Magnesium Oxide

E530; Magnesii oxidum; Magnesio, óxido de; Magnésium, oxyde de; Magnesiumoksidi; Magnesiumoxid; Magnezu tlenek; Magnezyum Oksit; Magnio oksidas; Nehéz magnézium; Oxid hořečnatý.

Магния Оксид

MgO = 40.30.

CAS — 1309-48-4.

ATC — A02AA02; A06AD02; A12CC10.

ATC Vet — QA02AA02; QA06AD02; QA12CC10.

Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.* Some pharmacopoeias include a single monograph that permits both the light and heavy varieties while some have 2 separate monographs for the 2 varieties.

Ph. Eur. 6.2 (Magnesium Oxide, Heavy; Magnesii Oxidum Ponderosum). A fine, white or almost white powder. 15 g has an apparent volume before settling of not more than 60 mL. Practically insoluble in water; dissolves in dilute acids with at most slight effervescence.

Ph. Eur. 6.2 (Magnesium Oxide, Light; Magnesii Oxidum Leve). A fine, white or almost white, amorphous powder. 15 g has an apparent volume before settling of at least 100 mL. Practically insoluble in water; dissolves in dilute acids with at most slight effervescence.

USP 31 (Magnesium Oxide). A very bulky, white powder, or a relatively dense, white powder, or a granulated powder. Practically insoluble in water; insoluble in alcohol; soluble in dilute acids. Store in airtight containers.

Profile

Magnesium oxide is an antacid with general properties similar to those of magnesium hydroxide (above). It is given in usual oral doses of about 400 mg. It is often given with aluminium-containing antacids such as aluminium hydroxide, which counteract its laxative effect.

Magnesium oxide has been used for its osmotic laxative properties in bowel preparation; oral doses of 3.5 g are given for this purpose, combined with bisacodyl or sodium picosulfate.

Magnesium oxide is also used as a magnesium supplement in deficiency states in oral doses of up to 800 mg (20 mmol) daily. It is also used as a food additive.

Preparations

USP 31: Alumina, Magnesium Carbonate, and Magnesium Oxide Tablets; Aromatic Cascara Fluidextract; Aspirin, Alumina, and Magnesium Oxide Tablets; Citric Acid, Magnesium Oxide, and Sodium Carbonate Irrigation; Magnesium Oxide Capsules; Magnesium Oxide Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Magneforte†; Polvo Roge; SG 33; ***Austria:*** Magnonorm; Magnotab; ***Denm.:*** Salilax; ***Fr.:*** Mag 2 Junior; Magocean; Sargemag; Thalamag; ***Ger.:*** Biolectra Magnesium 240; Biolectra Magnesium 365; Magium; Magnesium Diasporal; Magnesium Tonil; Magnetrans extra; Magnetrans forte; Magno Sanol; ***Hung.:*** Magnosolv; ***NZ:*** Mylanta Effervescent†; ***S.Afr.:*** Solumag; ***Swed.:*** Salilax; ***Thai.:*** Magoral; ***Turk.:*** Magnezi Kalsine; ***USA:*** Mag-200; Mag-Caps; Mag-Ox; Maox; Uro-Mag.

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

Used as an adjunct in: ***Arg.:*** Aspirina; Bufferin†; ***Braz.:*** Bufferin; ***Canad.:*** Aspirin with Stomach Guard; Bufferin; Tri-Buffered ASA; ***Ital.:*** Bufferin†; ***Pol.:*** Aspimag; Cardiofil; ***USA:*** Adprin-B; Bufferin; Cama Arthritis Pain Reliever; Extra Strength Bayer Plus.

Magnesium Trisilicate

E553(a); Magnesii trisilicas; Magnesio, trisilicato de; Magnésium, trisilicate de; Magnesiumtrisilikaatti; Magnesiumtrisilikat; Magnézium-trisziliká t; Magnezyum Trisilikat; Magnio trisilikatas; Trikřemičitan hořečnatý.

