Treatment of leukaemia. References<sup>1-5</sup> to and a review<sup>6</sup> of adverse effects in patients receiving arsenic trioxide for the treatment of acute promyelocytic leukaemia, including a report of sudden death occurring in 3 patients in a dose-finding study.

- 1. Huang SY, et al. Acute and chronic arsenic poisoning associated with treatment of acute promyelocytic leukaemia. *Br J Haematol* 1998; **103:** 1092–5.
- Huang CH, et al. Complete atrioventricular block after arsenic trioxide treatment in an acute promyelocytic leukemic patient. Pacing Clin Electrophysiol 1999; 22: 965–7.
   Camacho LH, et al. Leukocytosis and the retinoic acid syndrome
- in patients with acute promyelocytic leukemia treated with arsenic trioxide. J Clin Oncol 2000; 18: 2620-5.
- Ohnishi K, et al. Prolongation of the QT interval and ventricular tachycardia in patients treated with arsenic trioxide for acute promyelocytic leukemia. Ann Intern Med 2000; 133: 881–5.
- Westervelt P, et al. Sudden death among patients with acute promyelocytic leukemia treated with arsenic trioxide. Blood 2001; 98: 266-71.
- 6. Rust DM, Soignet SL. Risk/benefit profile of arsenic trioxide. Oncologist 2001; 6 (suppl 2): 29-32.

#### **Treatment of Adverse Effects**

Acute poisoning due to the ingestion of arsenic compounds should be treated by immediate gastric lavage if the patient presents within 1 hour and has not already vomited. Activated charcoal has been used to reduce absorption but is unlikely to be of benefit unless a significant amount of arsenic has been ingested. Intravenous replacement of fluids and electrolytes should be undertaken as necessary to correct dehydration and electrolyte imbalance; pressor agents may be required.

Chelation therapy should start immediately the cause of arsenic poisoning is suspected. The therapy of choice for acute poisoning is unithiol (p.1468) given intravenously in cases of gastrointestinal toxicity. Dimercaprol (p.1444) given intramuscularly is the second choice therapy if unithiol is unavailable. Oral therapy with unithiol or succimer (p.1466) should be substituted when gastrointestinal disturbances are no longer a problem. Oral penicillamine (p.1456) has also been used, including in conjunction with dimercaprol in severely ill patients, but its use in arsenic poisoning has been superseded by unithiol and succimer.

Patients suffering from chronic arsenic poisoning should be removed from the source of contamination as soon as possible. Initiation of oral chelation therapy with unithiol or succimer will depend on the patient's clinical condition and laboratory results of arsenic in urine, hair, and nails.

Chelation therapy should be continued until arsenic concentrations in urine have fallen to acceptable levels, although the therapeutic end-points of chelation therapy are poorly defined. If renal failure occurs haemodialysis may be required.

Poisoning. The treatment of 3 patients who had ingested massive doses of arsenic has been described.<sup>1,2</sup> An adult survived after ingesting 54 g of arsenic trioxide:1 in addition to standard supportive measures, attempts to remove the arsenic from his gastrointestinal tract included lavage, endoscopic removal, manual removal after gastrotomy, and cleansing enemas, plus chelation therapy. Of 2 siblings who ingested solubilised inorganic ar-senic in a pesticide solution,<sup>2</sup> one child (aged 4 months) was estimated to have ingested 428 mg/kg arsenic and died despite aggressive attempts at removal of the arsenic, including chelation therapy, extracorporeal membrane oxygenation, exchange transfusion, and haemodialysis. The other child, aged 2 years was estimated to have ingested 14.6 mg/kg arsenic, and survived following standard chelation therapy.

- 1. Dueñas-Laita A, et al. Acute arsenic poisoning. Lancet 2005;
- Lai MW, et al. Acute arsenic poisoning in two siblings. Pediatrics 2005; 116: 249–57.

### **Precautions**

Patients receiving arsenic trioxide for acute promyelocytic leukaemia should have their ECG blood sugar, electrolytes, blood count, and coagulation monitored at least twice weekly during induction and at least weekly during consolidation. More frequent monitoring may be needed in clinically unstable patients. Arsenic trioxide should be used with caution in renal impairment since renal excretion is the main route of elimination.

