In **hypertension** metoprolol tartrate is usually given in an initial oral dose of 100 mg daily, as a single dose or in two divided doses. The dose may be increased weekly, according to response; the usual maintenance dose is 100 to 200 mg daily, but up to 400 mg daily may be given.

The usual oral dose for **angina pectoris** is 50 to 100 mg two or three times daily.

In the treatment of **cardiac arrhythmias** the usual oral dose is 50 mg two or three times daily, increased if necessary up to 300 mg daily in divided doses.

For the emergency treatment of cardiac arrhythmias metoprolol tartrate may be given intravenously in an initial dose of up to 5 mg, at a rate of 1 to 2 mg/minute; this may be repeated, if necessary, at intervals of 5 minutes to a total dose of 10 to 15 mg. When acute arrhythmias have been controlled, maintenance therapy may be started 4 to 6 hours after intravenous therapy, at oral doses not exceeding 50 mg three times daily.

Arrhythmias may be prevented on induction of anaesthesia, or controlled during anaesthesia, by the slow intravenous injection of 2 to 4 mg; further injections of 2 mg may be repeated as necessary to a maximum total dose of 10 mg.

Metoprolol is also used as an adjunct in the early management of acute **myocardial infarction.** Treatment should be given within 12 hours of the onset of chest pain; metoprolol tartrate 5 mg should be given intravenously at 2-minute intervals to a total of 15 mg, where tolerated. After 15 minutes, in patients who have received the full intravenous dose, oral treatment should be started; 50 mg is given every 6 hours for 2 days. In patients who have failed to tolerate the full intravenous dose a reduced oral dose should be given as, and when, their condition permits. Subsequent maintenance dosage is 100 mg given twice daily by mouth. In patients who did not receive metoprolol by intravenous injection as part of the early management of myocardial infarction, metoprolol may be started once the clinical condition of the patient stabilises, in a dose of 200 mg daily in 2 or 4 divided doses.

In the management of stable, symptomatic **heart failure** metoprolol succinate may be given as an oral modified-release preparation. The initial dose is the equivalent of metoprolol tartrate 12.5 to 25 mg once daily, increased as tolerated, at intervals of 2 weeks, with a target dose of 200 mg once daily.

As an adjunct in the treatment of **hyperthyroidism** metoprolol tartrate may be given in oral doses of 50 mg four times daily. Doses of 100 to 200 mg are given daily in divided doses for **migraine** prophylaxis.

◊ General references.

1. Plosker GL, Clissold SP. Controlled release metoprolol formulations: a review of their pharmacodynamic and pharmacokinetic properties, and therapeutic use in hypertension and ischaemic heart disease. *Drugs* 1992; **43:** 382–414.
2. Prakash A, Markham A. Metoprolol: a review of its use in chronic heart failure. *Drugs* 2000; **60:** 647–78.
3. Tangeman HJ, Patterson JH. Extended-release metoprolol succinate in chronic heart failure. *Ann Pharmacother* 2003; **37:** 701–10.

Administration in children. Metoprolol has been used in children, although experience is limited. A study[1] in children aged 6 to 16 years with hypertension found that modified-release metoprolol succinate was well tolerated in doses of up to the equivalent of metoprolol tartrate 2 mg/kg daily, although efficacy was not established. US licensed product information nevertheless allows the use of oral doses of metoprolol succinate once daily in children aged 6 to 16 years; the initial dose is the equivalent of metoprolol tartrate 1 mg/kg daily (maximum 50 mg), adjusted according to response to a maximum of 2 mg/kg (not more than 200 mg) daily.

The *BNFC* recommends that for hypertension children aged 1 month to 12 years may be given standard formulations of metoprolol tartrate in an initial dose of 1 mg/kg twice daily orally, increased if necessary to a maximum dose of 8 mg/kg daily in 2 to 4 divided doses. Children over 12 years may be given the adult dose (see above).

1. Batisky DL, *et al.* Efficacy and safety of extended release metoprolol succinate in hypertensive children 6 to 16 years of age: a clinical trial experience. *J Pediatr* 2007; **150:** 134–9.

