**Effects on the skin.** Skin reactions and photodermatitis have followed application of home-made decoctions of fig leaves to the skin. <sup>1,2</sup>

- Ozdamar E, et al. An unusual cause of burn injury: fig leaf decoction used as a remedy for a dermatitis of unknown etiology. J Burn Care Rehabil 2003; 24: 229–33.
- Bassioukas K, et al. Erythrodermic phytophotodermatitis after application of aqueous fig-leaf extract as an artificial suntan promoter and sunbathing. Contact Dermatitis 2004; 51: 94–5.

### **Preparations**

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Austria: Carilax; Frugelletten; Herbelax; Neda Fruchtewurfel; Braz.: Bilifel†; Denm.: Figen; Fr.: Carres Parapsyllium; Preservation; Ger.: florabio Mann-Feigen-Sirup mit Senna†; florabio Manna-Feiger, Switz.: Agarol Soft; Dragees aux figues avec du sene; Fruttasan; Pursana; Valverde Constipation dragees; Valverde Constipation sirop; UK: Califig.

# Fosaprepitant (rINN)

Fosaprépitant; Fosaprepitantum. {3-[((2R,35)-2-{(1R)-1-[3,5-bis(Trifluoromethyl)phenyl]ethoxy}-3-(4-fluorophenyl)morpholin-4-yl)methyl]-5-oxo-4,5-dihydro-1H-1,2,4-triazol-1-yl}phosphonic acid.

Фозапрепитант

 $C_{23}H_{22}F_7N_4O_6P = 614.4.$ CAS — 172673-20-0.

# Fosaprepitant Meglumine (HNNM)

Fosaprepitant Dimeglumine; Fosaprepitant meglumina; Fosaprepitant Méglumine; Meglumini Fosaprepitantum; MK-0517. I-Deoxy-I-(methylamino)-D-glucitol  $3-[(2R,35)-2-\{(1R)-I-[3.5-bis(trifluoromethyl])-heny]]ethoxy}-3-(4-fluorophenyl)-4-morpholinyl)methyl]- 2,5-dihydro-5-oxo-I<math>H$ -1,2,4-triazol-I-yl}phosphonate.

Меглумина Фозапрепитант

 $C_{23}H_{22}F_7N_4O_6P$ ,  $2C_7H_{17}NO_5 = 1004.8$ . CAS — 265121-04-8.

**Stability.** US licensed product information states that, once reconstituted and diluted as directed in sodium chloride 0.9%, a solution of fosaprepitant meglumine is stable for 24 hours at room temperature (at or below 25°).

# **Adverse Effects and Precautions**

As for Aprepitant, p.1708.

# Interactions

As for Aprepitant, p.1708.

# **Pharmacokinetics**

Fosaprepitant is rapidly converted to aprepitant; for the pharmacokinetics of aprepitant, see p.1708.

# **Uses and Administration**

Fosaprepitant is a prodrug of the antiemetic aprepitant (p.1708), which is a neurokinin-1 receptor antagonist. Fosaprepitant meglumine is used for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic or moderately emetogenic cancer chemotherapy. Doses are expressed in terms of the base; 188 mg of fosaprepitant meglumine is equivalent to about 115 mg of fosaprepitant. A dose of fosaprepitant meglumine equivalent to 115 mg fosaprepitant may be given intravenously instead of oral aprepitant, with a corticosteroid and a 5-HT<sub>3</sub> antagonist (for details, see Administration, under Aprepitant, p.1709). The reconstituted dose of fosaprepitant is diluted in 110 mL of sodium chloride 0.9% to a final concentration of 1 mg/mL and infused over 15 minutes.

# ♦ References

 Navari RM. Fosaprepitant (MK-0517): a neurokinin-1 receptor antagonist for the prevention of chemotherapy-induced nausea and vomiting. Expert Opin Invest Drugs 2007; 16: 1977-85.

# Preparations

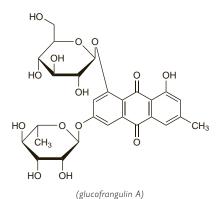
**Proprietary Preparations** (details are given in Part 3) **Cz.:** Ivemend; **Port.:** Ivemend; **UK:** Ivemend; **USA:** Emend.

