

laemia. This may cause or exacerbate hypertension, heart failure, oedema, alkalosis, and muscle weakness and damage, and systemic carbenoxolone should therefore be used with caution, if at all, in patients with cardiovascular disease. If hypokalaemia is prolonged, renal impairment can occur. Care is needed in pre-existing hepatic or renal impairment. Regular monitoring of weight and blood pressure is advised; if hypokalaemia, oedema, or a significant rise in blood pressure occurs, carbenoxolone therapy should be stopped. Potassium depletion may be corrected with potassium supplements. Systemic use of carbenoxolone sodium is contra-indicated in patients with hypokalaemia, in pregnancy, in the elderly, and in children.

◇ Muscle weakness,¹⁻⁵ muscle necrosis,⁴ myopathy,¹ hypertension,² headache,² cardiac failure,² mental confusion,⁴ areflexia,³ renal tubular dysfunction,⁵ and acute tubular necrosis⁴ have all been associated with carbenoxolone-induced hypokalaemia. Carbenoxolone-induced hypertension may have precipitated the onset of fatal polyarteritis in a patient predisposed to this condition.⁶

1. Fyfe T, et al. Myopathy and hypokalaemia in carbenoxolone therapy. *BMJ* 1969; **3**: 476.
2. Davies GJ, et al. Complications of carbenoxolone therapy. *BMJ* 1974; **3**: 400-2.
3. Royston A, Prout BJ. Carbenoxolone-induced hypokalaemia simulating Guillain-Barré syndrome. *BMJ* 1976; **2**: 150-1.
4. Descamps C, et al. Rhabdomyolysis and acute tubular necrosis associated with carbenoxolone and diuretic treatment. *BMJ* 1977; **1**: 272.
5. Dickinson RJ, Swaminathan R. Total body potassium depletion and renal tubular dysfunction following carbenoxolone therapy. *Postgrad Med J* 1978; **54**: 836-7.
6. Sloan J, Weaver JA. A case of polyarteritis developing after carbenoxolone therapy. *Ir Med J* 1968; **1**: 505-7.

Handling. Carbenoxolone sodium powder is irritant to nasal membranes.

Interactions

Because of the risk of toxicity, carbenoxolone should not be taken with digitalis glycosides unless serum-electrolyte concentrations are measured at weekly intervals and precautions are taken to avoid hypokalaemia.

Although amiloride or spironolactone relieve sodium and water retention, they antagonise the efficacy of systemic carbenoxolone and should not be used with it. The hypokalaemia associated with diuretics may be exacerbated by carbenoxolone.

Pharmacokinetics

Carbenoxolone sodium is absorbed from the gastrointestinal tract, mainly from the stomach. It is highly bound to plasma proteins. Carbenoxolone is chiefly excreted in the faeces via the bile. It appears to undergo enterohepatic circulation.

Uses and Administration

Carbenoxolone sodium is a synthetic derivative of glycyrrhizic acid (p.2316) that was formerly used as a mucosal protectant in peptic ulcer disease and has been given with antacids and alginate acid in gastro-oesophageal reflux disease.

Carbenoxolone sodium is one of many topical treatments for the symptomatic management of mouth ulceration (p.1700). It is usually used as a 2% gel; a 1% mouthwash has been used.

Mental function. High cortisol concentrations have been associated with poorer memory and neuronal loss in some patients. Carbenoxolone inhibits 11- β -hydroxysteroid dehydrogenase type 1, and thus may selectively lower intracellular cortisol. In a small crossover study in 10 healthy elderly men, carbenoxolone 100 mg three times daily by mouth for 4 weeks significantly improved verbal fluency compared with placebo, but did not influence visual or verbal memory, nonverbal reasoning, or processing speed. Twelve patients with stable type 2 diabetes were given carbenoxolone at the same dose for 6 weeks. Verbal memory was significantly improved compared with placebo, but verbal fluency and other scores were unaltered. All subjects were given amiloride 10 mg daily to prevent mineralocorticoid adverse effects (but see Interactions, above).¹

1. Sandeep TC, et al. 11- β -Hydroxysteroid dehydrogenase inhibition improves cognitive function in healthy elderly men and type 2 diabetes. *Proc Natl Acad Sci U S A* 2004; **101**: 6734-9.

Preparations

Proprietary Preparations (details are given in Part 3)

Austral.: Bioral; **Austria:** Rowadermat; **Hong Kong:** Herpesan; **Hung.:** Carbosan; **Ir.:** Carbosan; **Malaysia:** Herpesan; **Philipp.:** Rowagel; **Singapore:** Herpesan; **Spain:** Sanodin; **UK:** Bioplex†; Bioral†.

Multi-ingredient: **Ir.:** Pyrogastrone; **UK:** Pyrogastrone†.

