tion of acute and delayed nausea and vomiting associated with highly emetogenic or moderately emetogenic cancer chemotherapy (for details, see Administration, below).

For the prevention of postoperative nausea and vomiting a single oral dose of aprepitant 40 mg may be given within the 3 hours before induction of anaesthesia.

Administration. Licensed product information for aprepitant suggests the following 4-day regimen for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cancer chemotherapy:

- day 1: aprepitant 125 mg (given 1 hour before chemotherapy) with oral dexamethasone 12 mg and intravenous ondansetron 32 mg (both 30 minutes before chemotherapy)
- days 2 and 3: aprepitant 80 mg with oral dexamethasone 8 mg in the morning
- day 4: oral dexamethasone 8 mg in the morning.

In patients receiving moderately emetogenic chemotherapy, a 3-day regimen has been suggested as follows:

- day 1: aprepitant 125 mg (given 1 hour before chemotherapy) with oral dexamethasone 12 mg (30 minutes before chemotherapy); ondansetron is given in 2 doses of 8 mg by mouth, one taken 30 to 60 minutes before chemotherapy, and one taken 8 hours after the first dose
- days 2 and 3: aprepitant 80 mg in the morning.

Administration in renal impairment. A study in 8 patients with severe renal impairment (24-hour creatinine clearance less than 30 mL/minute per 1.73 m^2) and 8 patients with end-stage renal disease requiring haemodialysis found that pharmacokinetic parameters of aprepitant were not sufficiently different from those in 16 matched controls to warrant dosage adjustment in renal impairment.[1] Licensed product information concurs with this.

1. Bergman AJ, *et al.* Effect of impaired renal function and haemodialysis on the pharmacokinetics of aprepitant. *Clin Pharmacokinet* 2005; **44:** 637–47.

Nausea and vomiting. Studies[1-8] and reviews.[9,10]

1. Campos D, *et al.* Prevention of cisplatin-induced emesis by the oral neurokinin-1 antagonist, MK-869, in combination with granisetron and dexamethasone or with dexamethasone alone. *J Clin Oncol* 2001; **19:** 1759–67.
2. Poli-Bigelli S, *et al.* Addition of the neurokinin 1 receptor antagonist aprepitant to standard antiemetic therapy improves control of chemotherapy-induced nausea and vomiting: results from a randomized, double-blind, placebo-controlled trial in Latin America. *Cancer* 2003; **97:** 3090–8.
3. de Wit R, *et al.* Addition of the oral NK antagonist aprepitant to standard antiemetics provides protection against nausea and vomiting during multiple cycles of cisplatin-based chemotherapy. *J Clin Oncol* 2003; **21:** 4105–11.
4. Hesketh PJ, *et al.* The oral neurokinin-1 antagonist aprepitant for the prevention of chemotherapy-induced nausea and vomiting: a multinational, randomized, double-blind, placebo-controlled trial in patients receiving high-dose cisplatin—the Aprepitant Protocol 052 Study Group. *J Clin Oncol* 2003; **21:** 4112–19.
5. Warr DG, *et al.* Efficacy and tolerability of aprepitant for the prevention of chemotherapy-induced nausea and vomiting in patients with breast cancer after moderately emetogenic chemotherapy. *J Clin Oncol* 2005; **23:** 2822–30. Correction. *ibid.*; 5851. [dosage error in abstract]
6. Warr DG, *et al.* The oral NK antagonist aprepitant for the prevention of acute and delayed chemotherapy-induced nausea and vomiting: pooled data from 2 randomised, double-blind, placebo controlled trials. *Eur J Cancer* 2005; **41:** 1278–85.
7. Herrstedt J, *et al.* Efficacy and tolerability of aprepitant for the prevention of chemotherapy-induced nausea and emesis over multiple cycles of moderately emetogenic chemotherapy. *Cancer* 2005; **104:** 1548–55.
8. Diemunsch P, *et al.* Preventing postoperative nausea and vomiting: post hoc analysis of pooled data from two randomized active-controlled trials of aprepitant. *Curr Med Res Opin* 2007; **23:** 2559–65.
9. Dando TM, Perry CM. Aprepitant: a review of its use in the prevention of chemotherapy-induced nausea and vomiting. *Drugs* 2004; **64:** 777–94.
10. Massaro AM, Lenz KL. Aprepitant: a novel antiemetic for chemotherapy-induced nausea and vomiting. *Ann Pharmacother* 2005; **39:** 77–85.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Emend; ***Austral.:*** Emend; ***Belg.:*** Emend; ***Braz.:*** Emend; ***Cz.:*** Emend; ***Denm.:*** Emend; ***Fin.:*** Emend; ***Fr.:*** Emend; ***Ger.:*** Emend; ***Gr.:*** Emend; ***Hong Kong:*** Emend; ***Hung.:*** Emend; ***Irl.:*** Emend; ***Ital.:*** Emend; ***Malaysia:*** Emend; ***Norw.:*** Emend; ***NZ:*** Emend; ***Port.:*** Emend; ***Rus.:*** Emend (Эмена); ***S.Afr.:*** Emend; ***Singapore:*** Emend; ***Spain:*** Emend; ***Swed.:*** Emend; ***Switz.:*** Emend; ***Thai.:*** Emend; ***UK:*** Emend; ***USA:*** Emend; ***Venez.:*** Emend.