#### Frangula Bark

Alder Buckthorn Bark; Amieiro Negro; Bourdaine; Faulbaumrinde; Frángula, corteza de; Frangulabark; Frangulae cortex; Kora kruszyny; Krušinová kůra; Kutyabengekéreg; Paatsamankuori; Rhamni Frangulae Cortex; Šaltekšnių žievė.

Кора Крушины

CAS — 8057-57-6 (frangula extract)



NOTE. The name Buckthorn Bark has also been used; distinguish Frangula Bark from Buckthorn (p.1713) and from Sea Buckthorn (p.2384).

Pharmacopoeias. In Eur. (see p.vii).

**Ph. Eur. 6.2** (Frangula Bark). The dried, whole or fragmented bark of the stems and branches of *Rhamnus frangula* (=*Frangula alnus*). It contains not less than 7.0% of glucofrangulins, expressed as glucofrangulin A  $(C_{27}H_{30}O_{14}=578.5)$  and calculated with reference to the dried drug. Protect from light.

#### Profile

Frangula bark is an anthraquinone stimulant laxative with actions and uses similar to those of senna (p.1769).

**Homoeopathy.** Frangula bark has been used in homoeopathic medicines under the following names: Frangula; Rhamnus frangula; Rham. fr.

# **Preparations**

Ph. Eur.: Frangula Bark Dry Extract, Standardised.

**Proprietary Preparations** (details are given in Part 3)

Fr.: Depuratif des Alpes; **Switz.:** Arkocaps†; Elixir frangulae compositum.

Multi-ingredient: Austral.: Granocol†, Normacol Plus, Austria: Abfuhrtee†; Artin; Dragees Neunzehn†; Gallesyn; Laxalpin; Laxolind; Mag Kofuhrtee†; Artin; Dragees Neunzehn†; Gallesyn; Laxalpin; Laxolind; Mag Kottas Krauterexpress Abfuhrtee; Mag Kottas May-Cur-Tee; Planta Lax; Waldheim Abfuhrdragees mild; Belg: Depuratif des Alpes; Grains de Vals; Normacol Plus†; Canad.: Extra Strong Formula 12†; Herbal Laxative; Herbalax†; Cz.: Abdomilon†; Abfuhr-Heilkrautertee†; Cholagol; Reduktan; The Salvat; Denm: Ferroplex-frangula; Fr.: Dragees Fuza; Dragees VegelaeS Rex; Mediflor Tisane Antirhumatismale No 2; Mediflor Tisane Circulation du Sang No 12; Normacol a la Bourdaine†; Tonilax; Ger.: Heumann Abfurthtes Solubilax N†; Hevertolax duo†; Hong Kong: Hepatofalk; Normacol Plus; Hung: Cholagol; India: Kanormai; Int.: Normacol Plus; Isroel: Encypalmed; Relsv, Ital.: Draverex; Fave di Fuza; Frangulina†; Lactolas; Neoform†; Mex.: Normacol Plus; Alax; Cholavsol; Cholesol; Gastro; Laxantol; Rhelax; Senalax K; Tablette Przeciv Niestrawnosci; Tabulette Laxantes; Port.: Normacol Plus; S.Afr:: Normacol Plus; Singepore: Normacol Plus; Solita; Colosan plus; Lapidar 10; Linoforce; Linofled; Normacol avec bourdaine nouvelle formule†; Padma-Lax; Padmed Laxan; Phyto-Laxia; Phytolaxin; UK: Herbulax; Lustys Herbalene; Natewen; Normacol Plus; Politarene; Normacol Plus; Lapidar 10; Linoforce; Linofled; Normacol Bus; Phytolaxin; UK: Herbulax; Lustys Herbalene; Natewen; Normacol Plus; Polita; Phytolaxin; UK: Herbulax; Lustys Herbalene; Natewen; Normacol Plus; Politarene; Normacol Plus; Politare

# Gefarnate (BAN, rINN)

DA-688; Géfarnate; Gefarnato; Gefarnatum; Geranyl Farnesylacetate. A mixture of stereoisomers of 3,7-dimethylocta-2,6-dienyl 5,9,13-trimethyltetradeca-4,8,12-trienoate.