### **Pharmacokinetics**

Water-soluble arsenic acids and their salts are more rapidly absorbed from the gastrointestinal tract than poorly soluble arsenicals such as arsenic trioxide. The absorption of arsenic trioxide is dependent upon the physical form of the compound and coarsely powdered material may be eliminated in the faeces before significant dissolution and absorption can occur. Soluble arsenic salts may also be absorbed following inhalation and through skin.

Once absorbed, arsenic is stored mainly in the liver, kidneys, heart, and lungs, with smaller amounts in the muscles and nervous tissue. About 2 weeks after ingestion, arsenic is deposited in the hair and nails and remains fixed to the keratin for years. It is also deposited in the bones and skin.

Although pentavalent arsenic is reduced to some degree in vivo to the more toxic trivalent form, trivalent arsenic is slowly and extensively oxidised to pentavalent arsenic. Both forms are methylated and excreted in the urine, mainly as dimethylarsinic acid, with smaller amounts appearing as monomethylarsonic acid and inorganic arsenic compounds. Although about 60% of a dose may be eliminated in the urine within 8 days, small amounts may continue to be excreted for several weeks after a single dose. Less significant amounts of arsenic are excreted in the faeces and sweat and via the lungs and skin. It is also distributed into breast milk and readily crosses the placenta.

#### Uses and Administration

Arsenic trioxide is used for induction of remission and consolidation in acute promyelocytic leukaemia (see below). It is given as an intravenous infusion over 1 to 2 hours to patients who are refractory to, or who have relapsed from, conventional therapy with retinoids and antineoplastics; if acute vasomotor reactions occur, the rate of infusion may be slowed and up to 4 hours may be taken. For induction, a dose of 150 micrograms/kg is given once daily until remission occurs; no more than 50 doses should be given (in the USA, the maximum number of induction doses allowed is 60). Treatment for consolidation must begin 3 to 4 weeks after completion of induction (or 3 to 6 weeks in the USA). The dose for consolidation is 150 micrograms/kg once daily given for 25 doses spread over a period of up to 5 weeks; the regimen suggested in the UK is to give the daily dose for 5 days each week followed by 2 days without dosing.

Arsenic trioxide is used in certain Asian herbal remedies. Arsenic anhydride has also been used.

Arsenic trioxide has been widely used as a constituent of weedkillers and sheepdips and as a rodenticide.

Arsenic trioxide and arsenic triiodide were formerly used internally as solutions or externally as ointments in the treatment of various skin diseases, but such use is generally no longer recommended. Externally, arsenic trioxide has a caustic action.

Homoeopathy. Arsenic trioxide has been used in homoeopathic medicines under the following names: Arsenious trioxide; Arsenici trioxidum; Arsenicum album; Acidum arsenicosum;

Acute myeloid leukaemias. The use of arsenic trioxide in the management of patients with acute promyelocytic leukaemia (p.652) has been reviewed. 1-4 Remission was achieved in patients who had relapsed despite conventional therapy with retin-oids and antineoplastics. <sup>5,6</sup> Arsenic trioxide is also being investigated for postremission therapy and in conjunction with transplantation.<sup>4</sup> Treatment was also successful in newly-diagnosed patients but severe liver toxicity occurred in some cases.

For references to adverse effects occurring in patients receiving arsenic trioxide for acute promyelocytic leukaemia, see under Adverse Effects, above.