Attapulgite

Atapulgit; Atapulgita.

Аттапульгит

CAS — 1337-76-4; 12174-11-7.

ATC — A07BC04.

ATC Vet — QA07BC04.

Pharmacopoeias. In *Br.*

Activated attapulgite is included in *Br.*, *It.*, and *US*. Colloidal activated attapulgite is included in *US*.

BP 2008 (Attapulgite). A purified native hydrated aluminium magnesium silicate essentially consisting of the clay mineral palygorskite. A light, cream or buff, very fine powder, free or almost free from gritty particles. A 5% suspension in water has a pH of 7.0 to 9.5.

BP 2008 (Activated Attapulgite). Attapulgite that has been carefully heated to increase its adsorptive capacity.

USP 31 (Activated Attapulgite). Processed native aluminium magnesium silicate which has been carefully heated. It is a cream-coloured, micronised, nonswelling powder, free from gritty particles. Insoluble in water.

USP 31 (Colloidal Activated Attapulgite). A native aluminium magnesium silicate that has been purified. It is a cream-coloured, micronised, nonswelling powder, free from gritty particles. Insoluble in water. A 10% suspension in water has a pH of 7.0 to 9.5.

◊ NOTE. Another native aluminium magnesium silicate is described on p.2141.

Profile

Attapulgite is highly adsorbent and is used in a wide range of products including fertilisers, pesticides, and pharmaceuticals. Activated attapulgite is an adsorbent antidiarrhoeal used as an adjunct in the management of diarrhoea (p.1694) in a daily dose of up to 9 g orally in divided doses.

Preparations

Proprietary Preparations (details are given in Part 3)

Belg.: Actapulgite; ***Canad.:*** Fowlers; Kaopectate; ***Fr.:*** Actapulgite; ***Hong Kong:*** Gastrosorb; ***Indon.:*** Biodiar; Enterogit; Kaotate; New Diatabs; Teradi; ***Malaysia:*** Entox-P†; ***Philipp.:*** Polymagma; ***Rus.:*** Neointestopan (Неоинтестопан); ***Switz.:*** Actapulgite; ***Thai.:*** Entox-P†; ***Turk.:*** Diyasorb; ***UAE:*** Kaptin II; ***USA:*** Diasorb; Kaopectate Advanced Formula†; Kaopectate Maximum Strength; Rheaban Maximum Strength†; ***Venez.:*** Streptomagma.

Multi-ingredient: *Arg.:* Enterobacticel; ***Austral.:*** Diareze; ***Braz.:*** Diazol; Dispeptrin; ***Chile:*** Diaren; Diarfin†; Entero Micinovo; Enterol; Liracol; Nifurat†; ***Fr.:*** Gastropulgite; Mucipulgite; ***Hong Kong:*** Enterocin Compound; ***Indon.:*** Andikap; Arcapec; Diagit; Entrogard; Fitodiar; Licopec; Molagit; Neo Diastop; Neo Entrostop; Neo Koniform; ***Ital.:*** Streptomagma; ***S.Afr.:*** Kantrexil; ***Switz.:*** Gastropulgite†; Mucipulgite†; ***Turk.:*** Streptomagma; ***UK:*** Diocalm Dual Action; ***Venez.:*** Micyn-2; Mycin-2†; Strediazin c Atapulguita†; Streptomagma.