Магния Трисиликат

CAS — 14987-04-3 (anhydrous magnesium trisilicate); 39365-87-2 (magnesium trisilicate hydrate).

Description. Magnesium trisilicate is a hydrated magnesium silicate. The code E553(a) has been applied to both magnesium silicate and to magnesium trisilicate.

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

Ph. Eur. 6.2 (Magnesium Trisilicate). It has a variable composition corresponding approximately to the formula $Mg_2Si_3O_8.xH_2O$ containing not less than 29% of magnesium oxide and not less than the equivalent of 65% of silicon dioxide, both calculated with reference to the ignited substance. A white or almost white powder. Practically insoluble in water and in alcohol.

USP 31 (Magnesium Trisilicate). A compound of magnesium oxide and silicon dioxide with varying proportions of water. It contains not less than 20% of magnesium oxide and not less than 45% of silicon dioxide. A fine, white, odourless, powder, free from grittiness. Insoluble in water and in alcohol. It is readily decomposed by mineral acids.

Profile

Magnesium trisilicate is a hydrated magnesium silicate. It is an antacid with general properties similar to those of magnesium hydroxide (p.1743). It may be given in typical oral doses of up to about 500 mg as required, although higher doses have been given.. When given orally it reacts more slowly with hydrochloric acid in the stomach than magnesium hydroxide. Magnesium trisilicate is often given with aluminium-containing antacids such as aluminium hydroxide, which counteract its laxative effect.

Magnesium trisilicate is also used as a food additive and as a pharmaceutical excipient.

Effects on the kidneys. The formation of renal calculi containing silica is unusual, but has been reported in a small number of patients. In most of these cases, stone formation was attributed to the prolonged, and sometimes excessive, intake of antacids that contained magnesium trisilicate.[1,2]

1. Haddad FS, Kouyoumdjian A. Silica stones in humans. *Urol Int* 1986; **41:** 70–6.
2. Lee M-H, *et al.* Silica stone—development due to long time oral trisilicate intake. *Scand J Urol Nephrol* 1993; **27:** 267–9.

Preparations

BP 2008: Compound Magnesium Trisilicate Oral Powder; Compound Magnesium Trisilicate Tablets; Magnesium Trisilicate Mixture;
USP 31: Alumina and Magnesium Trisilicate Oral Suspension; Alumina and Magnesium Trisilicate Tablets; Magnesium Trisilicate Tablets.

Proprietary Preparations (details are given in Part 3)

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

Used as an adjunct in: ***Swed.:*** Deltison.

Manna

Maná; Manne en Larmes.

Манна

Profile

Manna is the dried exudation from the bark of the European flowering ash, *Fraxinus ornus* (Oleaceae), containing about 40 to 60% of mannitol (p.1330). It has been used as an osmotic laxative.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: *Cz.:* Dr Theiss Rheuma Creme†; Dr Theiss Schweden Krauter; Naturland Grosser Swedenbitter†; ***Ger.:*** florabio Mann-Feigen-Sirup mit Senna†; florabio Manna-Feigen; Infi-tract†.

Mebeverine Hydrochloride *(BANM, USAN, rINNM)*

CSAG-144; Hidrocloruro de mebeverina; Mébévérine, chlorhydrate de; Mebeverini hydrochloridum. 4-[Ethyl(4-methoxy-α-methylphenethyl)amino]butyl veratrate hydrochloride.

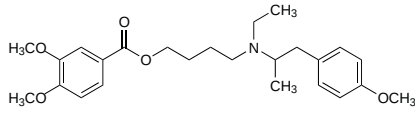
Мебеверина Гидрохлорид

$C_{25}H_{35}NO_5.HCl$ = 466.0.

CAS — 3625-06-7 (mebeverine); 2753-45-9 (mebeverine hydrochloride).

ATC — A03AA04.

ATC Vet — QA03AA04.



