4. Hellstern A, *et al.* Absolute bioavailability of metoclopramide given orally or by enema in patients with normal liver function or with cirrhosis of the liver. *Arzneimittelforschung* 1987; **37:** 733–6.
5. Magueur E, *et al.* Pharmacokinetics of metoclopramide in patients with liver cirrhosis. *Br J Clin Pharmacol* 1991; **31:** 185–7.

Blood disorders. Responses to treatment with metoclopramide have been reported in patients with Diamond-Blackfan anaemia, probably through induction of prolactin release, although the mechanism by which prolactin affects erythropoiesis is unclear.[1,2] In a pilot study, 3 out of 9 evaluable patients responded after 12 to 15 weeks of therapy; high serum ferritin, pituitary dysfunction, male sex, and younger age may have contributed to the poor response to metoclopramide in other patients.[1] In another case, response was seen by the fourth week of treatment; at the time of the report, the patient had remained asymptomatic and transfusion independent for 8 months.[2]

1. Abkowitz JL, *et al.* Response of Diamond-Blackfan anemia to metoclopramide: evidence for a role for prolactin in erythropoiesis. *Blood* 2002; **100:** 2687–91.
2. Akiyama M, *et al.* Successful treatment of Diamond-Blackfan anemia with metoclopramide. *Am J Hematol* 2005; **78:** 295–8.

Hiccup. Metoclopramide has been used in the management of intractable hiccup. For a discussion of hiccup and its management see p.976.

Lactation induction. Metoclopramide has been used[1,2] in doses of 10 mg three times daily for its dopamine antagonist properties to stimulate lactation in women who wish to breast feed and in whom mechanical stimulation of the nipple alone is inadequate, including mothers of adopted babies or babies born to surrogates.[3,4] However, pharmacological lactation induction should be viewed as adjunctive to mechanical methods and the duration of therapy should probably be limited to 7 to 14 days.[1,2] In addition, the efficacy of metoclopramide in stimulating lactation in women with preterm deliveries has been questioned by a controlled study.[5] Young women are at increased risk of extrapyramidal effects from metoclopramide—see under Adverse Effects, above. There has also been concern about the presence of the drug in breast milk. For a discussion of lactation inhibition and induction, see p.2003.

1. Anderson PO, Valdés V. Increasing breast milk supply. *Clin Pharm* 1993; **12:** 479–80.
2. Gabay MP. Galactogogues: medications that induce lactation. *J Hum Lact* 2002; **18:** 274–9.
3. Cheales-Siebenaler NJ. Induced lactation in an adoptive mother. *J Hum Lact* 1999; **15:** 41–3.
4. Biervliet FP, *et al.* Induction of lactation in the intended mother of a surrogate pregnancy: case report. *Hum Reprod* 2001; **16:** 581–3.
5. Hansen WF, *et al.* Metoclopramide effect on breastfeeding the preterm infant: a randomized trial. *Obstet Gynecol* 2005; **105:** 383–9.

Migraine. Metoclopramide is used in the treatment of migraine (p.616) to alleviate nausea and vomiting and gastric stasis, which commonly develop as a migraine attack progresses and can lead to poor absorption of oral antimigraine preparations. It may also be given to counteract nausea and vomiting from the use of ergotamine. Metoclopramide is included in some combination analgesic preparations for the treatment of acute attacks of migraine. In a study, oral lysine aspirin with metoclopramide was as effective as oral sumatriptan in the treatment of migraine.[1] Metoclopramide with sumatriptan may be effective in patients unresponsive to a triptan alone.[2]

Parenteral metoclopramide has also been shown to be an effective treatment for acute migraine; it reduces pain, and to some extent nausea (although other antiemetics may be more effective), and a systematic review concluded that it should be considered a first-line treatment for migraine in the emergency department.[3] A later study found intravenous metoclopramide (with intermittent doses of diphenhydramine) to be comparable to subcutaneous sumatriptan in terms of pain relief at both 2 and 24 hours after treatment.[4]

1. Tfelt-Hansen P, *et al.* The effectiveness of combined oral lysine acetylsalicylate and metoclopramide compared with oral sumatriptan for migraine. *Lancet* 1995; **346:** 923–6.
2. Schulman EA, Dermott KF. Sumatriptan plus metoclopramide in triptan-nonresponsive migraineurs. *Headache* 2003; **43:** 729–33.
3. Colman I, *et al.* Parenteral metoclopramide for acute migraine: meta-analysis of randomised controlled trials. *BMJ* 2004; **329:** 1369–72.
4. Friedman BW, *et al.* A trial of metoclopramide vs sumatriptan for the emergency department treatment of migraines. *Neurology* 2005; **64:** 463–8.