- Soignet SL. Clinical experience of arsenic trioxide in relapsed acute promyelocytic leukemia. Oncologist 2001; 6 (suppl 2): 11-6.
- 2. Murgo AJ. Clinical trials of arsenic trioxide in hematologic and solid tumors: overview of the National Cancer Institute ative Research and Development Studies. Oncologist 2001; 6 (suppl 2): 22-8.
- Slack JL, et al. Advances in the management of acute promyelo-cytic leukemia and other hematologic malignancies with arsenic trioxide. Oncologist 2002; 7 (suppl 1): 1–13.
- 4. Douer D, Tallman MS. Arsenic trioxide: new clinical experience with an old medication in hematologic malignancies. *J Clin On-*col 2005; **23**: 2396–2410.
- 5. Niu C, et al. Studies on treatment of acute promyelocytic leukemia with arsenic trioxide: remission induction, follow-up, and mal with assette thoract. Chaission induction, notw-up, and molecular monitoring in 11 newly diagnosed and 47 relapsed acute promyelocytic leukemia patients. *Blood* 1999; **94:** 3315–24.
- 6. Soignet SL, et al. United States multicenter study of arsenic trioxide in relapsed acute promyelocytic leukemia. *J Clin Oncol* 2001; **19:** 3852–60.

Multiple myeloma. Arsenic trioxide is under investigation for the treatment of relapsed or refractory multiple myeloma (p.658).

### References.

- 1. Munshi NC. Arsenic trioxide: an emerging therapy for multiple myeloma. *Oncologist* 2001; **6** (suppl 2): 17–21.
- 2. Munshi NC, et al. Clinical activity of arsenic trioxide for the treatment of multiple myeloma. Leukemia 2002; 16: 1835-7.
- 3. Bahlis NJ, et al. Feasibility and correlates of arsenic trioxide combined with ascorbic acid-mediated depletion of intracellular glutathione for the treatment of relapsed/refractory multiple myeloma. Clin Cancer Res 2002; 8: 3658-68.
- Berenson JR, Yeh HS. Arsenic compounds in the treatment of multiple myeloma: a new role for a historical remedy. Clin Lym-phoma Myeloma 2006; 7: 192–8.

Myelodysplastic syndromes. The use of arsenic trioxide for the treatment of myelodysplastic syndromes (p.654) is also under investigation.

- 1. List A, et al. Opportunities for Trisenox (arsenic trioxide) in the treatment of myelodysplastic syndromes. *Leukemia* 2003; **17**: 1499–1507.
- 2. Vey N. Arsenic trioxide for the treatment of myelodysplastic syndromes. Expert Opin Pharmacother 2004; 5: 613–21.
- 3. Schiller GJ, et al. Phase II multicenter study of arsenic trioxide in patients with myelodysplastic syndromes. J Clin Oncol 2006;
- Vey N, et al. Arsenic trioxide in patients with myelodysplastic syndromes: a phase II multicenter study. J Clin Oncol 2006; 24: 2465–71.
- 5. Sekeres MA. New data with arsenic trioxide in leukemias and myelodysplastic syndromes. Clin Lymphoma Myeloma 2007; 8 (suppl 1): S7-S12.

#### **Preparations**

Proprietary Preparations (details are given in Part 3)
Austria: Trisenox, Belg.: Trisenox, Cz.: Trisenox, Fr.: Trisenox, Gr.: Trisenox, Ital.: Trisenox, Jpn: Trisenox, Neth.: Trisenox, Spain: Trisenox, UK:
Trisenox, USA: Trisenox.

Multi-ingredient: Ital.: Pasta Arsenicale.

#### Arsine

Arsenic Trihydride; Arsina; Hydrogen Arsenide.  $AsH_3 = 77.95.$  CAS = 7784-42-1.

#### **Profile**

Arsine is a heavy colourless gas with a garlic-like odour, which has no clinical uses but is an environmental or occupational hazard. It is highly toxic and causes severe haemolysis which may result in acute renal failure. It is potentially toxic below the odour threshold of 0.5 ppm and dangerously toxic after exposure to as little as 3 ppm; there may be a latent period of up to 24 hours following exposure before symptoms develop. Symptoms of arsine gas poisoning include generalised weakness, muscle cramps, thirst, headache, abdominal pain, nausea, vomiting, anorexia, jaundice, bronze skin coloration, haemolytic anaemia, haematuria, oliguria, and anuria. Pulmonary oedema, ECG abnormalities, and neurological disorders have also been reported. Treatment involves exchange transfusions and haemodialysis; dimercaprol and other chelating agents have been used but are of no value in the acute stage and do not prevent haemolysis.