Preparations

BP 2008: Metoprolol Injection; Metoprolol Tartrate Tablets;
USP 31: Metoprolol Succinate Extended-Release Tablets; Metoprolol Tartrate and Hydrochlorothiazide Tablets; Metoprolol Tartrate Injection; Metoprolol Tartrate Oral Solution; Metoprolol Tartrate Oral Suspension; Metoprolol Tartrate Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Beloc†; Belozok; Lopresor; ***Austral.:*** Betaloc; Lopresor; Metohexal; Metolol†; Metrol; Minax; Toprol; ***Austria:*** Beloc; Lanoc; Metohexal; MetoMed; Metopal†; Metostadol; Metotyrol†; Seloken; ***Belg.:*** Lopresor; Selo-Zok; Seloken; Slow-Lopresor; ***Braz.:*** Lopressor; Selo-Zok; Seloken; ***Canad.:*** Betaloc; Lopresor; Novo-Metoprol; Nu-Metop; ***Cz.:*** Betaloc; Corvitol†; Egilok; Emzok; Metohexal†; Vasocardin; ***Denm.:*** Dura-Zok†; Mepronet; Metocar; Metozoc†; Selo-Zok; Seloken; ***Fin.:*** Metblock†; Metoprolin; Metozoc†; Seloken; Seloken ZOC; Selopral; Spesicor; ***Fr.:*** Lopressor; Seloken; Selozok; ***Ger.:*** Azumetop†; Beloc; Beloc-Zok; Jeprolol; Jutabloc; Lopresor; Meprolol; Meto; Meto-Succinat; Meto-Tablinen; Metobeta; Metodoc; Metodura; Metohexal; Metok†; Metomerck†; Metoprogamma; Prelis; Sigaprolol†; ***Gr.:*** Lopresor; ***Hong Kong:*** Betaloc; CP-Metolol; Denex†; Minax; Novo-Metoprol; Sefloc; ***Hung.:*** Betaloc; Egilok; Huma-Metoprol†; Ritmetol†; ***India:*** Betaloc; Metolar; Revelol; Selopres; ***Indon.:*** Cardiosel; Lopresor; Loprolol; Seloken; ***Irl.:*** Betaloc; Lopresor; Metocor; Metop; ***Israel:*** Lopresor; Metopress†; Neobloc; ***Ital.:*** Lopresor; Seloken; ***Jpn:*** Seloken; ***Malaysia:*** Beatrolol†; Betaloc; Betatab†; Denex; ***Mex.:*** Bioprol; Eurolol; Futaline; Kenaprol; Lopresor; Metopresol; Proken M†; Prolaken; Promiced; Prontol; Ritmolol; Selectadril†; Seloken; Sermetrol; Synadrenol†; ***Neth.:*** Lopresor; Selokeen; ***Norw.:*** Metozoc†; Selo-Zok; Seloken; ***NZ:*** Betaloc; Lopresor; Slow-Lopresor; ***Philipp.:*** Betaloc; Betaryx; Betazok; Cardiosel; Cardiostat; Cardiotab; Metocare; Metoprim; Metospec; Metostad; Montebloc; Neobloc; Prolohex; Valvexin; ***Pol.:*** Betaloc; Beto; Metocard; Metohexal; ***Port.:*** Lopresor; ***Rus.:*** Betaloc ZOK (Беталок ЗОК); Corvitol (Корвадил); Egilok (Эгилок); Emzok (Эмзок); Metocard (Метокард); Serdol (Сердол); Vasocardin (Вазокардин); ***S.Afr.:*** Lopresor; ***Singapore:*** Betaloc; Denex; ***Spain:*** Beloken; Lopresor; ***Swed.:*** Seloken; Seloken ZOC; ***Switz.:*** Beloc; Beloc COR†; Beloc-Zok; Lopresor; Metopress; ***Thai.:*** Betaloc; Cardeloc; Cardoxone; Denex†; Melol; Metoblock; Metolol; Minax; Sefloc; ***Turk.:*** Beloc; Lopresor; Problok; ***UK:*** Betaloc; Lopresor; ***USA:*** Lopressor; Toprol; ***Venez.:*** Lopresor.