(mebeverine)

Pharmacopoeias. In *Br.*

BP 2008 (Mebeverine Hydrochloride). A white or almost white crystalline powder. Very soluble in water; freely soluble in alcohol; practically insoluble in ether. A 2% solution in water has a pH of 4.5 to 6.5. Store in airtight containers at a temperature not exceeding 30°. Protect from light.

Adverse Effects and Precautions

Although adverse effects appear rare, gastrointestinal disturbances, dizziness, headache, insomnia, anorexia, and decreased heart rate have been reported in patients receiving mebeverine. Cases of hypersensitivity, including erythematous rash, urticaria, and angioedema, have also been reported. Mebeverine should be avoided in patients with paralytic ileus. Based on theoretical concerns, it should be used with care in patients with marked hepatic or renal impairment, and those with cardiac disorders such as heart block.

Cystic fibrosis. A 24-year-old man with cystic fibrosis, given mebeverine hydrochloride for lower abdominal pain and constipation, was found to have a perforated stercoral ulcer with generalised peritonitis.[1] It was suggested that mebeverine produced colonic stasis, which predisposed the patient to ulceration,[1] but the manufacturers[2] considered that the development of constipation and distal intestinal syndrome (meconium ileus equivalent) in this patient precipitated the development of stercoral ulceration. It was recommended[1] that antispasmodics such as mebeverine should not be used for the symptomatic treatment of distal intestinal syndrome in cystic fibrosis.

1. Hassan W, Keaney N. Mebeverine-induced perforated colon in distal intestinal syndrome of cystic fibrosis. *Lancet* 1990; **335:** 1225.
2. Whitehead AM. Perforation of colon in distal intestinal syndrome of cystic fibrosis. *Lancet* 1990; **336:** 446.

Porphyria. Mebeverine hydrochloride is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

Pharmacokinetics

Mebeverine is rapidly absorbed after oral doses with peak plasma concentrations occurring in 1 to 3 hours. It is 75% bound to albumin in plasma. Mebeverine is completely metabolised by hydrolysis to veratric acid and mebeverine alcohol, the latter of which may then be conjugated. The metabolites are excreted in the urine.

Uses and Administration

Mebeverine hydrochloride is an antispasmodic with a direct action on the smooth muscle of the gastrointestinal tract. It is used in conditions such as irritable bowel syndrome (p.1699) in a usual oral dose of 135 mg three times daily before meals; 100 mg three times daily has also been used. A modified-release preparation is also available, taken as 200 mg twice daily. The embonate is also used for oral liquid preparations in a dose equivalent to 150 mg of the hydrochloride three times daily. The *BNFC* suggests that the following hydrochloride-equivalent doses may be given three times daily, based on age:

- 25 mg for those aged 3 to 4 years
- 50 mg for those 4 to 8 years
- 100 mg for those 8 to 10 years
- 135 to 150 mg for those over 10 years

Preparations

BP 2008: Mebeverine Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Duspatalin; ***Austral.:*** Colese; Colofac; ***Austria:*** Colofac; ***Belg.:*** Duspatalin; Spasmonal†; ***Braz.:*** Duspatalin; ***Chile:*** Doloverina; Duspatal; Evadol; Meditoina; ***Cz.:*** Duspatalin; ***Denm.:*** Duspatalin; ***Fr.:*** Colopriv; Duspatalin; Spasmopriv; ***Ger.:*** Duspatal; Mebemerck; ***Gr.:*** Duspatalin; Gastromins†; ***Hong Kong:*** Duspatalin; ***Hung.:*** Duspatalin; ***India:*** Colospa; ***Indon.:*** Duspatalin; Irbosyd; ***Irl.:*** Colofac; ***Israel:*** Colotal; ***Ital.:*** Duspatal; ***Malaysia:*** Duspatalin; Lezpain; Mebetin; ***Mex.:*** Arluy; ***Neth.:*** Duspatal; ***NZ:*** Colofac; ***Philipp.:*** Duspatalin; ***Pol.:*** Duspatalin; ***Port.:*** Duspatal; ***Rus.:*** Duspatalin (Дюспаталин); ***S.Afr.:*** Bevispas; Colofac; ***Singapore:*** Duspatalin; Mebetin; ***Spain:*** Duspatalin; ***Switz.:*** Duspatalin; ***Thai.:*** Colofac; Duspatin; Menosor; ***Turk.:*** Duspatalin; Duspaverin; ***UK:*** Colofac; Equilon†; IBS Relief†.

