Preparations

BP 2008: Compound Rhubarb Tincture.

Proprietary Preparations (details are given in Part 3)
Cz.: Bukosan†; ***Ger.:*** Phytoestrol N; ***Pol.:*** Laxitab; Radirex; Rzewex.

Multi-ingredient: ***Arg.:*** Calculina†; LX-30; Oralsone Topic; Parodium; Pyralvex; ***Austral.:*** Betaine Digestive Aid; Neo-Cleanse; Pyralvex†; ***Austria:*** Abfuhrtee†; Eucarbon; Eucarbon Herbal; Novocholin; Pyralvex; Sabatif; Silberne; ***Belg.:*** Pyralvex; ***Braz.:*** Bilifel†; Bisuisan†; Boldopeptan†; Camomila; Eparema; Regulador Xavier N-2†; ***Canad.:*** Extra Strong Formula 12†; Herbal Laxative; Herbalax†; Herbolax; ***Cz.:*** Abdomilon†; Cynarosan†; Dr Theiss Rheuma Creme†; Dr Theiss Schweden Krauter; Dr Theiss Schwedenbitter; Pyralvex; Species Cholagogae Planta; Zlucnikova Cajova Smes; ***Fr.:*** Carres Parapsyllium; Depuratum; Parodium; Pyralvex; Resource Rhubagil; ***Ger.:*** Pyralvex; ***Gr.:*** Pyralvex; ***Hong Kong:*** Hepatofalk; Pyralvex; ***Hung.:*** Bolus Laxans; ***Indon.:*** Pyralvex; ***Irl.:*** Pyralvex; ***Israel:*** Davilla; Encypalmed; Eucarbon; Novicarbon; ***Ital.:*** Amaro Medicinale; Caramelle alle Erbe Digestive; Colax; Critichol; Digelax†; Dis-Cinil Complex; Eparema; Eparema-Levul; Eucarbon; Eupatol; Frerichs Maldifassi†; Lactolas; Lassatina†; Lassativi Vetegali; Magisbile†; Mepalax; Neoform†; Puntualax†; Pyralvex; Schiasamaro Medicinale†; Stimolfit; ***Malaysia:*** Eucarbon†; ***Neth.:*** Pyralvex; ***Philipp.:*** Boie Carminative (Carminasen); Pyralvex; ***Pol.:*** Betasol; Digestonic; Laxantol; Rhelax; ***Port.:*** Pyralvex; ***Rus.:*** Parodium (Пародиум); ***S.Afr.:*** Helmontskruie; Lewensessens; Moultons Herbal Extract; Pyralvex; Rubilax†; Wonderkroonessens; ***Singapore:*** Pyralvex; ***Spain:*** Crislaxo; Laxante Bescansa Aloico; Menabil Complex†; Pyralvex; Solucion Schoum; ***Switz.:*** Padma-Lax; Padmed Laxan; Pyralvex; Schweden-Mixtur H nouvelle formulation; ***Thai.:*** Pyralvex; ***Turk.:*** Eucarbon; Karboseptin; Piraldyne; Pyralvex; ***UK:*** Acidosis; Digestive; Fam-Lax; Fam-Lax Senna; HRI Golden Seal Digestive; Indian Brandee; Jacksons Herbal Laxative; Pegina; Pyralvex; Rhuaka; Stomach Mixture; Wind & Dyspepsia Relief; ***USA:*** Black-Draught†; ***Venez.:*** Cynascool; Natrossil; Orafilm†; Pinvex; Pyralvex†; Rheu-Tarx 1.

Roxatidine Acetate Hydrochloride

(BANM, USAN, rINNM)

Hidrocloruro de acetato de roxatidina; Hoe-760; Hoe-062 (roxatidine); Pifatidine Hydrochloride; Roxatidine, Acétate Chlorhydrique de; Roxatidini Acetati Hydrochloridum; TZU-0460. *N*-{3-[(α-Piperidino-*m*-tolyl)oxy]propyl}glycolamide acetate monohydrochloride.