Multi-ingredient: ***Arg.:*** Diubeloc†; ***Austria:*** Beloc comp; Metoprolol compositum; Seloken retard Plus; Triloc; ***Belg.:*** Logimat; Logroton; Selozide; Zok-Zid; ***Braz.:*** Selopress; ***Cz.:*** Logimax†; ***Denm.:*** Logimax; Zok-Zid; ***Fin.:*** Logimax; Selocomp ZOC; Seloken ZOC/ASA†; ***Fr.:*** Logimax; Logroton; ***Ger.:*** Azumetop HCT†; Belnif; Beloc-Zok comp; Meprolol Comp; Meto comp†; Meto-Isis comp†; meto-thiazid†; Metobeta comp; Metodura comp; Metohexal comp; Metoprolol comp; Metostad Comp; Mobloc; Prelis comp; Treloc; ***Gr.:*** Logimax; ***Hong Kong:*** Betaloc Comp; CP-Metolol Co; Logimax; ***Hung.:*** Logimax; ***India:*** Metolar-H; ***Irl.:*** Co-Betaloc; ***Israel:*** Logimax; ***Ital.:*** Igroton-Lopresor; Selozide†; ***Malaysia:*** Logroton; ***Mex.:*** Logimax; Selopres; ***Neth.:*** Logimax; Selokomb; ***Philipp.:*** Betazide; Logimax; ***Rus.:*** Logimax (Логимакс); ***Spain:*** Higrotensin; Logimax; Selopresin†; ***Swed.:*** Logimax; Seloken ZOC/ASA†; ***Switz.:*** Logimax; Logroton; ***UK:*** Co-Betaloc†; ***USA:*** Lopressor HCT.

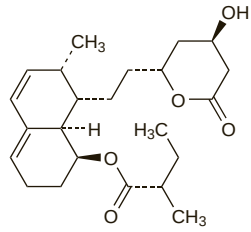
Mevastatin *(rINN)*

Compactin; CS-500; Mevastatina; Mévastatine; Mevastatinum; ML-236B. (1*S*,7*S*,8*S*,8a*R*)-1,2,3,7,8,8a-Hexahydro-7-methyl-8-{2-[(2*R*,4*R*)-tetrahydro-4-hydroxy-6-oxo-2*H*-pyran-2-yl]ethyl}-1-naphthyl (*S*)-2-methylbutyrate.

Мевастатин

$C_{23}H_{34}O_5$ = 390.5.

CAS — 73573-88-3.



Profile

Mevastatin is a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor (or statin) (see Simvastatin, p.1390) that has been isolated from *Penicillium citrinum*. It is a lipid regulating drug but is no longer used in clinical practice because of reports of toxicity in *animals*.

Mexiletine Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de mexiletina; Kö-1173; Meksiletiinihydrokloridi; Meksiletin Hidroklorür; Meksiletino hidrochloridas; Mexilétine, chlorhydrate de; Mexiletin-hidroklorid; Mexiletin-hydrochlorid; Mexiletinhydroklorid; Mexiletini hydrochloridum. 1-Methyl-2-(2,6-xylyloxy)ethylamine hydrochloride.

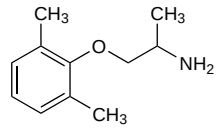
Мексилетина Гидрохлорид

$C_{11}H_{17}NO,HCl$ = 215.7.

CAS — 31828-71-4 (mexiletine); 5370-01-4 (mexiletine hydrochloride).

ATC — C01BB02.

ATC Vet — QC01BB02.



(mexiletine)

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Jpn*, and *US.*
Ph. Eur. 6.2 (Mexiletine Hydrochloride). A white or almost white, crystalline powder. It exhibits polymorphism. Freely soluble in water and in methyl alcohol; sparingly soluble in dichloromethane. A 10% solution in water has a pH of 4.0 to 5.5.
USP 31 (Mexiletine Hydrochloride). A white powder. Freely soluble in water and in dehydrated alcohol; practically insoluble in ether; slightly soluble in acetonitrile. A 10% solution in water has a pH of between 3.5 and 5.5. Store in airtight containers.

Adverse Effects and Treatment

Mexiletine has a narrow therapeutic ratio; many adverse effects of mexiletine are dose-related and will respond to dosage reduction but may be severe enough to force mexiletine to be stopped and symptomatic and supportive therapy to be given. Toxicity is common with oral or parenteral loading doses when plasma concentrations are high.

