulant laxative that has been used for the treatment of constipation (p.1693) and for bowel evacuation before investigational procedures or surgery. It has been withdrawn in many countries because of concern over its carcinogenic potential after reports of tumours in *rodents*.

It has been given in pills or tablets, and as an emulsion with liquid paraffin. Yellow phenolphthalein, an impure form, has been used similarly.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Fructines; ***Chile:*** Felaxen†; ***Cz.:*** Confetto Falqui†; ***Israel:*** Easylax; ***S.Afr.:*** Brooklax; Dr Mackenzies Veinoids; Laxador; Laxene; Laxicaps P†; SB Strong-Lax; Super-Tabs; Surge; ***Singapore:*** Regulim†; ***Switz.:*** Reguletts; ***Thai.:*** Purmolax†; Regulim; ***Turk.:*** Alin; Laksafenol; ***Venez.:*** Agarolax†.

Multi-ingredient: ***Arg.:*** Cascara Sagrada Bouzen†; Cascara Sagrada Puler†; Genolaxante; Veracolate; ***Austral.:*** Ford Pills; ***Austria:*** Waldheim Abfuhrdragees forte; ***Belg.:*** Grains de Vals; ***Braz.:*** Emagrex†; Fenogar†; Manolio†; Obesidex†; Obesifran†; Prisoventril†; ***Chile:*** Agarol; Bulgarolax; Fenokomp 39; Fenolftaleina Compuesta†; Oblax A-1-1; ***Ger.:*** Vencipon N†; ***Hung.:*** Artin†; Bilagit†; ***India:*** Agarol†; Jetomisol-P; ***Indon.:*** Laxadine; ***Israel:*** Laxative; Laxative Comp; ***Port.:*** Byl†; Caroid†; ***S.Afr.:*** Brooklax Pills; Redupon†; SB 3 Triple Action Pills; Veracolate†; ***Spain:*** Laxante Bescansa Aloico; Mahiou†; ***Switz.:*** Paragar; ***Thai.:*** Emulax; Veracolate; Zenda†; ***Turk.:*** Karboseptin; Musilaks; ***UK:*** Fam-Lax; ***USA:*** Agoral; Doxidan†; ***Venez.:*** Agarol†.

Pipenzolate Bromide *(BAN, rINN)*

Bromuro de pipenzolato; Pipenzolat Bromür; Pipenzolate, Bromure de; Pipenzolate Methylbromide; Pipenzolati Bromidum. 3-Benziloyloxy-1-ethyl-1-methylpiperidinium bromide.

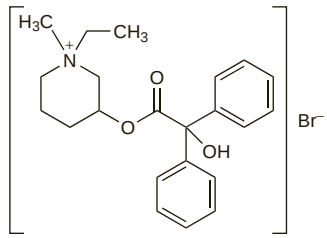
Пипензолата Бромид

$C_{22}H_{28}BrNO_3$ = 434.4.

CAS — 13473-38-6 (pipenzolate); 125-51-9 (pipenzolate bromide).

ATC — A03AB14.

ATC Vet — QA03AB14.



Profile

Pipenzolate bromide is a quaternary ammonium antimuscarinic with peripheral actions similar to those of atropine (p.1219). It has been used as an adjunct in the treatment of gastrointestinal disorders characterised by smooth muscle spasm.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Ila-med m; ***Mex.:*** Expal; Pipzen; ***Turk.:*** Piptalin.

Multi-ingredient: ***Chile:*** Baldmin; Gasorbol; Sinpasmon; ***Indon.:*** Piptal; ***Mex.:*** Espasal; Espasin†; Expal Compuesto; Finprob; ***Turk.:*** Asilon; Libkol; ***UAE:*** Alinal†.

Piperidolate Hydrochloride *(BANM, rINNM)*

Hidrocloruro de piperidolato; Pipéridolate, Chlorhydrate de; Piperidolati Hydrochloridum. 1-Ethyl-3-piperidyl diphenylacetate hydrochloride.

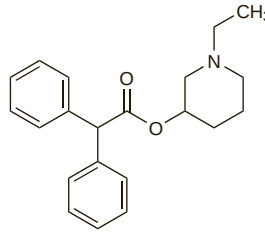
Пиперидолата Гидрохлорид

$C_{21}H_{25}NO_2$,HCl = 359.9.

CAS — 82-98-4 (piperidolate); 129-77-1 (piperidolate hydrochloride).