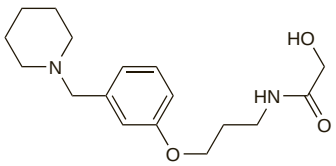
Роксатидина Ацетат Гидрохлорид

$C_{17}H_{26}N_2O_3,C_2H_2O,HCl$ = 384.9.

CAS — 78273-80-0 (roxatidine); 97900-88-4 (roxatidine hydrochloride); 78628-28-1 (roxatidine acetate); 93793-83-0 (roxatidine acetate hydrochloride).

ATC — A02BA06.

ATC Vet — QA02BA06.



(roxatidine)

Pharmacopoeias. In *Jpn.*

Stability. The stability of roxatidine acetate hydrochloride in parenteral nutrition solutions was influenced by storage temperature and amino acid content and composition.[1]

1. Oh J, *et al.* Stability of roxatidine acetate in parenteral nutrient solutions containing different amino acid formulations. *Am J Health-Syst Pharm* 2005; **62:** 289–91.

Adverse Effects and Precautions

As for Cimetidine, p.1716.

Interactions

Unlike cimetidine (p.1718) roxatidine does not appear to affect cytochrome P450, and therefore is considered to have little effect on the metabolism of other drugs. However, like other H_2-antagonists its effects on gastric pH may alter the absorption of some other drugs.

Pharmacokinetics

Roxatidine acetate hydrochloride is rapidly and almost completely absorbed from the gastrointestinal tract with peak concentrations in plasma occurring about 1 to 3 hours after doses by mouth. It is rapidly hydrolysed to the active desacetyl metabolite, roxatidine, by esterases in the liver, small intestine, and serum.

Over 90% of a dose is excreted in the urine as roxatidine and other metabolites. The elimination half-life of roxatidine is about 6 hours and is prolonged in renal impairment.

Small amounts of roxatidine have been reported to be distributed into breast milk.

Uses and Administration

Roxatidine acetate hydrochloride is an H_2-antagonist with actions and uses similar to those of cimetidine (p.1719).

In the management of peptic ulcer disease the oral dose is 150 mg at bedtime or 75 mg twice daily for 4 to 6 weeks. Where appropriate a maintenance dose of 75 mg at bedtime may be given to prevent the recurrence of ulcers. In gastro-oesophageal reflux disease the recommended dose is 150 mg at bedtime or 75 mg twice daily for 6 to 8 weeks. Gastritis has been managed with 75 mg once daily in the evening, and a dose of 75 mg twice daily has been used for Zollinger-Ellison syndrome.

When used as a pre-anaesthetic medication, an oral dose of roxatidine acetate hydrochloride 75 mg is given in the evening on the day before surgery and repeated 2 hours before the induction of anaesthesia; alternatively a single dose of 150 mg may be given the night before surgery.

Roxatidine acetate hydrochloride may also be given intravenously for the treatment of upper gastrointestinal tract haemorrhage in a dose of 75 mg twice daily by slow intravenous injection or by intravenous infusion.

For dosage in renal impairment, see below.

◊ Reviews.

1. Murdoch D. Roxatidine acetate: a review of its pharmacodynamic and pharmacokinetic properties, and its therapeutic potential in peptic ulcer disease and related disorders. *Drugs* 1991; **42:** 240–60.

Administration in renal impairment. The dosage of roxatidine acetate hydrochloride should be reduced in patients with renal impairment. Suggested oral doses, based on creatinine clearance (CC), for patients on acute therapy are:

- CC 20 to 50 mL/minute: 75 mg at bedtime
- CC less than 20 mL/minute: 75 mg every 2 days

However, results in 6 patients with chronic renal failure and CC less than 20 mL/minute indicated that giving the recommended dose of roxatidine acetate hydrochloride, 75 mg every other day, was inadequate to maintain gastric pH above 4 for more than 6 hours. Subsequent study in 8 patients showed that a dose of 75 mg daily was well tolerated and effective.[1]

1. Gladziwa U, *et al.* Pharmacokinetics and pharmacodynamics of roxatidine in patients with renal insufficiency. *Br J Clin Pharmacol* 1995; **39:** 161–7.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Roxit†; ***Gr.:*** Roxane†; ***India:*** Rotane; ***Ital.:*** Gastralgin; Neo H2; Roxit; ***Jpn:*** Altat; ***Neth.:*** Roxit†; ***S.Afr.:*** Roxit†; ***Spain:*** Roxiwas†; Zarocs.