Гефарнат

 $C_{27}H_{44}O_2 = 400.6.$  CAS - 51-77-4. $ATC - A02B \times 07.$ 

ATC Vet — QA02BX07.

$$H_3C$$
 $H_3C$ 
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 $H_3C$ 
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 $H_3C$ 
 $H_3C$ 

#### Profile

Gefarnate is a cytoprotective that has been used in the treatment of peptic ulcer disease and gastritis. An ophthalmic preparation is under investigation for the treatment of corneal and conjunctival epithelial disorders.

# Ginger

Gengibre; Gingembre; Gyömbér gyökértörzs; Imbierų šakniastiebiai; Ingefära; Ingwer; Inkivääri; Jengibre; Zázvorový oddenek; Zingib; Zingiber; Zingiberis rhizoma.

Имбирь

**Pharmacopoeias.** In *Chin., Eur.* (see p.vii), *Jpn*, and *US. US* also includes the powdered form.

**Ph. Eur. 6.2** (Ginger). The dried, whole or cut rhizome of *Zingiber officinale*, with the cork removed, either completely or from the wide flat surfaces only. Whole or cut, it contains not less than 1.5% of essential oil, calculated with reference to the anhydrous drug. It has a characteristic aromatic odour. Protect from light.

The BP 2008 states that ginger may be known in commerce as unbleached ginger.

**USP 31** (Ginger). The scraped, partially scraped, or unscraped rhizome of *Zingiber officinale* (Zingiberaceae), known in commerce as unbleached ginger. It contains not less than 4.5% of alcohol-soluble extractive and not less than 10% of water-soluble extractive. Store at 8° to 15°. Protect from light and moisture.

#### Profile

Ginger has carminative properties. It is used as a flavouring agent and has been tried for the prophylaxis of motion sickness and nausea and vomiting in pregnancy, although it does not seem to be effective for postoperative nausea and vomiting (p.1700).

Ginger oil is used in aromatherapy.

**Homoeopathy.** Ginger has been used in homoeopathic medicines under the following names: Zingiber; Zingiber officinale; Zing.

#### Nausea and vomiting. References.

- Arfeen Z, et al. A double-blind randomized controlled trial of ginger for the prevention of postoperative nausea and vomiting. Anaesth Intensive Care 1995; 23: 449–52.
- Ernst E, Pittler MH. Efficacy of ginger for nausea and vomiting: a systematic review of randomized clinical trials. Br J Anaesth 2000; 84: 367–71.
- 3. Grant KL, Lutz RB. Ginger. Am J Health-Syst Pharm 2000; 57: 945–7.
- Vutyavanich T, et al. Ginger for nausea and vomiting in pregnancy: randomized, double-masked, placebo-controlled trial. Obstet Gynecol 2001; 97: 577–82.
- Smith C, et al. A randomized controlled trial of ginger to treat nausea and vomiting in pregnancy. Obstet Gynecol 2004; 103: 639–45.
- Boone SA, Shields KM. Treating pregnancy-related nausea and vomiting with ginger. Ann Pharmacother 2005; 39: 1710–13.
- Chaiyakunapruk N, et al. The efficacy of ginger for the prevention of postoperative nausea and vomiting: a meta-analysis. Am J Obstet Gynecol 2006; 194: 95–9.

# **Preparations**

BP 2008: Aromatic Cardamom Tincture; Strong Ginger Tincture; Weak Ginger Tincture; USSP 31: Ginger Capsules; Ginger Tincture.

Proprietary Preparations (details are given in Part 3)

Austral.: Travacalm Natural; Canad.: Gravol Natural Source; Ger.: Zintona; Switz.: Zintona; Thai.: Zinaxin†; UK: Travel Sickness; Zinaxin.

