

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 m²) 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. Studies¹⁻⁸ 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 NK₁ 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 NK₁ 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 (Эмента); **S.Afr.:** Singapore; **Spain:** Emend; **Swed.:** Emend; **Switz.:** Emend; **Thai.:** Emend; **UK:** Emend; **USA:** Emend; **Venez.:** Emend.

Attapulgite

Atapulgit; Atapulgita.

Атталульгит

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 (Attapulgit). 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 Attapulgit). Attapulgit that has been carefully heated to increase its adsorptive capacity.

USP 31 (Activated Attapulgit). 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 Attapulgit). 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

Attapulgit is highly adsorbent and is used in a wide range of products including fertilisers, pesticides, and pharmaceuticals. Activated attapulgit 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.: Actapulgit; **Canad.:** Fowlers; Kaopectate; **Fr.:** Actapulgit; **Hong Kong:** Gastroisorb; **Indon.:** Biodiar; Enterogit; Kaotate; New Diatabs; Tera-di; **Malaysia:** Entox-P†; **Philipp.:** Polymagma; **Rus.:** Neointestopan (Неоинтестопан); **Switz.:** Actapulgit; **Thai.:** Entox-P†; **Turk.:** Diyasorb; **UAE:** Kaplin II; **USA:** Diisorb; Kaopectate Advanced Formula†; Kaopectate Maximum Strength; Rheaban Maximum Strength†; **Venez.:** Streptomagma.

Multi-ingredient: **Arg.:** Enterobactil; **Austral.:** Diareze; **Braz.:** Diazol; Dispeptrin; **Chile:** Diaren; Diarlin†; Entero Micinovo; EnteroL; Liracol; Nifurac†; **Fr.:** Gastropulgit; Mucipulgit; **Hong Kong:** Enterocin Compound; **Indon.:** Andikap; Arcapac; Diagit; Entrogard; Fitodiar; Licopec; Molagit; Neo Diastop; Neo Entropep; Neo Koniform; **Ital.:** Streptomagma; **S.Afr.:** Kantrexil; **Switz.:** Gastropulgit†; Mucipulgit†; **Turk.:** Streptomagma; **UK:** Diocalm Dual Action; **Venez.:** Micyn-2; Mycin-2†; Strediazin c Atapulgit†; Streptomagma.

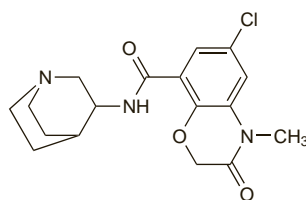
Azasetron Hydrochloride (rINN)

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

Азасетрона Гидрохлорид

C₁₇H₂₀ClN₃O₃.HCl = 386.3.

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



(azasetron)

Profile

Azasetron is a 5-HT₃ 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 Sodium; Balsalazine Disodium; BX-661A; Natrii Balsalazidum. 5-[4-(2-Carboxyethylcarbamoyl)phenylazo]salicylic acid, disodium salt, dihydrate.

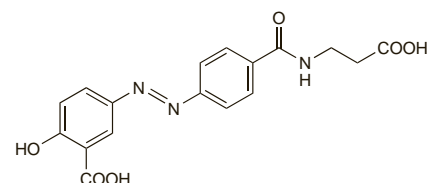
Натрий Балсалазид

C₁₇H₁₃N₃Na₂O₆.2H₂O = 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

for up to 12 weeks. For maintenance, 1.5 g twice daily is recommended, adjusted according to response up to a maximum of 6 g daily.

In the USA, licensed doses in children aged 5 to 17 years are 750 mg three times daily by mouth, or 2.25 g three times daily; treatment may be continued for up to 8 weeks.

Preparations

Proprietary Preparations (details are given in Part 3)

Arg.: Benoquin; **Austral.:** Colazide; **Cz.:** Colazide†; **Denm.:** Premid; **Ital.:** Balzide; **Norw.:** Colazid; **UK:** Colazide; **USA:** Colazal.

Multi-ingredient: **Swed.:** Colazid.