Orthostatic hypotension. Metoclopramide has been tried in the management of some patients with orthostatic hypotension, as mentioned on p.1530.

Tourette's syndrome. A small, short-term study in children and adolescents with Tourette's syndrome (see Tics, p.954) or chronic tic disorders found that treatment with oral metoclopramide (up to 40 mg daily) significantly reduced tic score and severity compared with placebo.[1]

1. Nicolson R, *et al.* A randomized, double-blind, placebo-controlled trial of metoclopramide for the treatment of Tourette's disorder. *J Am Acad Child Adolesc Psychiatry* 2005; **44:** 640–6.

Variceal haemorrhage. Metoclopramide 20 mg intravenously controlled bleeding from oesophageal varices within 15 minutes in 10 of 11 patients compared with 4 of 11 patients given placebo; all patients were treated by sclerotherapy.[1] Lower oesophageal sphincter pressure is increased by metoclopramide, thus reducing blood flow to varices and achieving haemostasis; another study[2] found use of metoclopramide with intravenous glyceryl trinitrate to be more effective than glyceryl trinitrate alone in reducing intravariceal pressure.

For a discussion of variceal haemorrhage and its management, see p.2346.

1. Hosking SW, *et al.* Pharmacological constriction of the lower oesophageal sphincter: a simple method of arresting variceal haemorrhage. *Gut* 1988; **29:** 1098–1102.
2. Sarin SK, Saraya A. Effects of intravenous nitroglycerin and nitroglycerin and metoclopramide on intravariceal pressure: a double blind, randomized study. *Am J Gastroenterol* 1995; **90:** 48–53.

Preparations

BP 2008: Metoclopramide Injection; Metoclopramide Oral Solution; Metoclopramide Tablets;
USP 31: Metoclopramide Injection; Metoclopramide Oral Solution; Metoclopramide Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Celit†; Fonderyl; Lizarona; Metoc; Midatenk; Novomit; Praux; Primavera-N; Primperil; Reliveran; Rilaquin; Rupemet; Saften; Sintegran; ***Austral.:*** Maxolon; Pramin; ***Austria:*** Gastro-Timelets; Gastronerton; Gastrosil; Metogastron; Paspertin; Pramidin; ***Belg.:*** Dibertil; Docmetoclo; Movistal†; Primperan; ***Braz.:*** Aristopramida; Citroplus†; Clopra†; Emetic; Eucil; Flucil; Metoclosan; Metoplamin; Metovit†; Nausil†; Neolasil; No-Vomit; Plagex; Plamida; Plamidasil; Plamivon; Plasil; Pramil; Vopax†; ***Canad.:*** Apo-Metoclop; ***Chile:*** Hemibe; Itan; ***Cz.:*** Cerucal; Degan; MCP; Pramidin†; ***Denm.:*** Emperal; Gastro-Timelets; Primperan; ***Fin.:*** Metopram; Primperan; ***Fr.:*** Anausin; Primperan; ***Ger.:*** Cerucal; Gastronerton; Gastrosil†; Gastrotranquil†; Hyrin†; MCP; MCPham†; Paspertin; ***Gr.:*** Primeran†; Primperan; ***Hong Kong:*** Manil; Martomide; Maxolon; Metocyl†; Metram; Primperan; ***Hung.:*** Cerucal; Paspertin†; ***India:*** Maxeron; Metocontin; Perinorm; Reglan; Tomid†; Vominorm; ***Indon.:*** Clopramel; Damaben; Emeran; Ethiferan; Gavistal; Lexapram; Mepramide; Metolon; Nilatika; Nofoklam; Normastin; Obteran; Opram; Piralen; Plasil; Praminal; Primperan; Raclonid; Reguloop; Sotatic; Tivomit; Tomit; Vertivom; Vilapon; Vomidex; Vomipram; Vomitrol; Zumatrol; ***Irl.:*** Antimet; Gastrobid Continus; Maxolon; Metocyl; ***Israel:*** Pramin; ***Ital.:*** Citroplus†; Clopan†; Delipramil; Isaprandil; Plasil; Pramidin; Randum; ***Jpn:*** Primperan; ***Malaysia:*** Manil; Maxolon; Metocyl†; Primperan; Pulin; ***Mex.:*** Biopram; Carnotprim; Cirulan; Clorimet-Z; Dolmisin; Eudiges; Gigemet; Hopram; Meclomid; Midetol; Mipramid; Plasil; Polcotec; Pradex; Pramilem; Pramotil†; Primperan; Propace; Synespramid; ***Neth.:*** Primperan; ***Norw.:*** Afipran; Primperan; ***NZ:*** Maxolon; Metamide; ***Philipp.:*** Biclomet; Novom; Plasil; ***Pol.:*** Pramidin; ***Port.:*** Metoclan†; Primperan; Reglan†; ***Rus.:*** Apo-Metoclop (Апо-метоклоп); Cerucal (Церукал); Perinorm (Перинорм); ***S.Afr.:*** Acumet; Ametic†; Betaclopramide; Clopamon; Contromet; Maxolon; Metalon; Perinorm; Pramalon; Setin; ***Singapore:*** Manil; Maxolon†; Metocyl†; Metolon†; Primperan; Pulin; ***Spain:*** Metagliz†; Primperan; ***Swed.:*** Primperan; ***Switz.:*** Gastrosil; Paspertin; Primperan; ***Thai.:*** Emetal; Gensil; H-Peran; Hawkperan†; Manil; Meramide†; Met-Sil; Metoclor; Nausil; Plasil; ***Turk.:*** Metoklamide; Metpamid; Primperan; ***UAE:*** Premosan; ***UK:*** Gastrobid Continus†; Gastroflux†; Maxolon; Primperan; ***USA:*** Clopra†; Maxolon†; Octamide; Reclomide; Reglan; ***Venez.:*** Clodoxin; Clop†; Irtopan; Mepramida; Peremid†; Pradamin†; Pramide; Primperan; Vibralen†.