Multi-ingredient: Austral.: Bioglan Ginger-Vite Forte; Bioglan Psylli-Mucil Plus; Boswellia Complex; Boswellia Compound; Broncafect; Cal Allyline; Diaco; Digestive Aid; Dyzco; Extralife Arthri-Care; Feminine Herbal Complex; Ginkgo Plus Herbal Plus Formula 10†; Herbal Cleanset; Herbal Digestive Formula; Lifesystem Herbal Plus Formula 1 I Ginkgo; PC Regulax; Peritone; PMS Support; PMT Complex; Travelaide; Austria: Mariazeller; Braz.: Broncot: Tussifien†; Canad.: Cayenne Plus; Chase Kolik Gripe Water; Cz.: Klosterfrau Melisana; Naturland Grosser Swedenbitter†; Fr.: Arthrollib; Evacrine; Ger.: Fovysat†; Gallexier; Gastricard†; Gastrosecur†; Gastrysat; JuViton†; Majocarmin forte†; Preselin Dyspeptikum†; Unex Amarumf; Hong Kong; Magesto; India: Carmicide; Happy Yüzer; Papytazyme; Tummy Base; Well-Beeing†; Indon.: Avogin; Pectum; Pregnaseq; Kal.: Donalg; Lozione Same Urto; Pik Gel; Malaysia: Dandelion Complex†; Strepsils Cough Lozenge, Strepsils Cough Syrup; Total Man†; Zinaxin Plus; Philipp.: Bo-D-Fense; Ruflex; Pol.: Melisana Klosterfrau; Rus.: Diana (Aµmana): Doktor Mom (Доктор Mow); Doktor Mom Herbal Cough Lozenges (Доктор Мом Растительные Пастими От Кашлч); Maraslavin (Мараславин); Original Grosser Bittner Balsam (Оригинальный Большой Балазам Биттнера); Suprima-Broncho (Суприма-брормо;): S.Afr.: Helmontskruie; Lewensessens; Wonderkroonessens; Singapore: Artrex†; Switz.: Padma-Lax Padmed Laxan; Tisane pour les problemes de prostate; Thai.: Carmicide†; Flatulence; Magesto; Mesto-Of; Papytazyme†; Zinaxin

Plus; **UK:** Arheumacare; Digestive; HRI Golden Seal Digestive; Indian Brandee; Indigestion Relief; Neo Baby Gripe Mixture; Neo Gripe Mixture; Traveleeze; Wind & Dyspepsia Relief; Zinopin; **Venez.:** Ervossil; Jengimiel;

# **Granisetron Hydrochloride**

(BANM, USAN, rINNM)

BRL-43694A; Granisétron, chlorhydrate de; Granisetron-hydrochlorid: Granisetronhydroklorid: Granisetroni hydrochloridum: Granisetronihydrokloridi: Granisetrono hidrochloridas: Hidrocloruro de granisetrón. I-Methyl-N-(9-methyl-9-azabicyclo[3.3.1]non-3-yl)-1H-indazole-3-carboxamide hydrochloride.

Гранисетрона Гидрохлорид

 $C_{18}H_{24}N_4O$ , HCI = 348.9.

CAS — 109889-09-0 (granisetron); 107007-99-8 (granisetron hydrochloride).

ATC - A04AA02. ATC Vet - QA04AA02.

(granisetron)

Pharmacopoeias. In Chin. and Eur. (see p.vii). Ph. Eur. 6.2 (Granisetron Hydrochloride). A white or almost white powder. Freely soluble in water; sparingly soluble in dichloromethane; slightly soluble in methyl alcohol. A 1% solution in water has a pH of 4.0 to 6.5.

# **Adverse Effects and Precautions**

As for Ondansetron, p.1757, although no dosage reduction is considered necessary in renal or hepatic impairment.

Carcinogenicity. The manufacturer (Roche) has reported an increased incidence of hepatic neoplasms in rodents given very high doses of granisetron for prolonged periods, but the clinical relevance of these results is unknown. Although mutagenicity and genotoxicity have not been seen in some tests, others have reported an increased incidence of polyploidy or unscheduled DNA synthesis in exposed cells.

Effects on the cardiovascular system. For a discussion of the effects of 5-HT<sub>3</sub> antagonists on the cardiovascular system, see under Ondansetron, p.1757.

# **Interactions**

The metabolism of granisetron is induced by phenobarbital.

# **Pharmacokinetics**

Granisetron is rapidly absorbed after oral doses, with peak plasma concentrations occurring after about 2 hours. Oral bioavailability is about 60% as a result of first-pass hepatic metabolism. Granisetron has a large volume of distribution of around 3 litres/kg; plasma protein binding is about 65%. The pharmacokinetics exhibit considerable interindividual variation, and the elimination half-life after an intravenous dose is reported to be around 4 to 5 hours in healthy subjects but about 9 to 12 hours in cancer patients. It is metabolised in the liver, primarily by N-demethylation, with less than 20% of a dose recovered unchanged in urine, the remainder being excreted in faeces and urine as metabolites. Granisetron clearance is not affected by renal impairment, but is lower in the elderly and in patients with hepatic impairment.