ATC — A03AA30.

ATC Vet — QA03AA30.



(piperidolate)

Profile

Piperidolate hydrochloride is a tertiary amine antimuscarinic with effects similar to those of atropine (p.1219). It has been given in the symptomatic treatment of smooth muscle spasm associated with gastrointestinal disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Mex.: Dactil OB.

Multi-ingredient: ***Braz.:*** Dactil OB.

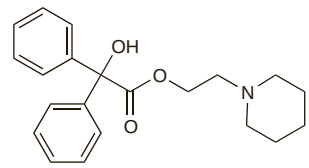
Pipethanate Ethobromide *(rINNM)*

Ethylpipethanate Bromide; Etobromuro de pipetanato; Piperilate Ethobromide; Pipéthanate, Ethobromure de; Pipethanati Ethobromidum. 1-(2-Benziloyloxyethyl)-1-ethylpiperidinium bromide.

Пипетаната Этобромид

$C_{23}H_{30}BrNO_3$ = 448.4.

CAS — 4546-39-8 (pipethanate); 23182-46-9 (pipethanate ethobromide).



(pipethanate)

Profile

Pipethanate ethobromide is an antimuscarinic with actions similar to those of atropine (p.1219). It has been used in the symptomatic treatment of visceral spasms in oral doses of up to 160 mg daily in divided doses. Pipethanate ethobromide has also been given intramuscularly or intravenously in doses of 10 to 20 mg daily and rectally in doses of 60 or 120 mg daily.

Preparations

Proprietary Preparations (details are given in Part 3)
Chile: Nospasmin; ***Ital.:*** Spasmodil; ***Jpn:*** Panpurol†.

Multi-ingredient: ***Chile:*** Nospasmin Compuesto.

Pirenzepine Hydrochloride *(BANM, USAN, rINNM)*

Hidrocloruro de pirenzepina; LS-519 (pirenzepine); LS-519-Cl2; Pirentsepiinidihydrokloridimonohydraatti; Pirenzepin-dihidrokloridmonohidrát; Pirenzepin-dihydrochlorid monohydrát; Pirenzepindihydrokloridmonohydrat; Pirenzépine, Chlorhydrate de; Pirenzépine (dichlorhydrate de) monohydraté; Pirenzepini dihydrochloridum monohydricum; Pirenzepini Hydrochloridum; Pirenzepino dihidrochloridas monohidratas. 5,11-Dihydro-11-(4-methylpiperazin-1-ylacetyl)pyrido[2,3-*b*][1,4]benzodiazepin-6-one dihydrochloride monohydrate.

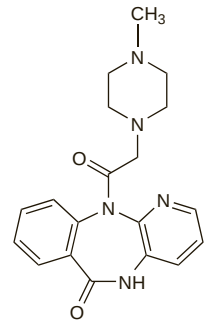
Пирензепина Гидрохлорид

$C_{19}H_{21}N_5O_2$,2HCl,H_2O = 442.3.

CAS — 28797-61-7 (pirenzepine); 29868-97-1 (pirenzepine hydrochloride).

ATC — A02BX03.

ATC Vet — QA02BX03.



(pirenzepine)

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

Ph. Eur. 6.2 (Pirenzepine Dihydrochloride Monohydrate; Pirenzepine Hydrochloride BP 2008). A white or yellowish crystalline powder. Freely soluble in water; very slightly soluble in dehydrated alcohol; practically insoluble in dichloromethane; slightly soluble in methyl alcohol. A 10% solution in water has a pH of 1.0 to 2.0. Protect from light.

Adverse Effects and Precautions

Dry mouth and blurred vision have been reported but the risk of antimuscarinic effects (see Atropine Sulfate, p.1219) may be reduced. Pirenzepine should be used with caution in patients with renal impairment, particularly those with end-stage renal failure.

Effects on the blood. Thrombocytopenia in one patient and agranulocytosis in another was probably associated with the use of pirenzepine.[1]

1. Stricker BHC, *et al.* Blood disorders associated with pirenzepine. *BMJ* 1986; **293:** 1074.

Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220).

Pharmacokinetics

Pirenzepine is absorbed from the gastrointestinal tract but the bioavailability is reported to be only about 20 to 30%, and is decreased to about 10 to 20% when taken with food. Very little pirenzepine is metabolised. About 10% of an oral dose is excreted unchanged in the urine, the remainder being excreted in the faeces.