Multi-ingredient: *Hong Kong:* Fybogel Mebeverine†; ***Irl.:*** Fybogel Mebeverine; ***UK:*** Fybogel Mebeverine.

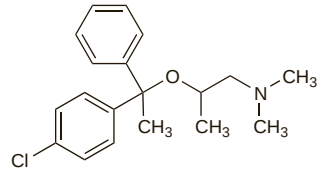
Mecloxamine Citrate *(rINNM)*

Citrato de mecloxamina; Mécloxamine, Citrate de; Mecloxamini Citras. 2-[1-(4-Chlorophenyl)-1-phenylethoxy]-*N*,*N*-dimethyl-1-propanamine citrate.

Меклоксамина Цитрат

$C_{19}H_{24}ClNO.C_6H_8O_7$ = 510.0.

CAS — 5668-06-4 (mecloxamine); 56050-03-4 (mecloxamine citrate).



(mecloxamine)

Profile

Mecloxamine citrate is reported to have antimuscarinic properties and has been used for its antiemetic action in antimigraine preparations.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: *Austria:* Avamigran; ***Turk.:*** Avmigran.

Mepenzolate Bromide *(BAN, rINN)*

Bromuro de mepenzolato; Mepentsolaattibromidi; Mepenzolatbromid; Mépenzolate, Bromure de; Mepenzolate Methylbromide; Mepenzolati Bromidum; Mepenzolone Bromide. 3-Benziloyloxy-1,1-dimethylpiperidinium bromide.

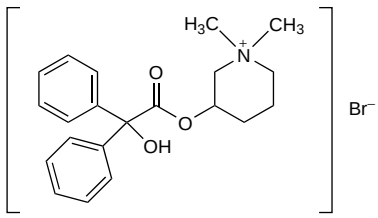
Мепензолата Бромид

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

CAS — 25990-43-6 (mepenzolate); 76-90-4 (mepenzolate bromide).

ATC — A03AB12.

ATC Vet — QA03AB12.



Pharmacopoeias. In *Jpn.*

Profile

Mepenzolate bromide is a quaternary ammonium antimuscarinic with peripheral actions similar to those of atropine (p.1219). It has been used in the relief of gastrointestinal disorders associated with smooth muscle spasm and as an adjunct in the treatment of peptic ulcer disease. Up to 200 mg daily may be given orally in divided doses.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Trancolon†; ***Swed.:*** Cantil†; ***USA:*** Cantil.

Multi-ingredient: ***Jpn:*** Trancolon P†.

Mesalazine *(BAN, rINN)*

5-Aminosalicylic Acid; 5-ASA; Fisalamine; Mesalamine *(USAN)*; Mesalatsiini; Mesalazin; Mesalazina; Mesalazinas; Mésalazine; Mesalazinum. 5-Amino-2-salicylic acid.

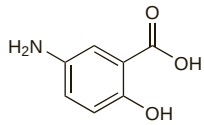
Месалазин

$C_7H_7NO_3$ = 153.1.

CAS — 89-57-6.

ATC — A07EC02.

ATC Vet — QA07EC02.



NOTE. Distinguish from 4-aminosalicylic acid (Aminosalicylic Acid, p.201) which is used in the treatment of tuberculosis.

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

Ph. Eur. 6.2 (Mesalazine). An almost white or light grey or light pink powder or crystals. Very slightly soluble in water; practically insoluble in alcohol. It dissolves in dilute solutions of alkali hydroxides and in dilute hydrochloric acid. Store in airtight containers. Protect from light.