# **Uses and Administration**

Granisetron is a 5-HT<sub>3</sub> antagonist with an antiemetic action similar to that of ondansetron (p.1757). It is used in the management of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy and for the prevention and treatment of postoperative nausea and vomiting (p.1700). Granisetron is given as the hydrochloride, but doses are expressed in terms of the base. Granisetron hydrochloride 1.1 mg is equivalent to about 1 mg of granisetron base.

For acute nausea and vomiting associated with chemotherapy granisetron is used in prevention and treatment in similar doses.

- In the UK, a dose equivalent to 3 mg of granisetron is diluted to a volume of 20 to 50 mL with a suitable infusion solution and given intravenously over 5 minutes before the start of chemotherapy; alternatively this dose may be given in 15 mL of infusion solution as a bolus over not less than 30 seconds. The dose may be repeated up to twice in 24 hours; doses should be given at least 10 minutes apart and a total daily dose of 9 mg should not be exceeded. The efficacy of granisetron may be enhanced by the use of dexamethasone. The recommended oral dose is 1 to 2 mg within one hour before therapy begins, then 2 mg daily as a single dose or in 2 divided doses.
- · For use in children, an intravenous infusion of 40 micrograms/kg, up to a maximum total dose of 3 mg, has been recommended, diluted in 10 to 30 mL of infusion fluid and given over 5 minutes. This dose may be repeated once within 24 hours, but at least 10 minutes after the original infusion. Alternatively, children may be given 20 micrograms/kg (up to 1 mg) orally twice daily for up to 5 days during therapy; the first dose should be given within 1 hour before the start of chemotherapy.
- · In the USA, lower intravenous doses of the equivalent of granisetron 10 micrograms/kg are recommended in both adults and children over 2 years of age, beginning within 30 minutes before chemotherapy. Oral doses are the same as those described for the UK above.

For the prevention of nausea and vomiting associated with radiotherapy the recommended adult oral dosage is 2 mg daily taken within 1 hour of irradiation. The drug has also been given intravenously for the treatment and prevention of nausea and vomiting associated with radiotherapy, in similar doses to those recommended above for emetogenic chemotherapy. In the UK, the BNFC has recommended similar oral and intravenous doses to those given above (for chemotherapy-induced nausea and vomiting) in both the treatment and prevention of radiotherapy-induced nausea and vomiting in children.

For the prevention of postoperative nausea and vomiting in adults 1 mg is diluted to 5 mL and given by intravenous injection over 30 seconds. Injection should be completed before induction of anaesthesia. The same dose may be given up to twice daily for the treatment of established postoperative nausea and vomit-

Transdermal and intranasal formulations of granisetron are under investigation.

◊ References.

- Adams VR, Valley AW. Granisetron: the second serotonin-re-ceptor antagonist. Ann Pharmacother 1995; 29: 1240–51. Correction. ibid. 1996; 30: 1043.
- 2. Wilson AJ, et al. Single-dose i.v. granisetron in the prevention of postoperative nausea and vomiting. Br J Anaesth 1996; **76:** 515–18.
- 3. Taylor AM, et al. A double-blind, parallel-group, placebo-controlled, dose-ranging, multicenter study of intravenous graniset-ron in the treatment of postoperative nausea and vomiting in patients undergoing surgery with general anesthesia. J Clin Anesth
- Blower PR. Granisetron: relating pharmacology to clinical effi-cacy. Support Care Cancer 2003; 11: 93–100.
- 5. Minami M. Granisetron: is there a dose-response effect on nausea and vomiting? Cancer Chemother Pharmacol 2003; 52:
- 6. Prentice HG. Granisetron in the control of nausea and vomiting associated with bone marrow transplantation: a review of its efficacy and tolerability. Support Care Cancer 2003; 11: 501–8.
- Corman SL, et al. Low-dose granisetron for postoperative nausea and vomiting prophylaxis. Ann Pharmacother 2004; **38**: 710–13.