Senna

Alexandriai szenna termés (senna pods, Alexandrian); Listek senesu (senna leaf); Plod kasie ostrolisté (senna pods, Alexandrian); Plod kasie úzkolisté (senna pods, Tinnevelly); Sen; Séné de Khartoum ou d'Alexandrie, fruit de (senna pods, Alexandrian); Séné de l'Inde ou de Tinnevelly, fruit de (senna pods, Tinnevelly); Séné, feuille de (senna leaf); Sennabalja, alexandrinsk (senna pods, Alexandrian); Sennabalja, Tinnevelley- (senna pods, Tinnevelley); Sennae folium (senna leaf); Sennae fructus acutifoliae (senna pods, Alexandrian); Sennae fructus angustifoliae (senna pods, Tinnevelly); Sennanpalko, Aleksandrian (senna pods, Alexandrian); Sennanpalko, Tinnevelleyn (senna pods, Tinnevelley); Sennový list (senna leaf); Senų lapai (senna leaf); Senų vaisiai (senna pods, Alexandrian); Siauralapių senų vaisiai (senna pods, Tinnevelly); Sinameki; Szennalevél (senna leaf); Tinevelly szenna termés (senna pods, Tinnevelly).

Кассия Остролистная (Alexandrian senna); Сенна Остролистная (Alexandrian senna); Александрийский Лист (Alexandrian senna leaf)

CAS — 8013-11-4.

ATC — A06AB06.

ATC Vet — QA06AB06.

Description. Senna obtained commercially from *Cassia senna* (*C. acutifolia*) (Leguminosae) is known as Alexandrian senna or Khartoum senna and that from *Cassia angustifolia* (Leguminosae) as Tinnevelly senna.

Pharmacopoeias. Senna fruit, from Alexandrian and Tinnevelly senna is included in *Eur.* (see p.vii), *Int.*, and *US.* Senna leaf, from Alexandrian or Tinnevelly senna or both, is included in *Chin.*, *Eur.*, *Int.*, *Jpn*, and *US.*

Ph. Eur. 6.2 (Senna Pods, Alexandrian; Sennae Fructus Acutifoliae; Alexandrian Senna Fruit BP 2008). The dried fruit of *Cassia senna* (*Cassia acutifolia*) containing not less than 3.4% of hydroxyanthracene glycosides, calculated as sennoside B ($C_{42}H_{38}O_{20}$ = 862.7) with reference to the dried drug. Protect from light and moisture.

Ph. Eur. 6.2 (Senna Pods, Tinnevelly; Sennae Fructus Angustifoliae; Tinnevelly Senna Fruit BP 2008). The dried fruit of *Cassia angustifolia* containing not less than 2.2% of hydroxyanthracene glycosides, calculated as sennoside B ($C_{42}H_{38}O_{20}$ = 862.7) with reference to the dried drug. Protect from light and moisture.

Ph. Eur. 6.2 (Senna Leaf; Sennae Folium). The dried leaflets of *Cassia senna* (=*Cassia acutifolia*), known as Alexandrian or Khartoum senna, or *Cassia angustifolia*, known as Tinnevelly senna, or a mixture of the two species. It contains not less than 2.5% of hydroxyanthracene glycosides, calculated as sennoside B ($C_{42}H_{38}O_{20}$ = 862.7) with reference to the dried drug. Protect from light and moisture.

USP 31 (Senna Leaf). The dried leaflet of *Cassia acutifolia*, known in commerce as Alexandria senna, or *Cassia angustifolia*, known in commerce as Tinnevelly senna (Leguminosae). Protect from moisture and from light.