USP 31 (Mesalamine). Light tan to pink needle-shaped crystals, odourless or with a slight characteristic odour. The colour may darken on exposure to air. Slightly soluble in water; very slightly soluble in dehydrated alcohol, in acetone, and in methyl alcohol; practically insoluble in butyl alcohol, in chloroform, in dichloromethane, in ether, in ethyl acetate, in *n*-hexane, and in propyl alcohol; soluble in dilute hydrochloric acid and in dilute alkali hydroxides. A 2.5% suspension in water has a pH of 3.5 to 4.5. Store in airtight containers. Protect from light.

Adverse Effects and Precautions

Mesalazine may cause headache and gastrointestinal disturbances, such as nausea, diarrhoea, and abdominal pain. Hypersensitivity reactions may occasionally occur. Some patients may experience exacerbation of symptoms of colitis. There are some reports of myocarditis, pericarditis, pancreatitis, interstitial nephritis, nephrotic syndrome, allergic lung reaction, increased liver enzyme values, hepatitis, lupus-like syndrome, skin reactions, alopecia, peripheral neuropathy, myalgia, and arthralgia. There have been rare reports of blood disorders including aplastic anaemia, agranulocytosis, leucopenia, neutropenia, thrombocytopenia, and methaemoglobinaemia.

Mesalazine should not be given to patients with severe renal or hepatic impairment, or salicylate hypersensitivity. It should be used with caution in the elderly, and in mild to moderate renal or hepatic impairment, active peptic ulceration, or sulfasalazine allergy.

If a blood dyscrasia is suspected treatment should be stopped immediately and a blood count performed. Patients or their carers should be told how to recognise signs of blood toxicity and should be advised to seek immediate medical attention if symptoms such as fever, sore throat, mouth ulcers, bruising, or bleeding develop. It is recommended that renal function is monitored before and during therapy (see Effects on the Kidneys, below).

◊ Many of the adverse effects associated with sulfasalazine (sulfapyridine linked to mesalazine) therapy have been attributed to the sulfapyridine moiety and most patients unable to tolerate sulfasalazine because of hypersensitivity or adverse reactions can be transferred to mesalazine without adverse effects occurring.[1-4] However, a small number of patients also have adverse effects while taking mesalazine and these are often very similar to those seen with sulfasalazine.[1-4] They may include nausea, abdominal discomfort or pain, exacerbation of diarrhoea, headache, fever, and rashes. Mesalazine is not generally associated with sulfasalazine's adverse effects on sperm (although there has been a case of reversible male infertility attributed to mesalazine—see under Sulfasalazine, p.1774). An analysis of adverse reactions reported to the UK CSM between 1991 and 1998 found no evidence of a significant difference in the frequency of serious adverse effects for mesalazine and sulfasalazine in the treatment of inflammatory bowel disease.[5] Reports of pancreatitis and interstitial nephritis (see Effects on the Kidneys, below), were more common with mesalazine. However, it has been pointed out that 80% of patients intolerant to sulfasalazine will tolerate mesalazine without problems.[6]

Mesalazine therapy should be started cautiously in patients with a history of sulfasalazine **hypersensitivity** and it should be withdrawn if signs of sensitivity develop or if there is diarrhoea or rectal bleeding. It has been suggested[2] that patients with a history of sulfasalazine hypersensitivity should be given test doses of mesalazine before starting a full course.

1. Dew MJ, *et al.* Treatment of ulcerative colitis with oral 5-aminosalicylic acid in patients unable to take sulphasalazine. *Lancet* 1983; **ii:** 801.
2. Campieri M, *et al.* 5-Aminosalicylic acid as rectal enema in ulcerative colitis patients unable to take sulphasalazine. *Lancet* 1984; **i:** 403.
3. Donald IP, Wilkinson SP. The value of 5-aminosalicylic acid in inflammatory bowel disease for patients intolerant or allergic to sulphasalazine. *Postgrad Med J* 1985; **61:** 1047–8.
4. Rao SS, *et al.* Clinical experience of the tolerance of mesalazine and olsalazine in patients intolerant of sulphasalazine. *Scand J Gastroenterol* 1987; **22:** 332–6.
5. Ransford RAJ, Langman MJS. Sulphasalazine and mesalazine: serious adverse reactions re-evaluated on the basis of suspected adverse reaction reports to the Committee on Safety of Medicines. *Gut* 2002; **51:** 536–9.
6. D'Haens G, van Bodegraven AA. Mesalazine is safe for the treatment of IBD. *Gut* 2004; **53:** 155.