The most common adverse effects involve the gastrointestinal tract and CNS. Effects on the gastrointestinal tract include nausea, vomiting, constipation, and diarrhoea; oesophageal ulceration has also been reported. Effects on the nervous system include tremor, confusion, lightheadedness, dizziness, blurred vision and other visual disturbances, sleep disturbances, and speech difficulties. The most frequent cardiovascular effects are hypotension, sinus bradycardia, heart block and AV dissociation, and atrial fibrillation. As with other antiarrhythmics mexiletine may exacerbate arrhythmias. Other adverse effects that have been reported include skin rashes, abnormal liver function tests, thrombocytopenia, positive antinuclear factor titres, and convulsions. The Stevens-Johnson syndrome has been reported rarely.

Incidence of adverse effects. In a study involving 100 patients with ventricular arrhythmias, mexiletine had to be stopped in 49 patients because of intolerable adverse effects.[1] The most common of these affected the gastrointestinal system (27%) and included nausea (10%), vomiting (6%), heartburn (6%), and oesophageal spasm (3%). Intolerable effects on the CNS occurred in 10% of patients and these were most commonly tremor (4%), ataxia (2%), dyskinesia (1%), and tinnitus (1%). When mexiletine was used with another antiarrhythmic, the incidence of intolerable effects was 56%.

Tolerable adverse effects with mexiletine alone were transient and dose-dependent and occurred in 18% of patients. They most often affected the gastrointestinal tract. No irreversible adverse effects were reported and no proarrhythmic effects were seen.

1. Kerin NZ, *et al.* Mexiletine: long-term efficacy and side effects in patients with chronic drug-resistant potentially lethal ventricular arrhythmias. *Arch Intern Med* 1990; **150:** 381–4.

Effects on the lungs. Pulmonary fibrosis has been reported in an elderly patient receiving mexiletine; the manufacturer was aware of 3 other cases.[1]

1. Bero CJ, Rihn TL. Possible association of pulmonary fibrosis with mexiletine. *DICP Ann Pharmacother* 1991; **25:** 1329–31.

Precautions

Mexiletine is contra-indicated in cardiogenic shock and in second- or third-degree AV block (unless the patient has a pacemaker). It should be used with caution in patients with sinus node dysfunction, other conduction disorders, bradycardia, hypotension, heart failure, or hepatic impairment. ECG and blood pressure monitoring should be carried out during treatment.

Absorption of oral mexiletine may be delayed in situations where gastric emptying is slowed, such as acute myocardial infarction.

Breast feeding. Mexiletine is distributed into human breast milk in higher concentrations than in maternal serum. A woman[1] given 200 mg of mexiletine three times daily during the last trimester of pregnancy (see below), went on to breast feed the infant. Concentrations of mexiletine in the maternal milk and serum were found to be 0.6 and 0.3 micrograms/mL respectively on the second day postpartum, and 0.8 and 0.7 micrograms/mL

respectively after 6 weeks. This represented a milk to serum ratio of 2.0 and 1.1 respectively. However, mexiletine was undetectable in the infant's serum on both occasions and no adverse effects were seen. In another report[2] a woman taking a similar dose of mexiletine for the last 5 months of her pregnancy also breast fed her infant. In samples of maternal milk and blood collected between the second and fifth day postpartum the milk to plasma ratio varied between 0.78 and 1.89 with a mean of 1.45. It was considered unlikely that the infant would ingest more than 1.25 mg of mexiletine in any 24-hour period, and this amount was not thought to be enough to cause adverse effects. Failure to feed was noted[3] in the first 17 days in an infant whose mother was taking 750 mg daily of mexiletine and 50 mg daily of atenolol. After maternal education and formula supplementation an acceptable growth curve was established. Breast feeding continued until the infant was 3 months old, and no adverse effects were seen at 10 months. The American Academy of Pediatrics[4] therefore considers that mexiletine is usually compatible with breast feeding.

1. Timmis AD, *et al*. Mexiletine for control of ventricular dysrhythmias in pregnancy. *Lancet* 1980; **ii:** 647–8.
2. Lewis AM, *et al.* Mexiletine in human blood and breast milk. *Postgrad Med J* 1981; **57:** 546–7.
3. Lownes HE, Ives TJ. Mexiletine use in pregnancy and lactation. *Am J Obstet Gynecol* 1987; **157:** 446–7.
4. 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 10/07/07)