#### ♦ References.

- Fowler BA, Weissberg JB. Arsine poisoning. N Engl J Med 1974; 291: 1171–4.
- 17/4, 231. 171—4.
  2. Hesdorffer CS, et al. Arsine gas poisoning: the importance of exchange transfusions in severe cases. Br J Ind Med 1986; 43:
- 3. Rael LT, et al. The effects of sulfur, thiol, and thiol inhibitor compounds on arsine-induced toxicity in the human erythrocyte membrane. *Toxicol Sci* 2000; **55:** 468–77.

#### **Asafetida**

Asafétida; Asafoetida; Asant; Devil's Dung; Gum Asafetida.

Pharmacopoeias. In Chin.

#### **Profile**

Asafetida is an oleo-gum resin obtained from various species of Ferula (Umbelliferae). It has been used as a carminative and antispasmodic. It was also formerly used as an expectorant. It is used in cooking and is an ingredient of certain foods.

## ♦ References.

Kelly KJ, et al. Methemoglobinemia in an infant treated with the folk remedy glycerited asafoetida. Pediatrics 1984; 73: 717–19.

### **Preparations**

**Proprietary Preparations** (details are given in Part 3) **S.Afr.:** Duiwelsdrekdruppels.

Multi-ingredient: India: Tummy Ease; S.Afr.: Entressdruppels HM; Stuidruppels; Thai.: Flatulence; UK: Daily Tension & Strain Relief.

### Asarabacca

Ásaro europeo; Hazelwort; Rhizoma Asari; Wild Nard.

NOTE Asarabacca has also been used as a common name for Aristolochia clematitis (see Aristolochia, p.2260).

Asarabacca is the dried rhizome, roots, and leaves of Asarum europaeum (Aristolochiaceae), which is an ingredient of snuffs. It is also an irritant emetic and has been used in rodent poisons. Asarabacca is an ingredient of preparations given for respiratory

Homoeopathy. Asarabacca has been used in homoeopathic medicines under the following names: Asarum: Asarum europaeum: Asar. eur.

## **Preparations**

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

## Asbestos

Amianto: Asbesto.

### **Profile**

The name asbestos is applied to several naturally occurring and widely distributed fibrous mineral silicates of the serpentine and amphibole groups. They include amosite (brown asbestos), anthophyllite, chrysotile (white asbestos), and crocidolite (blue asbestos).

Asbestos has properties of heat resistance, insulation, and reinforcement and has been used extensively for heat or electrical insulation, fire protection, in friction materials, and in the construction industry in a wide variety of materials including cement, pipes, and tiles.

When inhaled, asbestos fibres can cause asbestosis (pulmonary fibrosis), lung cancer, and mesothelioma of the pleura and peritoneum. Mesothelioma has been reported in persons exposed to relatively small amounts of asbestos after an average latent period of 30 to 40 years. An association between occupational exposure and an increased incidence of gastrointestinal, laryngeal, and other cancers has also been reported. Some types of asbestos are more hazardous than others; crocidolite (a member of the amphibole group) is considered to be the most dangerous.

- 1. Landrigan PJ, et al. The hazards of chrysotile asbestos: a critical review. *Ind Health* 1999; **37:** 271–80.

  2. Browne K, Gee JB. Asbestos exposure and laryngeal cancer. *Ann*
- Occup Hyg 2000; 44: 239–50.

  3. Bourdes V, et al. Environmental exposure to asbestos and risk of pleural mesothelioma: review and meta-analysis. Eur J Epidemiol 2000: 16: 411-7.
- 4. Bolton C, et al. Asbestos-related disease. Hosp Med 2002; 63: 148-51.
- 5. American Thoracic Society. Diagnosis and initial management of nonmalignant diseases related to asbestos. *Am J Respir Crit Care Med* 2004; **170:** 691–715. Also available at: http://www.thoracic.org/sections/publications/statements/pages/eoh/
- asbestos.html (accessed 24/07/08)

  6. Uibu T, et al. Asbestos exposure as a risk factor for retroperitoneal fibrosis. *Lancet* 2004; **363**: 1422–6.
- Hessel PA, et al. Asbestos, asbestosis, and lung cancer: a critical assessment of the epidemiological evidence. Thorax 2005; 60:
- 8. O'Reilly KM, et al. Asbestos-related lung disease. Am Fam Phy-
- sician 2007; 75: 683-8.

