Felodipine is given orally, generally in a modified-release formulation for use once daily in the morning. In **hypertension** the usual initial dose is 5 mg daily, adjusted as required; the usual maintenance dose is 2.5 to 10 mg daily and doses above 20 mg daily are not usually needed. In **angina** the usual initial dose is 5 mg daily increased if necessary to 10 mg daily.

Lower doses may be required in patients with hepatic impairment (see below) and in the elderly.

◊ Reviews.

1. Todd PA, Faulds D. Felodipine: a review of the pharmacology and therapeutic use of the extended release formulation in cardiovascular disorders. *Drugs* 1992; **44:** 251–77.
2. Walton T, Symes LR. Felodipine and isradipine: new calcium-channel-blocking agents for the treatment of hypertension. *Clin Pharm* 1993; **12:** 261–75.

Administration in hepatic impairment. In 9 patients with liver cirrhosis given felodipine 750 micrograms by intravenous infusion over 20 minutes and 10 mg orally as single doses on separate occasions the mean oral bioavailability was 17.1% which was not significantly different from published values in healthy subjects, but the maximum plasma concentrations were almost twice as high as normal, apparently due to reduced systemic clearance and volume of distribution.[1] The fact that bioavailability was not increased suggests that much pre-systemic metabolism takes place in the gut rather than the liver. Although increased adverse effects were not associated with the raised felodipine concentrations in this study it is recommended that therapy in cirrhotic patients begin at lower doses than in patients with normal liver function. US licensed product information recommends that an initial dose of 2.5 mg once daily should be used in patients with hepatic impairment.

1. Regårdh CG, *et al.* Pharmacokinetics of felodipine in patients with liver disease. *Eur J Clin Pharmacol* 1989; **36:** 473–9.

Preparations

USP 31: Felodipine Extended-Release Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Munobal; Plendil; ***Austral.:*** Agon†; Felodur; Plendil; ***Austria:*** Felodistad; Munobal; Plendil; ***Belg.:*** Plendil; Renedil; ***Braz.:*** Splendil; ***Canad.:*** Plendil; Renedil; ***Chile:*** Splendil; ***Cz.:*** Auronal; Felocor; Plendil; Presid; ***Denm.:*** Felodin; Hydac†; Plendil; Plendur; ***Fin.:*** Hydac; Plendil; ***Fr.:*** Flodil; ***Ger.:*** Felo-Puren; Felobeta; Felocor; Felogamma; Modip; Munobal; ***Gr.:*** Plendil; ***Hong Kong:*** Plendil; ***Hung.:*** Plendil; Presid; ***India:*** Felogard; ***Indon.:*** Nirmadil; Plendil; ***Irl.:*** Plendil; ***Israel:*** Penedil; ***Ital.:*** Feloday; Plendil; Prevex; ***Jpn:*** Splendil†; ***Malaysia:*** Plendil; ***Mex.:*** Fedin; Munobal; Plendil; ***Neth.:*** Plendil; Renedil; ***Norw.:*** Plendil; ***NZ:*** Felo; Plendil; ***Philipp.:*** Dilahex; Felim; Felop; Lodistad; Plendil; Versant; ***Pol.:*** Felohexal; Plendil; ***Port.:*** Mencor; Preslow; ***Rus.:*** Felodip (Фелодип); Plendil (Пленди́л); ***S.Afr.:*** Plendil; ***Singapore:*** Plendil; ***Spain:*** Fensel; Perfudal; Plendil; ***Swed.:*** Plendil; ***Switz.:*** Felodil; Munobal†; Plendil; ***Thai.:*** Felim; Felohexal; Feloten; Plendil; ***Turk.:*** Plendil; ***UK:*** Cardioplen; Felotens; Keloc; Neofel; Plendil; Vascalpha; ***USA:*** Plendil; ***Venez.:*** Munobal†; Plendil.

Multi-ingredient: ***Arg.:*** Nikion†; Triacor; ***Austral.:*** Triasyn; ***Austria:*** Triapin; Unimax; ***Belg.:*** Logimat; ***Cz.:*** Logimax†; Triasyn; Unimax†; ***Denm.:*** Logimax; ***Fin.:*** Logimax; Unimax; ***Fr.:*** Logimax; ***Ger.:*** Delmuno; Mobloc; Unimax; ***Gr.:*** Logimax; Triacor; Unitens; ***Hong Kong:*** Logimax; ***Hung.:*** Logimax; Triasyn; ***Irl.:*** Triapin; ***Israel:*** Logimax; ***Mex.:*** Logimax; Triacor; ***Neth.:*** Logimax; Triapin; Unimax; ***Philipp.:*** Logimax; Triapin; ***Port.:*** Unimax; ***Rus.:*** Logimax (Логимакс); ***S.Afr.:*** Tri-Plen; ***Spain:*** Logimax; ***Swed.:*** Logimax; ***Switz.:*** Logimax; Unimax; ***UK:*** Triapin; ***USA:*** Lexxel.