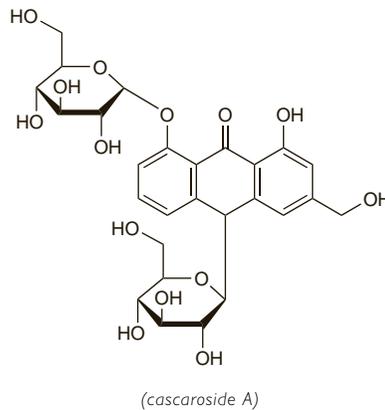
Casanthranol (USAN)

Casanthranol.

Казантранол

CAS — 8024-48-4.

The symbol † denotes a preparation no longer actively marketed



Pharmacopoeias. In US.

USP 31 (Casanthranol). It is obtained from cascara. It contains not less than 20% of total hydroxyanthracene derivatives calculated on the dried basis, of which not less than 80% consists of cascariosides, both calculated as cascarioside A (C₂₇H₃₂O₁₄ = 580.5).

It is a light tan to brown, amorphous, hygroscopic powder. Freely soluble in water with some residue; partially soluble in methyl alcohol and in hot isopropyl alcohol; practically insoluble in acetone. Store in airtight containers at a temperature not exceeding 30°. Protect from light.

Profile

Casanthranol is an anthraquinone stimulant laxative with general properties similar to those of senna (p.1769). It is given in usual oral doses of 30 to 60 mg daily with a faecal softener. In severe cases a dose of 90 mg daily, or 60 mg twice daily, may be given.

Preparations

Proprietary Preparations (details are given in Part 3)

Belg.: Cascaxal†; **Neth.:** Cascaxal.

Multi-ingredient: **Arg.:** Bil 13; En-Ga-Lax; **Canad.:** Peri-Colace†; **Spain:** Laxital; **USA:** Black-Draught†; Docusoft Plus; Genasoft Plus Softgels†; Laxative & Stool Softener; Peri-Dos Softgels†; Silace-C†.

Cascara

Amerikinių šaltėkšnių žievė; Cáscara sagrada; Cascaraninde; Chittam Bark; Kaszkarabokor kéreg; Kúra řešetlaku Purshova; Rhamni purshianae cortex; Rhamni Purshiani Cortex; Sacred Bark; Sagradabark; Sagradankuori.

Жостер Пурша; Крушина Пурша

CAS — 8047-27-6; 8015-89-2 (cascara sagrada extract).
ATC — A06AB07.

ATC Vet — QA06AB07.

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

Ph. Eur. 6.2 (Cascara). The dried, whole or fragmented bark of *Rhamnus purshianus* (= *Fragula purshiana*). It contains not less than 8.0% of hydroxyanthracene glycosides of which not less than 60% consists of cascariosides, both expressed as cascarioside A (C₂₇H₃₂O₁₄ = 580.5), and calculated with reference to the dried drug. Protect from light.

USP 31 (Cascara Sagrada). The dried bark of *Rhamnus purshianus* (Rhamnaceae). It contains not less than 7% of total hydroxyanthracene derivatives calculated on the dried basis, of which not less than 60% consists of cascariosides, both calculated as cascarioside A. It has a distinct odour.

Profile

Cascara is an anthraquinone stimulant laxative with general properties similar to those of senna (p.1769). It has been used in the treatment of constipation in oral doses equivalent to about 20 mg of total hydroxyanthracene derivatives daily.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving cascara, and the American Academy of Pediatrics considers¹ that it is therefore usually compatible with breast feeding.

1. 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 08/11/06)

Preparations

BP 2008: Cascara Dry Extract; Cascara Tablets;

USP 31: Aromatic Cascara Fluidextract; Cascara Sagrada Extract; Cascara Sagrada Fluidextract; Cascara Tablets.

Proprietary Preparations (details are given in Part 3)

Arg.: Natulax; **Braz.:** Laxotrin†; **Fr.:** Peristaltine; **Ger.:** Legapas; **Port.:** Laxolent†.

Multi-ingredient: **Arg.:** Bilidren; Calculina†; Cascara Sagrada Bouzen†; Cascara Sagrada Oligoplex†; Cascara Sagrada Puler†; Veracolate†; Yuyo; **Aust.:** Colax; Pertone; **Austria:** Cascara-Salax; Dragees Neunzehnt†; Sil-