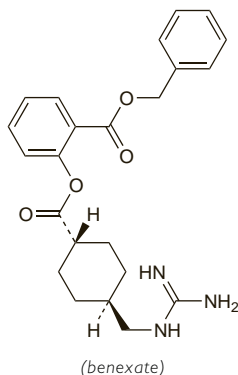
Benexate Hydrochloride (rINN)

Bénexate, Chlorhydrate de; Benexati Hydrochloridum; Hidrocloruro de benexato. Benzyl salicylate *trans*-4-(guanidinomethyl)cyclohexanecarboxylate hydrochloride.

Бенексат Гидрохлорид

$C_{22}H_{27}N_3O_4 \cdot HCl = 445.9$.

CAS — 78718-52-2 (benexate); 78718-25-9 (benexate hydrochloride); 91574-91-3 (benexate hydrochloride betadex).



Profile

Benexate hydrochloride is a mucosal protectant that has been used in the management of peptic ulcer disease. The β -cyclodextrin clathrate, benexate hydrochloride betadex, has been given in an oral dose of 400 mg twice daily.

Preparations

Proprietary Preparations (details are given in Part 3)

Jpn: Uligut.

Bisacodyl (BAN, rINN)

Bisacodilo; Bisacodylum; Bisakodil; Bisakodilisi; Bisakodyl; Bisakodyli; Bisakodil. 4,4'-(2-Pyridylmethylene)di(phenyl acetate).

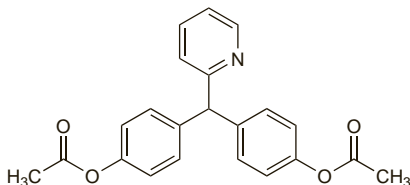
Бисакодил

$C_{22}H_{19}NO_4 = 361.4$.

CAS — 603-50-9.

ATC — A06AB02; A06AG02.

ATC Vet — QA06AB02; QA06AG02.



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

Ph. Eur. 6.2 (Bisacodyl). A white or almost white crystalline powder. Practically insoluble in water; sparingly soluble in alcohol; soluble in acetone. It dissolves in dilute mineral acids. Protect from light.

USP 31 (Bisacodyl). A white to off-white crystalline powder. Practically insoluble in water; soluble in benzene; soluble 1 in 210 of alcohol, 1 in 2.5 of chloroform, and 1 in 275 of ether; sparingly soluble in methyl alcohol.

Bisacodyl Tannex (BANM, USAN, rINN)

CAS — 1336-29-4.

ATC — A06AB02; A06AG02.

ATC Vet — QA06AB02; QA06AG02.

Adverse Effects

Bisacodyl and other stimulant laxatives may cause abdominal discomfort such as colic or cramps. Prolonged use or overdosage can result in diarrhoea with excessive loss of water and electrolytes, particularly potassium; there is also the possibility of developing an atonic non-functioning colon. Hypersensitivity reactions, including angioedema and anaphylactoid reactions, have been reported rarely. When given rectally, bisacodyl sometimes causes irritation and may cause proctitis or sloughing of the epithelium. To avoid gastric irritation bisacodyl tablets are enteric-coated.

Precautions

As with other laxatives, prolonged use should be avoided. Bisacodyl should not be given to patients with intestinal obstruction or acute abdominal conditions such as appendicitis; care should also be taken in patients with inflammatory bowel disease. It should not be used in patients with severe dehydration. The suppositories should preferably be avoided in patients with anal fissures, proctitis, or ulcerated haemorrhoids.

Handling. Inhalation of bisacodyl powder and contact with eyes, skin, and mucous membranes should be avoided.

Pharmacokinetics

On oral or rectal use bisacodyl is converted to the active desacetyl metabolite bis(*p*-hydroxyphenyl)-pyridyl-2-methane by intestinal and bacterial enzymes. Absorption from the gastrointestinal tract is minimal with enteric-coated tablets or suppositories; the small amount absorbed is excreted in the urine as the glucuronide. Bisacodyl is mainly excreted in the faeces.