Breast feeding. The concentrations of mesalazine in maternal plasma and breast milk in a woman taking 500 mg three times daily, were 410 and 110 nanograms/mL respectively.[1] Although it was considered that the amount of mesalazine distributed into breast milk was small and that it was safe during breast feeding,[2,3] maternal use of mesalazine 500 mg suppositories twice daily has been associated with watery diarrhoea in a breast-fed infant[2] and for this reason the American Academy of Pediatrics considers that mesalazine should be given with caution to breast-feeding mothers.[4]

1. Jenss H, *et al.* 5-Aminosalicylic acid and its metabolite in breast milk during lactation. *Am J Gastroenterol* 1990; **85:** 331.
2. Nelis GF. Diarrhoea due to 5-aminosalicylic acid in breast milk. *Lancet* 1989; **i:** 383.
3. Klotz U, Harings-Kaim A. Negligible excretion of 5-aminosalicylic acid in breast milk. *Lancet* 1993; **342:** 618–19.
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 28/02/06)

Effects on the blood. Although uncommon, mesalazine-associated adverse effects on the blood have been reported, including thrombocytopenia,[1,2] neutropenia,[3] severe aplastic anaemia,[4,5] and pancytopenia.[6] In July 1995 the UK CSM stated that it had been notified of 49 haematological reactions suspected of being associated with mesalazine,[7] including 5 reports of aplastic anaemia, 1 of agranulocytosis, 11 of leucopenia, and 17 of thrombocytopenia. There had been 3 fatalities. They recommended a blood count and immediate withdrawal of the drug if a dyscrasia was suspected. Intensive immunosuppressive treatment has been used in the management of mesalazine-associated aplastic anaemia.[5,8]

1. Daneshmend TK. Mesalazine-associated thrombocytopenia. *Lancet* 1991; **337:** 1297–8.
2. Farrell RJ, *et al.* Mesalamine-associated thrombocytopenia. *Am J Gastroenterol* 1999; **94:** 2304–6.
3. Wyatt S, *et al.* Filgrastim for mesalazine-associated neutropenia. *Lancet* 1993; **341:** 1476.
4. Abboudi ZH, *et al.* Fatal aplastic anaemia after mesalazine. *Lancet* 1994; **343:** 542.
5. Otsubo H, *et al.* Mesalazine-associated severe aplastic anemia successfully treated with antithymocyte globulin, cyclosporine and granulocyte colony-stimulating factor. *Int J Hematol* 1998; **68:** 445–8.
6. Kotanagi H, *et al.* Pancytopenia associated with 5-aminosalicylic acid use in a patient with Crohn's disease. *J Gastroenterol* 1998; **33:** 571–4.
7. Committee on Safety of Medicines/Medicines Control Agency. Blood dyscrasias and mesalazine. *Current Problems* 1995; **21:** 5–6. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2015619&RevisionSelectionMethod=LatestReleased (accessed 15/06/06)
8. Laidlaw ST, Reilly JT. Antilymphocyte globulin for mesalazine-associated aplastic anaemia. *Lancet* 1994; **343:** 981–2.

