Similar preparations are available in other countries, and in the USA a suspension enema containing 4 g of mesalazine has been used.

◊ References.

1. Clemett D, Markham A. Prolonged-release mesalazine: a review of its therapeutic potential in ulcerative colitis and Crohn's disease. *Drugs* 2000; **59:** 929–56.
2. Hanauer SB, Strömberg U. Oral Pentasa in the treatment of active Crohn's disease: a meta-analysis of double-blind, placebo-controlled trials. *Clin Gastroenterol Hepatol* 2004; **2:** 379–88.
3. Akobeng AK, Gardener E. Oral 5-aminosalicylic acid for maintenance of medically-induced remission in Crohn's Disease. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2005 (accessed 01/06/07).
4. Sutherland L, MacDonald JK. Oral 5-aminosalicylic acid for induction of remission in ulcerative colitis. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 01/06/07).
5. Sutherland L, MacDonald JK. Oral 5-aminosalicylic acid for maintenance of remission in ulcerative colitis. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2006 (accessed 01/06/07).
6. Bergman R, Parkes M. Systematic review: the use of mesalazine in inflammatory bowel disease. *Aliment Pharmacol Ther* 2006; **23:** 841–55.
7. van Bodegraven AA, Mulder CJ. Indications for 5-aminosalicylate in inflammatory bowel disease: is the body of evidence complete? *World J Gastroenterol* 2006; **12:** 6115–23.
8. Anonymous. Once-daily mesalamine (Lialda) for ulcerative colitis. *Med Lett Drugs Ther* 2007; **49:** 25–6.
9. McCormack PL, *et al.* Delayed-release Multi Matrix System (MMX) mesalazine: in ulcerative colitis. *Drugs* 2007; **67:** 2635–42.
10. Kale-Pradhan PB, *et al.* Multi-Matrix System Mesalamine: to use or not to use. *Ann Pharmacother* 2008; **42:** 265–9.

Administration. Because the release characteristics of different formulations of mesalazine vary, they should not be regarded as interchangeable.[1] This applies even to those formulations where the dosage is apparently similar.[2] However, a study established that an oral once-daily regimen was bioequivalent to a twice-daily regimen of the same product (*Pentasa (Ferring, France)*).[3]

1. Forbes A, Chadwick C. Mesalazine preparations. *Lancet* 1997; **350:** 1329.
2. Benbow AG, Gould I. Mesalazine preparations. *Lancet* 1998; **351:** 68.
3. Gandia P, *et al.* Is once-daily mesalazine equivalent to the currently used twice-daily regimen? A study performed in 30 healthy volunteers. *J Clin Pharmacol* 2007; **47:** 334–42.

Diverticular disease. In a study involving 218 patients with a history of recurrent attacks of acute diverticulitis (p.1695), half were assigned to treatment with oral rifaximin 400 mg twice daily for 7 days, and half received rifaximin plus a modified-release formulation of mesalazine 800 mg three times daily, again for 7 days. Courses were then repeated, with rifaximin at the same dose and mesalazine at 800 mg twice daily, for 7 days in each month, and patients followed for 12 months. The combination of rifaximin and mesalazine was significantly more effective in reducing symptomatic episodes and normalisation of bowel habit than rifaximin alone: 89 of 107 patients given the combination were symptom-free at 12 months, compared with 44 of 105 given just the antibacterial.[1] Similarly, the same group found that in patients with uncomplicated diverticular disease given 10 days of treatment with rifaximin and mesalazine (*Pentacol; Sofar, Ital.*) in the doses above, followed by mesalazine 1.6 g daily for 8 weeks, 70 of 86 completing the study were completely asymptomatic, suggesting that daily mesalazine alone was an effective maintenance therapy, although longer-term studies were needed.[2] Mesalazine has also been investigated in combination with a probiotic preparation of lactic-acid-producing organisms.[3]

1. Tursi A, *et al.* Long-term treatment with mesalazine and rifaximin versus rifaximin alone for patients with recurrent attacks of acute diverticulitis of colon. *Dig Liver Dis* 2002; **34:** 510–15.
2. Brandimarte G, Tursi A. Rifaximin plus mesalazine followed by mesalazine alone is highly effective in obtaining remission of symptomatic uncomplicated diverticular disease. *Med Sci Monit* 2004; **10:** PI70–PI73.
3. Tursi A, *et al.* Mesalazine and/or Lactobacillus casei in preventing recurrence of symptomatic uncomplicated diverticular disease of the colon: a prospective, randomized, open-label study. *J Clin Gastroenterol* 2006; **40:** 312–16.

Preparations

USP 31: Mesalamine Delayed-Release Tablets; Mesalamine Extended-Release Capsules; Mesalamine Rectal Suspension.