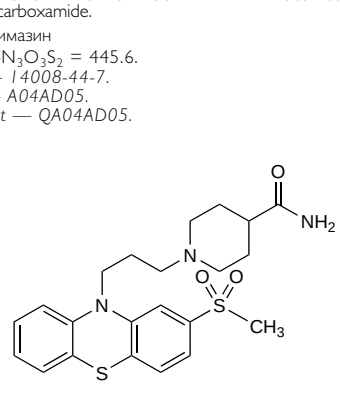
Multi-ingredient: ***Arg.:*** Bil 13 Enzimatico; Bitecain AA; Digesplen; Facilgest†; Factorine; Faradil; Faradil Enzimatico; Migral Compositum; Pakinase; Pankreon Total; Tetralgin; Vacuobil Plus; ***Austral.:*** Anagraine; Metomax; ***Austria:*** Ceolat Compositum; Paspertase; ***Belg.:*** Migpriv; ***Braz.:*** Cefalium; Diagrin†; Digeplus; Emetrol†; Enjool†; Essen; Estac†; Plagon; Plasil Enzimatico; Sintozima; Vominil†; ***Chile:*** Aero Itan; Aeroflat†; Aerogastrol; Digespar; Garceptol; Gaseofin†; No-Ref; Pangastren; ***Cz.:*** Cephalgan†; Migpriv†; Migranerton; ***Denm.:*** Migpriv†; ***Fin.:*** Migpriv; ***Fr.:*** Cephalgan†; Migpriv; ***Ger.:*** Migraeflux MCP; Migralave + MCP; Migrane-Neuridal; Migranerton; Paspertase†; ***Gr.:*** Premig; ***Hung.:*** Migpriv; ***India:*** Okanorm Plus; Pacimol-M; Paramet; ***Indon.:*** Primadol; Primperan Compositum; ***Irl.:*** Paramax; ***Ital.:*** Geffer; Migpriv; Migraprim; ***Mex.:*** Antigram; Digenor; Digenor Plus; Espaven MD; Espraden; Plasil Enzimatico; Pramigel; Primpesasy; ***Neth.:*** Migrafin; ***Norw.:*** Migpriv†; ***NZ:*** Paramax; ***Pol.:*** Migpriv; ***Spain:*** Aero Plus†; Aeroflat; Anti Anorex Triple; Novo Aerofil Sedante†; Paidozim; Salcemetic†; Suxidina; ***Swed.:*** Migpriv; ***Switz.:*** Migpriv; ***UK:*** Migramax; Paramax.

Metopimazine *(BAN, USAN, rINN)*

EXP-999; Metopimazina; Métopimazine; Metopimazinum; RP-9965. 1-[3-(2-Methylsulphonylphenothiazin-10-yl)propyl]piperidine-4-carboxamide.

Метопимазин

$C_{22}H_{27}N_3O_3S_2$ = 445.6.
CAS — 14008-44-7.
ATC — A04AD05.
ATC Vet — QA04AD05.