  9. British Thoracic Society Standards of Care Committee. BTS statement on malignant mesothelioma in the UK, 2007. *Thorax* 2007; 62 (suppl 2): iil-iil9. Also available at: http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Malignant%20Mesothelioma/Guidelines/statement%20on% 20malignant%20mesothelioma2007.pdf (accessed 24/07/08)

#### Ash

Askblad (ash leaf); Chinese Ash (Fraxinus chinensis); Common Ash; Esche; European Ash (Fraxinus excelsior); Fraxini folium (ash leaf); Frêne; Frêne, feuille de (ash leaf); Fresno; Jasanový list (ash leaf); Magas kőrisfa levél (ash leaf); Saamenlehti (ash leaf); Uosių lapai (ash leaf).

Pharmacopoeias. Chin. includes Ash Bark (Cortex Fraxini, Qinpi). Eur. (see p.vii) includes Ash Leaf.

Ph. Eur. 6.2 (Ash Leaf; Fraxini Folium). The dried leaf of Fraxinus excelsior or F. oxyphylla. It contains a minimum of 2.5% of total hydroxycinnamic acid derivatives, expressed as chlorogenic acid  $(C_{16}H_{18}O_9 = 354.3)$ , calculated with reference to the dried drug. Protect from light.

## **Profile**

The leaf of the European ash (Fraxinus excelsior) is included in herbal remedies for the treatment of rheumatic and joint disorders, urinary-tract disorders, and constipation. The leaf of F. oxyphylla is also used.

Ash bark has been used to reduce fever and as a tonic

The bark of the Chinese ash, F. chinensis or related species is used in traditional Chinese medicine for disorders including acute dysentery and diarrhoea.

# **Preparations**

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: Austral.: Phytodolor; Austria: Phytodolor; Cz.: Phytodolor; Fr.: Mediflor Tisane Antirhumatismale No 2; Mediflor Tisane Contre la Constipation Passagere No 7; Mediflor Tisane No 4 Diuretique; Obeflorine; Ger.: Phytodolor; Spain: Natusor Artilane†.

### Avena

Aven; Cultivated White Oats; Oatmeal; Oats.

Pharmacopoeias. US includes colloidal oatmeal.

USP 31 (Colloidal Oatmeal). The powder resulting from the grinding and further processing of whole oat grain. When dried at 120° for 4 hours it loses not more than 10% of its weight.

Avena is the grain of Avena sativa (Gramineae). It is used in herbal medicine and is reputed to have sedative activity.

A colloidal fraction extracted from avena is used in the preparation of emollient dermatological preparations

Whether avenin, a protein present in oats, is harmful to patients with coeliac disease is controversial.

Homoeopathy. Avena has been used in homoeopathic medicines under the following names: Avena sativa; Avena e planta tota; Aven. sat.

## **Preparations**

Proprietary Preparations (details are given in Part 3)

Proprietary Preparations (details are given in Part 3)

Arg.: Dermopan; Austral.: DermaVeen Bath; DermaVeen Dry Skin; Canad.: Aveeno Preparations; Life Brand Soothing Bath Treatment; Fr.: Sensifluid; Hong Kong: DermaVeen; Israel: Nutrasoothe†; Ital.: Avalon; Aveeno Preparations; Emulave; Micaveen; NZ: DermaVeen; Port.: Aveeno Preparations; Emulave; Singapore: DermaVeen Astr; DermaVeen Port.: Aveeno Skin; DermaVeen Moisturising; DermaVeen Oatmeal Shampoo; DermaVeen Soap Free; Switz.: Avenaforce†; UK: Aveeno Preparations; USA: ActiBath.