Fendiline Hydrochloride *(pINNM)*

Fendiline, Chlorhydrate de; Fendilini Hydrochloridum; Hidrocloruro de fendilina. *N*-(2-Benzhydrylethyl)-α-methylbenzylamine hydrochloride.

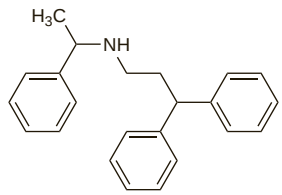
Фендилина Гидрохлорид

$C_{23}H_{25}N,HCl$ = 351.9.

CAS — 13042-18-7 (fendiline); 13636-18-5 (fendiline hydrochloride).

ATC — C08EA01.

ATC Vet — QC08EA01.



(fendiline)

Profile

Fendiline hydrochloride is a calcium-channel blocker used as a vasodilator in ischaemic heart disease.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Sensit†; ***Ger.:*** Sensit; ***Gr.:*** Sensit.

Fenofibrate *(BAN, rINN)*

Fenofibraatti; Fenofibrát; Fenofibrat; Fenofibratas; Fénofibrate; Fenofibrato; Fenofibratum; LF-178; Procetofen; Procetofene. Isopropyl 2-[4-(4-chlorobenzoyl)phenoxy]-2-methylpropionate.

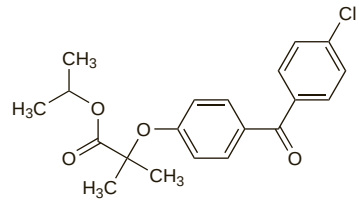
Фенофибрат

$C_{20}H_{21}ClO_4$ = 360.8.

CAS — 49562-28-9.

ATC — C10AB05.

ATC Vet — QC10AB05.



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

Ph. Eur. 6.2 (Fenofibrate). A white or almost white, crystalline powder. M.p. 79° to 82°. Practically insoluble in water; slightly soluble in alcohol; very soluble in dichloromethane. Protect from light.

USP 31 (Fenofibrate). A white or almost white, crystalline powder. M.p. 79° to 82°. Practically insoluble in water; slightly soluble in alcohol; very soluble in dichloromethane. Protect from light.

Adverse Effects and Precautions

As for Bezafibrate, p.1232.

Interactions

As for Bezafibrate, p.1232.

UK licensed product information for fenofibrate suggests that in patients taking oral anticoagulants, the dose of anticoagulant should be reduced by about one-third when treatment with fenofibrate is started, and then adjusted gradually if necessary.

Pharmacokinetics

Fenofibrate is readily absorbed from the gastrointestinal tract when taken with food; absorption may be reduced if fenofibrate is given on an empty stomach, although this depends on the formulation (see Bioavailability, below). It is rapidly hydrolysed to its active metabolite fenofibric acid which is about 99% bound to plasma albumin. The plasma elimination half-life is about 20 hours. Fenofibric acid is excreted mainly in the urine, mainly as the glucuronide conjugate, but also as a reduced form of fenofibric acid and its glucuronide. It is not removed by haemodialysis.

◊ References.

1. Chapman MJ. Pharmacology of fenofibrate. *Am J Med* 1987; **83** (suppl 5B): 21–5.

Bioavailability. Fenofibrate is poorly soluble in water and has a low bioavailability when given orally.[1] Bioavailability is increased by food, particularly if there is a high fat content, and fenofibrate is therefore usually given with meals. Changes to the formulation, particularly with regard to the particle size, have been made to improve solubility,[1] with the aim of increasing bioavailability and reducing the influence of food. Micronisation improves bioavailability to a certain extent, and allows a lower dose to be given; 300 mg of non-micronised fenofibrate is usually considered equivalent to about 200 mg of the standard micronised form. Microcoating may further improve bioavailability,[2] but absorption is still affected by the presence of food.[3] Nanoparticle,[4] stabilised microparticle,[3] or semi-solid formulations,[5] however, appear to have a more consistent bioavailability and may be given with or without food.

1. Vogt M, *et al.* Dissolution enhancement of fenofibrate by micronization, cogrinding and spray-drying: comparison with commercial preparations. *Eur J Pharm Biopharm* 2008; **68:** 283–8.
2. Guichard JP, *et al.* A new formulation of fenofibrate: suprabioavailable tablets. *Curr Med Res Opin* 2000; **16:** 134–8.
3. Guivarc'h PH, *et al.* A new fenofibrate formulation: results of six single-dose, clinical studies of bioavailability under fed and fasting conditions. *Clin Ther* 2004; **26:** 1456–69.
4. Sauron R, *et al.* Absence of a food effect with a 145 mg nanoparticle fenofibrate tablet formulation. *Int J Clin Pharmacol Ther* 2006; **44:** 64–70.
5. Sonet B, *et al.* Randomised crossover studies of the bioequivalence of two fenofibrate formulations after administration of a single oral dose in healthy volunteers. *Arzneimittelforschung* 2002; **52:** 200–4.

Uses and Administration

Fenofibrate, a fibric acid derivative, is a lipid regulating drug with actions on plasma lipids similar to those of bezafibrate (p.1233).