Pharmacopoeias. In *Fr.*

Profile

Metopimazine, a phenothiazine dopamine antagonist, is an antiemetic with general properties similar to those of chlorpromazine (p.969). It is used in the management of nausea and vomiting, including that associated with cancer chemotherapy (p.1700). It is given in usual oral doses of 15 to 30 mg daily, in 2 to 4 divided doses; similar daily doses have been given by rectum in 3 divided doses. It has also been given by injection in a dose of 10 to 20 mg daily, usually intramuscularly but occasionally by the intravenous route. Higher doses of 30 to 50 mg daily by intramuscular injection or intravenous infusion have been given for chemotherapy-induced nausea and vomiting.

Preparations

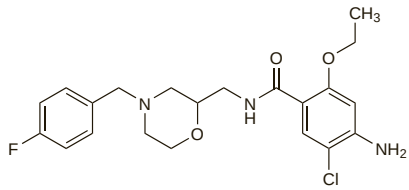
Proprietary Preparations (details are given in Part 3)
Denm.: Vogalene; ***Fr.:*** Vogalene; Vogalib.

Mosapride Citrate *(rINNM)*

AS-4370; Citrato de mosaprida; Mosapride, Citrate de; Mosapridi Citras; Rimopride Citrate. (±)-4-Amino-5-chloro-2-ethoxy-*N*-{[4-(*p*-fluorobenzyl)-2-morpholinyl]methyl}benzamide citrate dihydrate.

Мозаприда Цитрат

$C_{21}H_{25}ClFN_3O_3,C_6H_8O_7,2H_2O$ = 650.0.
CAS — 112885-41-3 (mosapride); 112885-42-4 (mosapride citrate).



(mosapride)

Profile

Mosapride is a substituted benzamide used for its prokinetic properties. It is reported to be an agonist at 5-HT_4 receptors, increasing acetylcholine release and stimulating gastrointestinal motility (see also Cisapride, p.1721), as well as having 5-HT_3 antagonist properties. It is given orally as the citrate dihydrate, but doses are expressed as the anhydrous citrate, and are 5 mg three times daily before or after meals.

◊ References.

1. Sakashita M, *et al.* Pharmacokinetics of the gastrokinetic agent mosapride citrate after single and multiple oral administrations in healthy subjects. *Arzneimittelforschung* 1993; **43:** 867–72.
2. Ruth M, *et al.* The effect of mosapride, a novel prokinetic, on acid reflux variables in patients with gastro-oesophageal reflux disease. *Aliment Pharmacol Ther* 1998; **12:** 35–40.
3. Ruth M, *et al.* The effect of mosapride on oesophageal motor function and acid reflux in patients with gastro-oesophageal reflux disease. *Eur J Gastroenterol Hepatol* 2003; **15:** 1115–21.
4. Asakawa H, *et al.* Effect of mosapride on glycemic control and gastric emptying in type 2 diabetes mellitus patients with gastropathy. *Diabetes Res Clin Pract* 2003; **61:** 175–82.
5. Liu Z, *et al.* Mosapride citrate, a novel 5-HT4 agonist and partial 5-HT3 antagonist, ameliorates constipation in parkinsonian patients. *Mov Disord* 2005; **20:** 680–6.
6. He M, *et al.* Mosapride citrate prolongs survival in stroke patients with gastrostomy. *J Am Geriatr Soc* 2007; **55:** 142–4.
7. Curran MP, Robinson DM. Mosapride: in gastrointestinal disorders. *Drugs* 2008; **68:** 981–91.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Galopran; Intesul; Levusid; Lostapride; Mosar; Vagantyl; ***India:*** Mosafe; Mosapid; Mosart; Peripride; ***Jpn:*** Gasmotin.

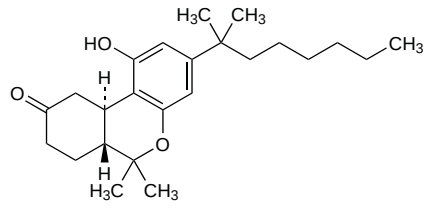
Multi-ingredient: ***Arg.:*** Gastrimet†; Mosar Enzimatico; Mosar Plus.

Nabilone *(BAN, USAN, rINN)* ⊗

Compound 109514; Lilly-109514; Nabilon; Nabilona; Nabiloni; Nabilonum. (±)-(6a*R*,10a*R*)-3-(1,1-Dimethylheptyl)-6a,7,8,9,10,10a-hexahydro-1-hydroxy-6,6-dimethyl-6*H*-benzo[*c*]chromen-9-one.

Набилон

$C_{24}H_{36}O_3$ = 372.5.
CAS — 51022-71-0.
ATC — A04AD11.
ATC Vet — QA04AD11.



Adverse Effects

Nabilone may produce adverse effects similar to those of cannabis (see p.2275). The most common adverse effects are drowsiness, vertigo, and dry mouth. Neurological effects have included