- 8. Goldsmith B. First choice for radiation-induced nausea and voi iting—the efficacy and safety of granisetron. *Acta Oncol* 2004; **43** (suppl 15): 19–22.
- 9. Aapro M. Granisetron: an update on its clinical use in the management of nausea and vomiting. Oncologist 2004; 9: 673-86.

Pain. For reference to the use of granisetron in various painful syndromes see under Uses and Administration of Ondansetron,

# **Preparations**

Proprietary Preparations (details are given in Part 3) Proprietary Preparations (details are given in Part 3)
Arg.: Aludal; Eumetic†, Granitron; Kytril†, Rigmoz†, Austral.: Kytril; Austral.: Kytril; Braz.: Kytril; Carad.: Kytril; Chile: Kytril; Cz.: Emegar; Kytril; Denm.: Kytril; Fin.: Kytril; Fir.: Kytril; Ger.: Kevatril; Gr.: Granitron; Kytril; Honm.: Kytril; Fin.: Kytril; Hung.: Granigen; Kytril; India: Granicip; Indon.: Kytril; India: Granicip; Indon.: Kytril; India: Kytril; Israel: Kytril; Norw.: Kytril; India: Granicip; Indon.: Kytril; Kytril; Israel: Kytril; Norw.: Kytril; India: Kytril; Norw.: Kytril; Norw.: Kytril; Singapore: Kytril; Spain: Kytril; Swed.: Kytril; Switz.: Kytril; Thai.: Kytril; Turk.: Kytril; Setron; UK: Kytril; USA: Kytril; Venez.: Granicip; Kytril; Rubrum.

#### Hydrotalcite (BAN, rINN)

Hidrotalcita; Hidrotalsit; Hydrotalcit; Hydrotalcitum; Hydrotalsiitti. Aluminium magnesium carbonate hydroxide hydrate

 $Mg_6Al_2(OH)_{16}CO_3, 4H_2O = 604.0.$ CAS — 12304-65-3. ATC — A02AD04. ATC Vet - QA02AD04.

NOTE. Compounded preparations of hydrotalcite may be represented by the following names:

Co-simalcite x/y (BAN)—where x and y are the strengths in milligrams of simeticone and hydrotalcite respectively.

# Pharmacopoeias. In Br.

BP 2008 (Hydrotalcite). A hydrated form of an aluminium magnesium basic carbonate corresponding to the formula  $Al_2Mg_6(OH)_{16}CO_3,4H_2O$ . It contains not less than 15.3% and not more than 18.7% of  $Al_2O_3$  and not less than 36.0% and not more than 44.0% of MgO. The ratio of Al<sub>2</sub>O<sub>3</sub> to MgO is not less than 0.40 and not more than 0.45. A white or almost white, freeflowing, granular powder. Practically insoluble in water; it dissolves in dilute mineral acids with slight effervescence. A 4% suspension in water has a pH of 8.0 to 10.0.

Hydrotalcite is an antacid (see p.1692) that is given in oral doses of up to about 1 g.

# **Preparations**

BP 2008: Hydrotalcite Tablets.

Proprietary Preparations (details are given in Part 3) Austria: Talcid; Talicid; Talcid; Tal

Multi-ingredient: Indon.: Promag, Jpn: Eki Cabe; Philipp.: Simeco; UK:

# Hyoscine (BAN)

Escopolamina; Hioscina; Hioscyna; Hyoscin; Hyoscinum; Hyoskiini; Scopolamine; Scopolaminum; Skopolamini; Skopolamin; Skopolamina; Tropato de epoxitropina. (-)-(15,3s,5R,6R,7S,8s)-6,7-Epoxy-3[(S)-tropoyloxy] tropane.

Гиосцин

 $C_{17}H_{21}NO_4 = 303.4.$ 

CAS - 51-34-3

ATC - A04AD01; N05CM05; S01FA02.

ATC Vet — QA04AD01; QN05CM05; QS01FA02.

NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of hyoscine: Burundanga.

# Pharmacopoeias. In Eur. (see p.vii).

Ph. Eur. 6.2 (Hyoscine). A white or almost white, crystalline powder or colourless crystals. M.p. 66° to 70°. Soluble in water; freely soluble in alcohol.

The symbol † denotes a preparation no longer actively marketed