Effects on the cardiovascular system. Myocarditis associated with chest pain and ECG abnormalities has been reported[1,2] in 2 patients taking mesalazine; 1 patient died in cardiogenic shock.[2] It has been suggested that mesalazine or sulfasalazine should be replaced by glucocorticoids if cardiac symptoms arise during treatment.[2] Pericarditis[3,4] with fever, rash, dyspnoea, pleural and pericardial effusions, and arthritis, has been described, and is considered to constitute a drug-induced lupus-like syndrome. Constrictive pericarditis with an absence of other lupus-like symptoms developed in a patient taking mesalazine for inflammatory bowel disease.[5] Based on reported cases of mesalazine-induced pericarditis, symptoms of this potentially life-threatening adverse effect have tended to arise 2 to 4 weeks after starting mesalazine, although symptom onset may be delayed by concurrent corticosteroid treatment.[6] Mesalazine cardiotoxicity presenting as an acute coronary syndrome, without myocarditis or pericarditis, has also been reported.[7]

1. Agnholt J, *et al.* Cardiac hypersensitivity to 5-aminosalicylic acid. *Lancet* 1989; **i:** 1135.
2. Kristensen KS, *et al.* Fatal myocarditis associated with mesalazine. *Lancet* 1990; **335:** 605.
3. Dent MT, *et al.* Mesalazine induced lupus-like syndrome. *BMJ* 1992; **305:** 159.
4. Lim AG, Hine KR. Fever, vasculitic rash, arthritis, pericarditis, and pericardial effusion after mesalazine. *BMJ* 1994; **308:** 113.
5. Oxentenko AS, *et al.* Constrictive pericarditis in chronic ulcerative colitis. *J Clin Gastroenterol* 2002; **34:** 247–51.
6. Waite RA, Malinowski JM. Possible mesalamine-induced pericarditis: case report and literature review. *Pharmacotherapy* 2002; **22:** 391–4.
7. Amin HE, *et al.* Mesalamine-induced chest pain: a case report. *Can J Cardiol* 2000; **16:** 667–9.

Effects on fertility. For a report of reversible male infertility occurring with mesalazine, see under Sulfasalazine, p.1774.

Effects on the hair. For a report of accelerated loss of scalp hair in 2 patients receiving mesalazine enemas, see under Sulfasalazine, p.1774.

Effects on the kidneys. Between February 1988 and December 1990 the UK CSM[1] received 9 reports of serious nephrotoxic reactions associated with the use of *Asacol*, a modified-release mesalazine preparation. The reactions included 4 cases of interstitial nephritis, 3 of severe renal failure, and 2 cases of nephrotic syndrome. A subsequent case report[2] indicated that by September 1998 the number of such reports for mesalazine totalled 104, including 35 cases of interstitial nephritis. The authors considered that monitoring of renal function was required in patients receiving mesalazine. A protocol for such monitoring was subsequently suggested,[3] and a similar protocol has been adopted in UK licensing information for mesalazine, with serum creatinine being estimated:

- before treatment
- every 3 months for the first year
- every 6 months for the next 4 years
- annually thereafter

The nephrotic syndrome[4] and interstitial nephritis[5] have also been reported with sulfasalazine, and interstitial nephritis with olsalazine (see p.1752). A large UK epidemiologic study found no difference in risk of renal disease between mesalazine and sulfasalazine. The study also concluded that the risk of renal disease associated with mesalazine and related compounds is low and may be partly attributable to the underlying disease.[6] Overall nephrotoxicity has been estimated to occur in about 1 in 4000 UK patients per year taking aminosalicylate-based therapy.[7]

1. Committee on Safety of Medicines. Nephrotoxicity associated with mesalazine (Asacol). *Current Problems 30* 1990. Also available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024448&RevisionSelectionMethod=LatestReleased (accessed 02/07/08)
2. Popoola J, *et al.* Late onset interstitial nephritis associated with mesalazine treatment. *BMJ* 1998; **317:** 795–7.
3. Corrigan G, Stevens PE. Review article: interstitial nephritis associated with the use of mesalazine in inflammatory bowel disease. *Aliment Pharmacol Ther* 2000; **14:** 1–6.
4. Barbour VM, Williams PF. Nephrotic syndrome associated with sulphasalazine. *BMJ* 1990; **301:** 818.
5. Dwarakanath AD, *et al.* Sulphasalazine induced renal failure. *Gut* 1992; **33:** 1006–1007.