Pregnancy. Mexiletine crosses the placenta but there have been several reports of its use in pregnant women with no apparent long-term effects on the infants. A normal infant was born to a woman given mexiletine with propranolol for the control of ventricular tachycardia during the third trimester of pregnancy.[1] During the first 6 hours after delivery the infant had a heart rate of only 90 beats/minute, probably due to the propranolol; it was normal thereafter. At delivery the serum concentration of mexiletine in mother and infant was the same. A woman[2] who received mexiletine and atenolol throughout pregnancy also delivered a normal infant; failure to feed was noted at 17 days but at 10 months no adverse effects were seen. In another case[3] where the mother took mexiletine throughout pregnancy, the infant had a low Apgar score at 1 minute and hypoglycaemia was also noted, but the relationship to mexiletine was unclear; cord and maternal blood concentrations at the time of delivery were 400 nanograms/mL and 600 nanograms/mL, respectively.

1. Timmis AD, *et al*. Mexiletine for control of ventricular dysrhythmias in pregnancy. *Lancet* 1980; **ii:** 647–8.
2. Lownes HE, Ives TJ. Mexiletine use in pregnancy and lactation. *Am J Obstet Gynecol* 1987; **157:** 446–7.
3. Gregg AR, Tomich PG. Mexilitene [sic] use in pregnancy. *J Perinatol* 1988; **8:** 33–5.

Interactions

Mexiletine undergoes extensive metabolism in the liver particularly by the cytochrome P450 isoenzymes CYP1A2 and CYP2D6, and possibly CYP3A4, and interactions may occur with other drugs metabolised by the same enzymes. Plasma concentrations of mexiletine may be reduced by hepatic enzyme inducers such as phenytoin and rifampicin; increased plasma concentrations may occur with enzyme inhibitors.

Absorption of mexiletine may be delayed by drugs that slow gastric emptying such as opioid analgesics and atropine. The rate of absorption may be increased by metoclopramide; the extent of absorption is unaffected.

Drugs that acidify or alkalinise the urine enhance or reduce the rate of elimination of mexiletine, respectively.

There may be an increased risk of arrhythmias if mexiletine is used with other antiarrhythmics or with arrhythmogenic drugs.

Mexiletine has been reported to increase theophylline concentrations (p.1142) and to precipitate lidocaine toxicity (p.1863).

Pharmacokinetics

Mexiletine is readily and almost completely absorbed from the gastrointestinal tract, with a bioavailability of about 90%, although absorption may be delayed in situations where gastric emptying is slowed, such as acute myocardial infarction.

Mexiletine is metabolised in the liver to a number of metabolites; metabolism may involve cytochrome P450 isoenzymes CYP1A2, CYP2D6, and CYP3A4, and genetic polymorphism in relation to CYP2D6 has been identified. Mexiletine is excreted in the urine, mainly in the form of its metabolites with about 10% excreted unchanged; clearance is increased in acid urine.

Mexiletine is widely distributed throughout the body and is about 50 to 70% bound to plasma proteins. Mexiletine crosses the placenta and is distributed into breast milk. It has an elimination half-life of about 10 hours in healthy subjects but this may be prolonged in patients with heart disease, hepatic impairment, or severe renal impairment. Its therapeutic effect has been correlated with plasma concentrations of 0.5 to 2 micrograms/mL, but the margin between therapeutic and toxic concentrations is narrow, and severe toxicity may occur within this range.

◊ References.

1. Labbé L, Turgeon J. Clinical pharmacokinetics of mexiletine. *Clin Pharmacokinet* 1999; **37:** 361–84.

Uses and Administration

Mexiletine is a class Ib antiarrhythmic (p.1153) with actions similar to those of lidocaine (p.1864), to which it is structurally related. Unlike lidocaine it undergoes little hepatic first-pass metabolism and can be given orally.

Mexiletine is used for the treatment of ventricular **arrhythmias** (p.1160). It is given orally or intravenously as the hydrochloride.

Mexiletine hydrochloride is given orally in a usual loading dose of 400 mg followed by 200 to 250 mg three or four times daily, starting 2 hours after the loading dose. The usual maintenance dosage is 600 to 900 mg daily in divided doses; doses up to 1.2 g daily may be given. Oral doses should be taken with food and swallowed with plenty of liquid to avoid oesophageal ulceration. Modified-release preparations have been used. Higher loading doses (for example, of 600 mg) may be necessary in patients after myocardial infarction to overcome delayed absorption, especially if they have received an opioid analgesic.