berne; **Belg.:** Grains de Vals; Vethoine; **Braz.:** Bilifelt†; Boldopeptan†; Chof-ranina; Composto Emagrecedor†; Emagrevit†; Eparema; Jurubleno†; Pilulas De Witt†; Prisovent†; Solovoli; Ventre Livre†; **Canad.:** Bicholate; Cholasyll; Cholasyll†; Control; Doulux; Extra Strong Formula 12†; Herbal Laxative; Herbal Laxative plus Yogurt; Herbal Laxative†; Herbalax†; Herbalax; Herborex; Laxaco; Laxative†; Mucinum†; Thunas Laxative†; **Chile:** Bulgorolax; **Fr.:** Dragees Fucal; Dragees Vegetales Rex; Grains de Vals; Imegull†; Mucinum a l'Extrait de Cascara; **Hong Kong:** Mucinum Cascara†; **Ital.:** Amaro Medicinale; Coladren; Combilax; Confeetti Lassativi CM; Critichol; Digelax†; Dis-Cinil Complex; Draverex; Eparema; Eparema-Leviv†; Eupatol; Fave di Fucal; Grani di Vals; Hepatos; Hepatos B12; Lassatina†; Magsibilet†; Mepalax; Schias-Amaro Medicinale†; Solovoli; Stimolift; Vadolax†; **Norw.:** Cosylan; **Port.:** Caroid†; Mucinum†; **S.Afr.:** Moultons Herbal Extract; Veracolate†; **Spain:** Crislaxo; Lipograsil; Menabil Complex†; Nico Hepatocyn; Pildoras Zeninas; **Swed.:** Emulax; **Switz.:** Padma-Lax Padmed Laxan; **Thai.:** Flatulence; Hemolax; Veracolate†; **UK:** Dual-Lax Extra Strong; Dual-Lax Normal Strength; Jacksons Herbal Laxative; Laxative Tablets; Modern Herbs Laxative; Modern Herbs Pile; Natural Herb Tablets; Out-of-Sorts; Pileabs; Piletabs; Rhuaka; Senokot Dual Relief; Skin Eruptions Mixture; **USA:** Concentrated Milk of Magnesia-Cascara; **Venez.:** Gameral.

Cassia Pulp

Fístula, pulpa de caña.

Мякоть АМАТАС

Profile

Cassia pulp is the evaporated aqueous extract of crushed ripe cassia fruits (cassia pods), *Cassia fistula* (Leguminosae). It is a mild anthraquinone stimulant laxative with general properties similar to those of senna (p.1769).

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Braz.:** Fitolax; Florlax; Fontolax; Forlax; Frutalax†; Laxarine†; Laxtam; Naturretti; Sene Composita†; Tamaril; Tamarine; Tamarix†; **Fr.:** Benetransit; **Ital.:** Miracolone; Tamarine; **Mex.:** Naturetti†; **S.Afr.:** Entressdruppels HM†; **Spain:** Pruina.

Cerium Oxalate

Cerii Oxalat; Cerio, oxalato de; Ceriumoksalaatti; Ceriumoxalat.

Церия Оксалаат

CAS — 139-42-4 (anhydrous cerous oxalate); 15053-73-3 (cerous oxalate decahydrate).

ATC — A04AD02.

ATC Vet — QA04AD02.

NOTE. Cerium oxalate has been defined as consisting of about 50% of cerous oxalate ((C₂O₄)₃Ce₂·10H₂O) with the oxalates of numerous other rare earths, especially lanthanum, praseodymium, and neodymium. Oxalates of the form (C₂O₄)₃Ce₂·xH₂O are also referred to as cerium or cerous oxalate.

Profile

Cerium oxalate has been used as an antiemetic.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: **Spain:** Novonausin†.

Certolizumab Pegol (BAN, USAN, rINN)

CDP-870; Certolizumab Pégoli; Certolizumabum Pegolum; PHA-738144.

Цертолизумаб Пегол

CAS — 428863-50-7.

ATC — L04AB05.

ATC Vet — QL04AB05.

Adverse Effects and Precautions

As for Infliximab, p.69.

Interactions

As for Infliximab, p.71

Uses and Administration

Certolizumab pegol is a pegylated tumour necrosis factor antibody fragment. It is used in the treatment of patients with moderate to severe, active Crohn's disease (p.1697) who have had an inadequate response to conventional treatment. The initial dose is 400 mg given as two subcutaneous injections of 200 mg, repeated after 2 and 4 weeks. Patients who have a clinical response may then receive a maintenance dose of 400 mg every 4 weeks. Certolizumab pegol is also under investigation in the treatment of rheumatoid arthritis and psoriasis.

References

1. Schreiber S, et al. A randomized, placebo-controlled trial of certolizumab pegol (CDP870) for treatment of Crohn's disease. *Gastroenterology* 2005; **129**: 807-18. Correction. *ibid.*; 1808. [dose]
2. Sandborn WJ, et al. PRECISE 1 Study Investigators. Certolizumab pegol for the treatment of Crohn's disease. *N Engl J Med* 2007; **357**: 228-38.
3. Schreiber S, et al. PRECISE 2 Study Investigators. Maintenance therapy with certolizumab pegol for Crohn's disease. *N Engl J Med* 2007; **357**: 239-50. Correction. *ibid.*; 1357.

Preparations

Proprietary Preparations (details are given in Part 3)

Switz.: Cimzia; **USA:** Cimzia.