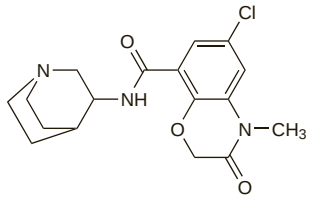
Azasetron Hydrochloride *(rINNM)*

Azasétron, Chlorhydrate d'; Azasetroni Hydrochloridum; Hidrocloruro de azasetrón; Nazasetron Hydrochloride; Y-25130. (±)-6-Chloro-3,4-dihydro-4-methyl-3-oxo-*N*-3-quinuclidinyl-2*H*-1,4-benzoxazine-8-carboxamide hydrochloride.

Азасетрона Гидрохлорид

$C_{17}H_{20}ClN_3O_3$,HCl = 386.3.

CAS — 123040-69-7 (azasetron); 141922-90-9 (azasetron hydrochloride).



(azasetron)

Profile

Azasetron is a 5-HT_3 antagonist with general properties similar to those of ondansetron (p.1756). It is used as an antiemetic in the management of nausea and vomiting induced by cytotoxic therapy. Azasetron hydrochloride is given in a usual dose of 10 mg once daily by mouth or intravenously.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Serotone†; ***Jpn:*** Serotone.

Balsalazide Sodium *(BANM, rINNM)*

Balsalazida sódica; Balsalazide Disodium *(USAN)*; Balsalazide Sodique; Balsalazine Disodium; BX-661A; Natrii Balsalazidum. 5-[4-(2-Carboxyethylcarbamoyl)phenylazo]salicylic acid, disodium salt, dihydrate.

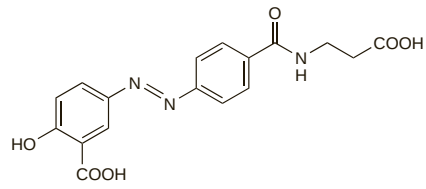
Натрий Балсалазид

$C_{17}H_{13}N_3Na_2O_6$,$2H_2O$ = 437.3.

CAS — 80573-04-2 (balsalazide); 150399-21-6 (balsalazide disodium dihydrate).

ATC — A07EC04.

ATC Vet — QA07EC04.



(balsalazide)

Adverse Effects and Precautions

As for Mesalazine, p.1745. 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 haematotoxicity and should be advised to seek immediate medical attention if symptoms such as fever, sore throat, mouth ulcers, bruising, or bleeding develop. Balsalazide should not be used in patients with severe hepatic impairment or moderate or severe renal impairment; care is required in those with lesser degrees of hepatic or renal impairment, and in asthma, bleeding disorders, or active peptic ulcer disease.

◊ Reviews.

1. Baker DE. Safety of balsalazide therapy in the treatment of inflammatory bowel disease. *Rev Gastroenterol Disord* 2005; **5:** 135–41.

Hypersensitivity. A case of acute pericarditis, cholestasis, and vasculitis resulting from hypersensitivity to balsalazide has been reported.[1] The authors noted similarities to mesalazine-associated pericarditis and lupus-like syndrome (see Effects on the Cardiovascular System, p.1745).

1. Adhiyaman V, *et al.* Hypersensitivity reaction to balsalazide. *BMJ* 2000; **320:** 613.

Pharmacokinetics

Very little of an oral dose of balsalazide is absorbed via the upper gastrointestinal tract, and almost the entire dose reaches its site of action in the colon intact. It is broken down by the colonic bacterial flora into 5-aminosalicylic acid (mesalazine), which is active, and 4-aminobenzoylalanine, which is considered to be an inert carrier. About 25% of the released mesalazine is absorbed and acetylated, as described under mesalazine (p.1746). A small proportion of 4-aminobenzoylalanine is absorbed and acetylated by first-pass metabolism through the liver. The acetylated metabolites are excreted in the urine.

Uses and Administration

Balsalazide consists of mesalazine linked to 4-aminobenzoylalanine via an azo bond. This bond is broken by colonic bacteria, releasing the active mesalazine (p.1746). Balsalazide sodium is given in the treatment of mild to moderate active ulcerative colitis (p.1697), in an oral dose of 2.25 g three times daily until remission or for up to 12 weeks. For maintenance of remission of ulcerative colitis a dose of 1.5 g twice daily is recommended, adjusted as necessary up to 6 g daily. For doses in children, see below.

◊ Reviews.

1. Muijsers RBR, Goa KL. Balsalazide: a review of its therapeutic use in mild-to-moderate ulcerative colitis. *Drugs* 2002; **62:** 1689–705.

Administration in children. Balsalazide sodium is not licensed in the UK for use in children under 18 years of age. However, the *BNFC* suggests that, in those aged 12 years and over, 2.25 g may be given orally three times daily for an acute attack of mild to moderate ulcerative colitis, until remission occurs, or