Mexiletine hydrochloride may be given by slow intravenous injection in doses of 100 to 250 mg at a rate of 25 mg/minute, followed by an infusion at a rate of 250 mg over 1 hour, 250 mg over the next 2 hours, and then at about 500 micrograms/minute for maintenance, according to response; when appropriate the patient may be transferred to oral therapy with doses of 200 to 250 mg three or four times daily. Alternatively, an initial intravenous dose of 200 mg at a rate of 25 mg/minute, may be followed by an oral dose of 400 mg on completion of the injection, with subsequent oral therapy as above.

Mexiletine has also been tried in the treatment of refractory neuropathic **pain** (see below).

Administration in children. Mexiletine may be effective for ventricular arrhythmias in children; a study[1] of 42 children and young adults (age range 5 months to 34 years) found that mexiletine, given orally in a dose of 1.4 to 5 mg/kg every 8 hours, was effective in 30 patients (71%), with long-term control reported in 18. Treatment was more effective in children with congenital heart disease than in those with cardiomyopathy or no heart disease. Another report[2] found that young children required higher mg/kg doses than adults; a 2-week-old girl and a 20-month-old boy required oral doses of 25 and 15 mg/kg daily, respectively, to produce therapeutic plasma concentrations and control of tachycardia.

1. Moak JP, *et al*. Mexiletine: an effective antiarrhythmic drug for treatment of ventricular arrhythmias in congenital heart disease. *J Am Coll Cardiol* 1987; **10:** 824–9.
2. Holt DW, *et al*. Paediatric use of mexiletine and disopyramide. *BMJ* 1979; **2:** 1476–7.

Administration in the elderly. The rate of absorption of mexiletine was slower in a group of 7 elderly subjects compared with 8 young subjects given mexiletine 100 mg by mouth, but the extent of absorption was probably not affected.[1] Elimination of mexiletine was not significantly different between the 2 groups and there was no pharmacokinetic basis for dosage modification of mexiletine in the elderly. An observational study[2] in patients receiving mexiletine found a small decrease in clearance with age, but again this was not considered to warrant dosage adjustment.

1. Grech-Bélanger O, *et al*. Pharmacokinetics of mexiletine in the elderly. *J Clin Pharmacol* 1989; **29:** 311–15.
2. Ueno K, *et al*. Pharmacokinetics of mexiletine in middle-aged and elderly patients. *Clin Pharm* 1993; **12:** 768–70.

Administration in renal impairment. The pharmacokinetics of mexiletine do not appear to be affected by renal impairment,[1] although one study[2] found that in patients with creatinine clearance below 10 mL/minute the steady-state plasma concentration and half-life were increased, suggesting that dosage should be adjusted according to plasma concentrations in such patients. Haemodialysis[1] and continuous ambulatory peritoneal dialysis[3] do not appear to affect mexiletine clearance.

1. Wang T, *et al*. Pharmacokinetics and nondialyzability of mexiletine in renal failure. *Clin Pharmacol Ther* 1985; **37:** 649–53.
2. El Allaf D, *et al.* Pharmacokinetics of mexiletine in renal insufficiency. *Br J Clin Pharmacol* 1982; **14:** 431–5.
3. Guay DRP, *et al*. Mexiletine clearance during peritoneal dialysis. *Br J Clin Pharmacol* 1985; **19:** 857–8.

Pain. Neuropathic pain (p.8) is often insensitive to opioid analgesics and various drugs, including mexiletine, have been tried. Mexiletine may be of benefit in diabetic neuropathy,[1] although studies have given conflicting results; two of the studies that reported no difference between treatment and placebo found that a subset of patients (those with stabbing or burning pain, heat sensations, and formication) appeared to benefit.[2,3] There have also been reports of improvement in patients with central post-stroke pain (thalamic pain syndrome),[4] and in neuropathic pain associated with cancer,[5-7] and a systematic review[8] concluded that mexiletine was safe and effective in various types of neuropathic pain.