Multi-ingredient: Arg.: Aveno; Cholesterol Reducing Plan†; Dermali-bour; Epithelial†; Epitheliale A-Derma; Epitheliale AH; Exomega; Purasoft; Valeriana Oligoplex; Austral.: Avena Complex; Bioglan The Blue One; Cal-

mo; DermaVeen Moisturising; DermaVeen Shower & Bath; Dong Quai Complex; Glycyrrhiza Complex; Pacifenity; Panax Complex; Chille: Fucus Compuesto; Homeofortin III; Cz.: Valofyt Neo; Fr.: A-Derma Lait Solaire; Biocarde; Cytelium; Dermlairin; Dermalibour; Epitheliale; Eryase; Exomega; Gonaxine; Menoxine; Septalibour; Ger.: Requiesan; Vollmers praparierter gruner N; Hong Kong; Aderma Dermalibour; Aderma Exomega; Aderma Ultra High Protection; Indon.: Menolia; Ital.: Acnaveen; Altadrine; Mex.: Aveendix; Bonaven; Suavene; Pol.: Sedomix; Port.: D'Aveia; Micaven; S.4fr.: Avena Sativa Comp; Singapore: DermaVeen Acnet; DermaVeen Shower & Bath; Switz.: Mucilar Avena; The a l'avoine sauvage de Vollmer; UK: Avena Sativa Comp; Daily Overwork & Mental Fatigue Relief; Daily Tension & Strain Relief; USA: Aveeno Cleansing Bar; Venez.: Avensyt; Bonaven; Cytelium; Dagenol; Dermopan; Epitheliale AH; Fiberful; Fibralash; mopan; Epitheliale AH; Fiberfull; Fibralax†.

Aguacate; Ahuacate; Alligator Pear.

Авокадо; Аллигаторова Груша

## **Profile**

Avocado, Persea americana (P. persea; P. gratissima) (Lauraceae), is included in herbal preparations mainly for respiratory-tract and hepatic disorders. Several parts of the plant, including the fruit and leaves, have been used for a variety of disorders

The fruit is a dietary source of vitamin E, vitamin B<sub>6</sub>, vitamin K,

Avocado oil is used topically as an emollient and as a neutral carrier for essential oils in aromatherapy. It may also be taken

### **Preparations**

Proprietary Preparations (details are given in Part 3) Arg.: Piascledine

Multi-ingredient: Arg.: Derrumal; Braz.: Abacateirol†; Lisian†; Chile: Codetol PM; Jarabe Palto Compuesto con Miel Adulto; Jarabe Palto Compuesto con Miel Infantil; Paltomiel; Paltomiel Plus; Pulmosina; NZ: Mr Nits; Port.: Biureol.

#### **Azadirachta**

Margosa: Neem: Nim.

Azadirachta is the dried stem bark, root bark, and leaves of Azadirachta indica (Melia azadirachta) (Meliaceae), which has been used as a bitter. It is widely used in South Asia and has been reported to have insecticidal, antimalarial, and spermicidal properties. Azadirachta oil (neem oil, margosa oil) expressed from the seeds has also been used.

Adverse Effects. EFFECTS ON THE SKIN. Report of a patient who developed contact dermatitis of the face and ears 1 week after she started using neem oil for the treatment of alopecia

Reutemann P, Ehrlich A. Neem oil: an herbal therapy for alo-pecia causes dermatitis. *Dermatitis* 2008; 19: E12–E15.

POISONING. Severe poisoning in Indian children given neem oil as a remedy for minor ailments.

Sinniah D, Baskaran G. Margosa oil poisoning as a cause of Reye's syndrome. Lancet 1981; i: 487–9.

## Uses. INSECT REPELLENT. References.

Prakash A, et al. A preliminary field study on repellency of neem oil against Anopheles dirus (Diptera:Culicidae) in Assam. J Commun Dis 2000; 32: 145–7.