Uses and Administration

Bisacodyl is a diphenylmethane stimulant laxative (p.1693) used for the treatment of constipation (p.1693) and for bowel evacuation before investigational procedures or surgery. Its action is mainly in the large intestine and it is usually effective within 6 to 12 hours after oral doses, within 15 to 60 minutes after rectal use by suppository, and within 5 to 20 minutes when given as an enema. Bisacodyl tablets should be swallowed whole and should not be taken within 1 hour of milk or antacids.

For constipation, bisacodyl is given in usual doses of 5 to 10 mg daily as enteric-coated tablets given at night or 10 mg as a suppository or enema given in the morning. Oral doses of 10 to 20 mg are given for complete bowel evacuation, followed by 10 mg as a suppository the next morning. For doses in children, see below.

A complex of bisacodyl with tannic acid (bisacodyl tannex) has been given with a barium sulfate enema before radiographic examination of the colon.

Administration in children. For constipation, the following oral doses of bisacodyl are recommended for children, to be taken at night:

- 4 to 10 years: 5 mg
- over 10 years: 5 to 10 mg

Alternatively, the following rectal doses are recommended, to be inserted in the morning:

- under 10 years: 5 mg
- over 10 years: 10 mg

The *BNFC* gives similar doses, but limits the use of suppositories in children to those aged over 2 years.

For bowel clearance before surgery or radiological investigation, the following doses are recommended:

- 4 to 10 years: 5 mg orally the night before, followed by 5 mg as a suppository the next morning
- over 10 years: 10 to 20 mg orally the night before, followed by 10 mg as a suppository the next morning

The *BNFC* gives similar doses but allows for the use of oral doses for 2 nights before the procedure, followed, if necessary, by the rectal dose 1 hour before the procedure.

Preparations

BP 2008: Bisacodyl Suppositories; Gastro-resistant Bisacodyl Tablets;

USP 31: Bisacodyl Delayed-release Tablets; Bisacodyl Rectal Suspension; Bisacodyl Suppositories.

Proprietary Preparations (details are given in Part 3)

Arg.: Dulcolax; Laxamin; Modaton; Tractoduo; **Austral.:** Bisalax; Dulcolax; **Austria:** Dulcolax; Laxbene; **Belg.:** Carters; Dulcolax; Henafurine; Muci-

num; Nosik-Lax; Purgo-Pil; **Braz.:** Bisalax; Cronoplex; Dislax†; Dulcolax; Fi-deine; Islax; Plesonax; **Canad.:** Alophen; Bisacolax; Carters Little Pills; Correctol; Dulcolax; Feen-A-Mint†; Gentlax; Laxcodyl†; Soflax; **Ex.:** **Chile:** Alysax; **Cz.:** Fenolax; **Fr.:** Xylax†; Stadalax; **Denm.:** Dulcolax; Penilax; Toilax; **Fin.:** Metalax; Toilax; **Gr.:** Contalax; Dulcolax; **Ger.:** Agaroletten; Bekunis Bisacodyl; Bisco-Zitron; Drix Bisacodyl; Dulcolax; Flonsan N; Laxagetten; Laxamin N†; Laxans-ratiopharm; Laxbene†; Laxoberal Bisa; Laxysat Burger; Marienbader Pillen N; Mediolax; Pynlax; Stadalax†; Tempolax; Tirgon; Vinco-Abfuhr-Perlen†; **Gr.:** Dulcolax; Flonsan N; **Hong Kong:** Dulcolax; Mar-cholax; **Hung.:** Dulcolax; Stadalax; **India:** Bo-Lax; Dulcolax; Julax; Julax-M†; **Indon.:** Bicolax; Dulcolax; Laxacol; Laxamex; Stolas; Dulcolax; Toilax; **Israel:** Atzirut X; Contalax; Laxadin; **Ital.:** Alaxa; Conifetto CM†; Dulcolax; Normalene; Stixenil; Vercolene CM; **Malaysia:** Beacolux†; Dulcolax; **Mex.:** Dulcolax; **Neth.:** Bekunis Bisacodyl; Dulcolax; Kruidvat Laxeert-abletten; Nounilax; Toilax; Trekpleister Laxeerdagees†; **Norw.:** Dulcolax; Toilax; **NZ:** Dulcolax; Fleet Laxative; **Philipp.:** Dulcolax; Vesilax; **Port.:** Dulcolax; Modierax; **Rus.:** Dulcolax (Дульколак); **S.Afr.:** Dulcolax; Megalax†; Penilax; **Singapore:** Dulcolax; **Spain:** Dulco Laxo; **Swed.:** Dulcolax; Toilax; **Switz.:** Bekunis Dragees; Demolaxin; Dulcolax; Muxol; Prontolax; Tavolax nouvelle formule; **Thail.:** Conlax; Dulcolax; Emulax; Gencolax; Kadolax; Laxcodyl; Laxitab; Vacolax; **Turk.:** Bisakol; Sekolax; **UAE:** Laxocodyl; **UK:** Biolax; Dulcolax; Entrolax; **USA:** Alophen; Bisa-Lax; Correctol; Doxidan; Dulcolax; Evac-Q-Tabs; Ex-Lax Ultra; Feen-A-Mint; Fleet Bisacodyl; Fleet Laxative; Gentlax; Modane; **Venez.:** Dulcolan.