Other painful states in which mexiletine has been reported to be of benefit include: Dercum's disease (a condition involving painful fatty deposits),[9] and erythromelalgia.[10,11]

1. Jarvis B, Coukell AJ. Mexiletine: a review of its therapeutic use in painful diabetic neuropathy. *Drugs* 1998; **56:** 691–707.
2. Stracke H, *et al*. Mexiletine in the treatment of diabetic neuropathy. *Diabetes Care* 1992; **15:** 1550–5.
3. Wright JM, *et al.* Mexiletine in the symptomatic treatment of diabetic peripheral neuropathy. *Ann Pharmacother* 1997; **31:** 29–34.
4. Awerbuch GI, Sandyk R. Mexiletine for thalamic pain syndrome. *Int J Neurosci* 1990; **55:** 129–33.
5. Colclough G, *et al.* Mexiletine for chronic pain. *Lancet* 1993; **342:** 1484–5.
6. Sloan P, *et al.* Mexiletine as an adjuvant analgesic for the management of neuropathic cancer pain. *Anesth Analg* 1999; **89:** 760–1.
7. Fassoulaki A, *et al.* The analgesic effect of gabapentin and mexiletine after breast surgery for cancer. *Anesth Analg* 2002; **95:** 985–91.
8. Challapalli V, *et al.* Systemic administration of local anesthetic agents to relieve neuropathic pain. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 24/01/07).
9. Petersen P, *et al*. Treating the pain of Dercum's disease. *BMJ* 1984; **288:** 1880.
10. Nathan A, *et al.* Primary erythromelalgia in a child responding to intravenous lidocaine and oral mexiletine treatment. Abstract: *Pediatrics* 2005; **115:** 1066. Full version: http://pediatrics.aappublications.org/cgi/content/full/115/4/e504 (accessed 10/07/07)
11. Kuhnert SM, *et al*. Lidocaine and mexiletine therapy for erythromelalgia. *Arch Dermatol* 1999; **135:** 1447–9.

Preparations

BP 2008: Mexiletine Capsules; Mexiletine Injection;
USP 31: Mexiletine Hydrochloride Capsules.

Proprietary Preparations (details are given in Part 3)
Arg.: Mexitilen; ***Austral.:*** Mexitil; ***Austria:*** Mexitil; ***Belg.:*** Mexitil; ***Braz.:*** Mexitil; ***Canad.:*** Mexitil†; ***Cz.:*** Katen; ***Fin.:*** Mexitil; ***Fr.:*** Mexitil†; ***Ger.:*** Mexitil; ***Gr.:*** Mexitil; Myovek†; ***Hong Kong:*** Mexitil†; ***Hung.:*** Ritalmex; ***India:*** Mexitil; ***Irl.:*** Mexitil; ***Israel:*** Mexilen; ***Ital.:*** Mexitil; ***Jpn:*** Mexitil; ***Mex.:*** Mexitil†; ***Neth.:*** Mexitil†; ***NZ:*** Mexitil; ***Pol.:*** Mexicord; ***S.Afr.:*** Mexitil†; ***Spain:*** Mexitil; ***Swed.:*** Mexitil†; ***Thai.:*** Mexitil†; ***Turk.:*** Mexitil; ***UK:*** Mexitil†; ***USA:*** Mexitil; ***Venez.:*** Tumetil.

Mibefradil Hydrochloride *(BANM, rINNM)*

Hidrocloruro de mibefradil; Mibéfradil, Chlorhydrate de; Mibefradil Dihydrochloride *(USAN)*; Mibefradili Hydrochloridum; Ro-40-5967 (mibefradil); Ro-40-5967/001 (mibefradil hydrochloride). (1*S*,2*S*)-(2-{[3-(2-Benzimidazolyl)propyl]methylamino}-ethyl)-6-fluoro-1,2,3,4-tetrahydro-1-isopropyl-2-naphthyl methoxyacetate dihydrochloride.

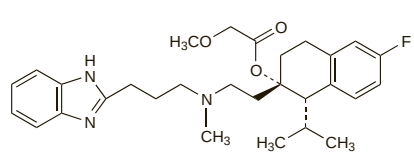
Мибефрадила Гидрохлорид

$C_{29}H_{38}FN_3O_3,2HCl$ = 568.6.

CAS — 116644-53-2 (mibefradil); 116666-63-8 (mibefradil hydrochloride).

ATC — C08CX01.

ATC Vet — QC08CX01.



(mibefradil)

Profile

Mibefradil is a calcium-channel blocker that acts principally on fast T-type calcium channels, unlike conventional calcium-channel blockers that act on slow L-type channels (see p.1154). Mibe-