## **Preparations**

Proprietary Preparations (details are given in Part 3) India: Nimbola†; Malaysia: Moz-Away; UK: Nice 'n Clean

Multi-ingredient: India: Flexi-muv; NZ: Mr Nits; UK: Dr Johnsons Nit

### Azapentacene Sulfonate Sodium

Disodium 5,12-dihydroquinoxalino[2,3-b]phenazine disulfonate.  $C_{18}H_{12}N_4O_6S_2,Na_2 = 490.4.$ 

1790-56-3 (azapentacene disulfonic acid); 3863-80-7 (azapentacene disulfonate disodium).

Azapentacene sulfonate sodium has been used in the management of cataracts.

### **Preparations**

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

Hong Kong: Quinax; Indon.: Pentacin; Mex.: Lutrax; Philipp.: Quinax; Pol.: Quinax; Rus.: Quinax (Квинакс); Singapore: Quinax; Thai.: Quinax.

# Azintamide (rINN)

Azintamida; Azintamidum; Azinthiamide; ST-9067. 2-[(6-Chloro-3-pyridazinyl) thio]-N,N- diethylacetamide.

Азинтамид

 $C_{10}H_{14}CIN_3OS = 259.8.$ CAS — 1830-32-6.

#### **Profile**

Azintamide has been used as a choleretic.

#### **Preparations**

Proprietary Preparations (details are given in Part 3) Gallin purum; **Port.:** Colerin.

Multi-ingredient: Arg.: Biluen Enzimatico; Austria: Ora-Gallin; Ora-Gallin compositum; Port.: Colerin-F; Spain: Oragalin Espasmolitico.

#### Azovan Blue (BAN)

Azovanum Caeruleum: Azul de Evans: Cl Direct Blue 53: Colour. Index No. 23860; Evans Blue; T-1824. Tetrasodium 1,1'-diamino-8,8'-dihydroxy-7,7'-(2,2'-dimethylbiphenyl-4,4'-diylbisdiazo)di-(naphthalene-2,4-disulphonate); Tetrasodium 6,6'-[3,3'-dimethylbiphenyl-4,4'-diylbis(azo)]bis[4-amino-5-hydroxynaphthalene-1,3-disulphonate].

 $C_{34}H_{24}N_6Na_4O_{14}S_4 = 960.8.$ CAS - 314-13-6.

#### Profile

Azovan blue is a dye that has been given intravenously for the determination of blood volume; it is firmly bound to plasma proteins and is slow to leave the circulation. Some patients may experience staining of the skin.

## **Azulene**

Atsuleeni; Azulen; Azuleno; Azulenum; Cyclopentacycloheptene.  $C_{10}H_8 = 128.2.$ CAS — 275-51-4.

NOTE. The name 'Azulene' has also been used for a number of derivatives of azulene including azulene sodium sulfonate, chamazulene, guaiazulene, and sodium gualenate.

## **Profile**

Azulene has been used in preparations for anorectal and skin disorders, and for oral hygiene. The sodium sulfonate salt has been used in preparations for mouth and throat disorders and for dyspepsia; sodium gualenate has also been used in gastrointestinal disorders.

Hypersensitivity. Allergic cheilitis occurred in a patient after long-term use of a toothpaste containing azulene.1

1. Balato N, et al. Allergic cheilitis to azulene. Contact Dermatitis

## **Preparations**

Proprietary Preparations (details are given in Part 3) Hong Kong: Azunol†; Israel: Kamil Blue: Jpn: Azunol.

Multi-ingredient: Arg.: Domuderm; Ninderm; Austria: Emser Nasensalbe; Braz.: Eritrex A; Proctosan; Ger.: Emser Nasensalbe N†; Israel: Kamil Blue; Ital.: AZ 15.

## **Bactericidal Permeability Increasing Protein**

Proteína bactericida incrementadora de la permeabilidad.

### Opebacan (BAN, USAN, rINN)

Opébacan; Opebacán; Opebacanum; rBPI-21. 132-L-Alanine-I-193-bactericidal/permeability-increasing protein (human). Опебакан

CAS — 206254-79-7.

### **Profile**

Bactericidal permeability increasing protein is produced by human leucocytes and possesses both Gram-negative bactericidal and endotoxin-neutralising properties. It also inhibits angiogenesis. Several derivatives have been developed and are under