Proprietary Preparations (details are given in Part 3)
Arg.: Bufexan; Pentasa; Salofalk; Suprimal; Xalazina; Yolecol; ***Austral.:*** Mesasal; Pentasa; Salofalk; ***Austria:*** Claversal; Pentasa; Salofalk; ***Belg.:*** Asacol†; Claversal; Colitofalk; Pentasa; ***Braz.:*** Asalit; Chron-ASA; Mesacol; Pentasa†; ***Canad.:*** Asacol; Mesasal; Pentasa; Salofalk; ***Chile:*** Pentasa; Salofalk; ***Cz.:*** Asacol; Pentasa; Salofalk; Samezil; ***Denm.:*** Asacol; Mesasal; Pentasa; ***Fin.:*** Asacol; Pentasa; Salofalk; ***Fr.:*** Fivasa; Pentasa; Rowasa; ***Ger.:*** Asacolitin; Claversal; Pentasa; Salofalk; ***Gr.:*** Asacol; Asalazin†; Crohnezine; Ectospasmol; Empenox; Enterin; Favorat; Laboxantryl; Mesagin†; Pentasa; Prozylex†; Salofalk; ***Hong Kong:*** Asacol; Pentasa; Salofalk; ***Hung.:*** Asacol; Huma-Col-Asa; Pentasa; Salofalk; Xalazin; ***India:*** Asacol; Mesacol; ***Indon.:*** Salofalk; ***Irl.:*** Asacolon; Pentasa; Salofalk; ***Israel:*** Asacol; Pentasa; Rafassal; ***Ital.:*** Asacol; Asalex; Asamax; Asavixin; Claversal; Enteraproct; Enterasin; Lextrasa; Mesaflor; Pentacol; Pentasa; Plimage; Quota; Salofalk†; Xalazin†; ***Jpn:*** Pentasa; ***Malaysia:*** Pentasa; Salofalk; ***Mex.:*** Asacol; Kenzomyl†; Pentasa; Salofalk; Seramine; ***Neth.:*** Asacol; Asamax; Claversal; Pentasa; Salofalk; ***Norw.:*** Asacol; Mesasal; Pentasa; ***NZ:*** Asacol; Pentasa; ***Philipp.:*** Pentasa; Salofalk; ***Pol.:*** Asamax; Colitan; Jucolon; Pentasa; Salofalk; ***Port.:*** Asacol; Claversal; Pentasa; Salofalk; ***Rus.:*** Mesacol (Месакол); Pentasa (Пентаса); Samezil (Самезил); ***S.Afr.:*** Asacol; Mesasal; Pentasa; ***Singapore:*** Asacol; Pentasa; Salofalk; ***Spain:*** Claversal; Lixacol; Pentasa; Salofalk; ***Swed.:*** Asacol; Mesasal; Pentasa; Salofalk; ***Switz.:*** Asacol; Asazine; Mesazine; Pentasa; Salofalk; ***Thai.:*** Asacol†; Mesacol; Salofalk; ***Turk.:*** Asacol; Salofalk; ***UK:*** Asacol; Ipocol; Mesren; Mezavant; Pentasa; Salofalk; ***USA:*** Asacol; Canasa; Lialda; Pentasa; Rowasa.

Methanthelinium Bromide *(BAN, pINN)*

Bromuro de metantelinio; Dixamonum Bromidum; Methantheline Bromide; Methanthelinii Bromidum; Méthanthélinium, Bromure de; MTB-51; SC-2910. Diethylmethyl[2-(xanthen-9-ylcarbonyloxy)ethyl]ammonium bromide.

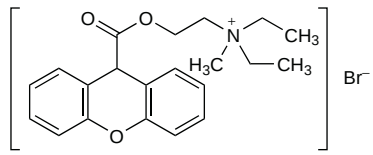
Метантелиния Бромид

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

CAS — 5818-17-7 (methanthelinium); 53-46-3 (methanthelinium bromide).

ATC — A03AB07.

ATC Vet — QA03AB07.



Profile
Methanthelinium bromide is a quaternary ammonium antimuscarinic with peripheral effects similar to those of atropine (p.1219). It has been used as an adjunct in the treatment of peptic ulcer disease, in gastrointestinal disorders associated with smooth muscle spasm, and in the management of urinary incontinence. A usual oral dose in gastrointestinal disorders is 50 mg three times daily.

Preparations
Proprietary Preparations (details are given in Part 3)
Ger.: Vagantin.

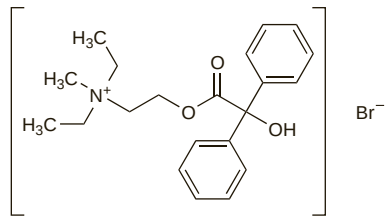
Methylbenactyzium Bromide *(rINN)*

Benactyzine Methobromide; Bromuro de metilbenacticio; Methylbenactyzii Bromidum; Méthylbénactyzium, Bromure de. Diethyl(2-hydroxyethyl)methylammonium bromide benzilate.