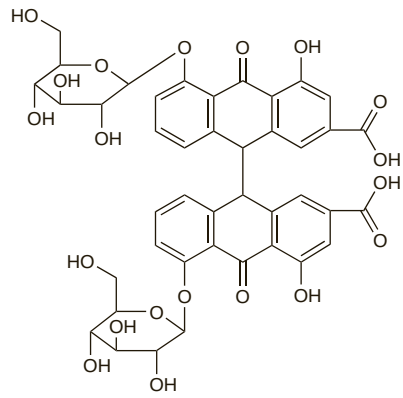
USP 31 (Senna Pods). The dried ripe fruit of *Cassia acutifolia* (Alexandrian senna) or *Cassia angustifolia* (Tinnevelly senna) containing not less than 3.4% or 2.2% respectively of anthraquinone glucosides, calculated as sennosides, on the dried basis. Protect from moisture and from light.

Sennosides

Senósidos.

Сеннозиды

CAS — 81-27-6 (sennoside A); 128-57-4 (sennoside B); 52730-36-6 (sennoside A, calcium salt); 52730-37-7 (sennoside B, calcium salt).



(sennoside A)

Pharmacopoeias. In *US.*

USP 31 (Sennosides). A partially purified natural complex of anthraquinone glucosides found in senna, isolated from *Cassia acutifolia* or *Cassia angustifolia* as calcium salts. It is a brownish powder. Soluble 1 in 35 of water, 1 in 2100 of alcohol, 1 in 3700 of chloroform, and 1 in 6100 of ether. A 10% solution in water has a pH of 6.3 to 7.3. Store at a temperature of 20° to 25°. Protect from moisture and from light.

Adverse Effects

Senna may cause mild 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. Anthraquinone derivatives may colour the urine yellowish-brown at acid pH, and red at alkaline pH. Reversible melanosis coli has been reported following chronic use.

Abuse. Prolonged use or abuse of senna laxatives has been associated with finger clubbing,[1-5] hypokalaemia[3] and tetany,[1] hypertrophic osteoarthropathy,[4,5] intermittent urinary excretion of aspartylglucosamine,[2] hypogammaglobulinaemia,[3] reversible cachexia,[3] and hepatitis[6] or hepatic failure.[7] In one case, nephrocalcinosis was attributed to hypercalcaemia caused by excessive ingestion of calcium sennosides.[5]

1. Prior J, White I. Tetany and clubbing in patient who ingested large quantities of senna. *Lancet* 1978; **ii:** 947.
2. Malmquist J, *et al.* Finger clubbing and aspartylglucosamine excretion in a laxative-abusing patient. *Postgrad Med J* 1980; **56:** 862–4.
3. Levine D, *et al.* Purgative abuse associated with reversible cachexia, hypogammaglobulinaemia, and finger clubbing. *Lancet* 1981; **i:** 919–20.
4. Armstrong RD, *et al.* Hypertrophic osteoarthropathy and purgative abuse. *BMJ* 1981; **282:** 1836.
5. Lim AKH, *et al.* Anorexia nervosa and senna misuse: nephrocalcinosis, digital clubbing and hypertrophic osteoarthropathy. *Med J Aust* 2008; **188:** 121–2.
6. Beuers U, *et al.* Hepatitis after chronic abuse of senna. *Lancet* 1991; **337:** 372–3.
7. Vanderperren B, *et al.* Acute liver failure with renal impairment related to the abuse of senna anthraquinone glycosides. *Ann Pharmacother* 2005; **39:** 1353–7.

Effects on the liver. Hepatitis has been reported in a patient drinking herbal tea containing senna. The patient was found to be a poor metaboliser for hepatic detoxification reactions; the authors cautioned against even small doses of herbal preparations in such patients.[1]

Hepatitis and hepatic failure have also been reported after abuse of senna laxatives, see Abuse, above.

1. Seybold U, *et al.* Senna-induced hepatitis in a poor metabolizer. *Ann Intern Med* 2004; **141:** 651.

Hypersensitivity. Hypersensitivity reactions manifesting as asthma and rhinoconjunctivitis have been reported in those manufacturing[1] or dispensing[2] senna products. However, a study of 125 workers involved in the manufacture of laxatives found only 4 cases of occupational asthma, although sensitisation to senna or ispaghula dust was present in 18 and 9 of the workers