Multi-ingredient: **Arg.:** En-Ga-Lax; Laxicon; Nigalax; **Austral.:** Coloxyl; Durolax X-Pack†; Go Kit; Go Kit Plus†; **Austria:** Laxbene; Prepacol; Purgazen; Purgat†; **Belg.:** Prepacol; Softene; **Canad.:** Bicholate; Extra Strong Formula 12†; Fruitatives†; Gentlax S; Royvac Kit; **Chile:** Laxogeno; **Cz.:** Prepacol; **Fr.:** Prepacol; **Ger.:** Potsilo N; Prepacol; **Gr.:** Florsan; **Hung.:** Laxbene; **NZ:** Coloxyl; **Port.:** Bekunis; **Spain:** Bekunis Complex; Boldolax-in†; **Thail.:** Bisolax; **Turk.:** Bekunis; **USA:** Dulcolax Bowel Prep Kit; Fleet Prep Kit No. 1; Fleet Prep Kit No. 2; Fleet Prep Kit No. 3; HalfLytely; X-Prep Bowel Evacuant Kit-1.

Bismuth Compounds

Bismuto, compuestos de.

Висмут Соединения

Bismuth compounds have been used for their astringent and antidiarrhoeal properties in a variety of gastrointestinal disorders, and have been applied topically in skin disorders and anorectal disorders such as haemorrhoids. Certain salts are active against *Helicobacter pylori* and are used in the treatment of peptic ulcer disease.

Bismuth Aluminate (USAN)

Aluminato de bismuto; Aluminum Bismuth Oxide.

Алюминат Висмута

$Bi_2(Al_2O_4)_3 \cdot 10H_2O = 952.0$.

CAS — 12284-76-3 (anhydrous bismuth aluminate).

Pharmacopoeias. In *Chin.* and *Fr.*

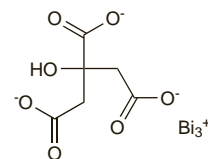
Bismuth Citrate

Citrato de bismuto.

Цитрат Висмута

$Bi_2C_6H_5O_7 = 398.1$.

CAS — 813-93-4.



NOTE. Do not confuse with bismuth subcitrate potassium (p.1711) or tripotassium dicitratobismuthate (colloidal bismuth subcitrate, p.1711).

Pharmacopoeias. In *US*.

USP 31 (Bismuth Citrate). A white, amorphous or crystalline powder. Insoluble in water and in alcohol; soluble in dilute ammonia solution and in solutions of alkali citrates. Store in airtight containers. Protect from light. Prevent exposure to temperatures above 40°.

Bismuth Oxide

Bismuth Trioxide; Óxido de bismuto.

Оксид Висмута

$Bi_2O_3 = 466.0$.

CAS — 1304-76-3.