Метилбенактизия Бромид

$C_{21}H_{28}BrNO_3$ = 422.4.

CAS — 3166-62-9.



Pharmacopoeias. In *Jpn.*

Profile
Methylbenactyzium bromide, a derivative of benactyzine (p.383), is an antimuscarinic with effects similar to those of atropine (p.1219). It has been given orally for the treatment of gastrointestinal spasm and nocturnal enuresis.

Preparations
Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Austria:*** Anxiolit plus.

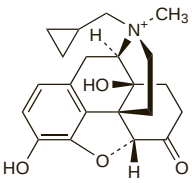
Methylnaltrexone Bromide *(USAN, rINN)*

Bromure de Méthylnaltrexone; Bromuro de Metilnaltrexona; Methylnaltrexonii Bromidum; MRZ-2663BR; Naltrexone Methobromide. (17*RS*)-17-(Cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxy-17-methyl-6-oxomorphinanium bromide.

Метинальтрексон Бромид

$C_{21}H_{26}BrNO_4$ = 436.3.

CAS — 83387-25-1 (methylnaltrexone); 73232-52-7 (methylnaltrexone bromide).



Br⁻ and epimer at N^+

Profile
Methylnaltrexone bromide is a selective peripherally acting antagonist of opioid μ-receptors that is used for the treatment of opioid-induced constipation in patients receiving palliative care for advanced illness, when response to usual laxative therapy is insufficient. It is also being studied for treatment of opioid-induced urinary retention and postoperative ileus.

For the treatment of opioid-induced constipation methylnaltrexone bromide may be given once every 48 hours by subcutaneous injection in the following doses according to body-weight: patients less than 38 kg in weight, 150 micrograms/kg; 38 to 62 kg, 8 mg; 62 to 114 kg, 12 mg; more than 114 kg, 150 micrograms/kg.

◊ References.

1. Yuan CS. Methylnaltrexone mechanisms of action and effects on opioid bowel dysfunction and other opioid adverse effects. *Ann Pharmacother* 2007; **41:** 984–93.
2. Reichle FM, Conzen PF. Methylnaltrexone, a new peripheral μ-receptor antagonist for the prevention and treatment of opioid-induced extracerebral side effects. *Curr Opin Investig Drugs* 2008; **9:** 90–100.
3. Thomas J, *et al.* Methylnaltrexone for opioid-induced constipation in advanced illness. *N Engl J Med* 2008; **358:** 2332–43.

Preparations
Proprietary Preparations (details are given in Part 3)
UK: Relistor; ***USA:*** Relistor.

Metoclopramide *(BAN, rINN)*

Metoclopramida; Métoclopramide; Metoclopramidum; Metoklopramid; Metoklopramidas; Metoklopramidi. 4-Amino-5-chloro-*N*-(2-diethylaminoethyl)-2-methoxybenzamide.

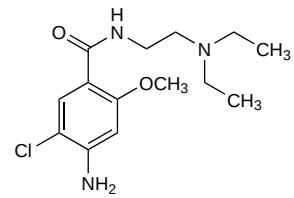
Метоклопрамид

$C_{14}H_{22}ClN_3O_2$ = 299.8.

CAS — 364-62-5.

ATC — A03FA01.

ATC Vet — QA03FA01.



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

Ph. Eur. 6.2 (Metoclopramide). A white or almost white, fine powder. It exhibits polymorphism. Practically insoluble in water; sparingly soluble to slightly soluble in alcohol; slightly soluble in dichloromethane.

Metoclopramide Hydrochloride *(BANM, USAN, rINNM)*

AHR-3070-C; DEL-1267; Hidrocloruro de metoclopramida; Métoclopramide, chlorhydrate de; Metoclopramidi hydrochloridum; Metoclopramidi Hydrochloridum Monohydricum; Metoklopramid Hidroklorür; Metoklopramid-hidroklorid; Metoklopramid-hydrochlorid monohydrát; Metoklopramidhydroklorid; Metoklopramidihydrokloridi; Metoklopramido hidrochloridas; Metoklopramidu chlorowodorek; MK-745.

Метоклопрамида Гидрохлорид

$C_{14}H_{22}ClN_3O_2$,HCl,H_2O = 354.3.

CAS — 7232-21-5 (anhydrous metoclopramide hydrochloride); 54143-57-6 (metoclopramide hydrochloride monohydrate); 2576-84-3 (anhydrous metoclopramide dihydrochloride).

ATC — A03FA01.

ATC Vet — QA03FA01.

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

Ph. Eur. 6.2 (Metoclopramide Hydrochloride). A white or almost white, crystalline powder or crystals. Very soluble in water; freely soluble in alcohol; sparingly soluble in dichloromethane. A 10% solution in water has a pH of 4.5 to 6.0. Protect from light.

USP 31 (Metoclopramide Hydrochloride). A white or practically white, odourless or practically odourless, crystalline powder.