It is used to reduce low-density lipoprotein (LDL)-cholesterol, total cholesterol, triglycerides, and apolipoprotein B, and to increase high-density lipoprotein (HDL)-cholesterol, in the management of hyperlipidaemias (p.1169), including type IIa, type IIb, type III, type IV, and type V hyperlipoproteinaemias.

Fenofibrate is given orally. It is usually given with food to improve bioavailability although this may not be necessary with all preparations (see Bioavailability, above). It is available in a range of formulations with differing bioavailabilities and the dose is therefore specific to the preparation.

Standard micronised formulations of fenofibrate are available as 67-mg capsules to be taken several times daily, or as 200- or 267-mg capsules for once daily dosage. The usual initial dose is 67 mg three times daily or 200 mg once daily; the dose may be reduced to 67 mg twice daily or increased to 67 mg four times daily or 267 mg once daily according to response.

Preparations with improved bioavailability may be given in doses of around 40 to 160 mg once daily.

Non-micronised formulations may also be available and are given in an initial dose of 200 to 300 mg daily in divided doses, adjusted according to response to between 200 and 400 mg daily; 100 mg of non-micronised fenofibrate is therapeutically equivalent to 67 mg of the standard micronised form.

The dose of fenofibrate should be reduced in renal impairment (see below). For the dose of fenofibrate in children, see also below.

◊ Reviews.

1. Keating GM, Croom KF. Fenofibrate: a review of its use in primary dyslipidaemia, the metabolic syndrome and type 2 diabetes mellitus. *Drugs* 2007; **67:** 121–53.

Administration in children. Experience with fenofibrate in children is limited and it should only be given under specialist advice. The dose depends on the formulation:

- For *standard micronised* fenofibrate the *BNFC* recommends that children are given the 67-mg capsule formulation. The oral dose is one 67-mg capsule per 20 kg body-weight daily for children aged 4 to 15 years; those aged 15 to 18 years may be given the adult dose (see above).
- *Non-micronised* fenofibrate is licensed for use in some countries in children from the age of 10 years, in an oral dose of 5 mg/kg daily.

Administration in renal impairment. A single-dose study[1] in patients with mild (creatinine clearance (CC) 30 to 50 mL/minute) or severe renal impairment (CC below 10 mL/minute or undergoing haemodialysis) found that the plasma elimination half-life of fenofibric acid was prolonged, with a range of 54 to 362 hours; no correlation was found between half-life and serum creatinine or CC. Fenofibrate metabolites were not removed by haemodialysis, and repeated dosing in patients undergoing regular haemodialysis led to significant accumulation of fenofibric acid.[1]

Fenofibrate is therefore not generally recommended in patients with severe renal impairment although UK licensed product information allows a dose of 134 mg of standard micronised fenofibrate daily for patients with CC between 20 and 60 mL/minute and 67 mg daily for patients with CC below 20 mL/minute. US licensed product information for improved bioavailability formulations suggests initial daily doses of about 40 to 50 mg (equivalent to about 67 mg of standard micronised fenofibrate) in patients with renal impairment, but contra-indicates use in those with severe impairment.

1. Desager JP, *et al.* Effect of hemodialysis on plasma kinetics of fenofibrate in chronic renal failure. *Nephron* 1982; **31:** 51–4.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Craveril; Fenobrate; Fenolip†; Lipidil†; Lipoplasmin†; Minuslip; Procetoken; Qualecon†; Sclerofin; ***Austral.:*** Lipidil; ***Austria:*** Fenolip; Lipcor; Lipsin; ***Belg.:*** Docfenofi; Fenofitop; Fenogal; Lipanthyl; ***Braz.:*** Lipanon; Lipidil; ***Canad.:*** Apo-Feno; Lipidil; ***Chile:*** Lipidil; ***Cz.:*** Apo-Feno; Febira; Fenofix; Grofibrat†; Hypolip†; Lipanthyl; Lipirex; Lipohexal; Suprelip; ***Fin.:*** Lipanthyl; ***Fr.:*** Fegenor; Lipanthyl; Lipirex; Secalip; ***Ger.:*** ClL; durafenat; Fenobeta; Fenofanton; Lipanthyl; Lipidil; Normalip pro; ***Gr.:*** Lipanthyl; Lipidil; Neo-Disterin; Planitrix†; Zerlubron†; ***Hong Kong:*** Apo-Feno-Micro; Fegenor; Lexemin; Lipanthyl; Qualipantyl; Trolip†; ***Hung.:*** Feno-Micro; Fenobrat; Lipanthyl†; Lipidil; ***India:*** Fenolip; Lipicard; ***Indon.:*** Evothyl; Felosma; Hyperchol; Lipanthyl; Trichol; Trolip; Yosenob; Zumafib; ***Irl.:*** Lipantil; ***Ital.:*** Fulcro; Lipanthyl†; Lipofene; Lipsin; Nolipax; Scleril; Tilene; Volutine†; ***Jpn:*** Tricor; ***Malaysia:*** Apo-Feno-Micro; Lexemin; Lipanthyl; ***Mex.:*** Controlip;