US market) were estimated to represent a rate of 1 case per 1000 patient-years. Serious complications of constipation did not seem to be increased in the population of alosetron users.

1. Chang L, *et al.* Incidence of ischemic colitis and serious complications of constipation among patients using alosetron: systematic review of clinical trials and post-marketing surveillance data. *Am J Gastroenterol* 2006; **101:** 1069–79.

Precautions

Alosetron should be stopped immediately in patients who develop constipation or symptoms of ischaemic colitis such as new or worsening abdominal pain or blood in the stool. Treatment with alosetron should not be resumed in patients who develop ischaemic colitis.

Alosetron should not be used in patients with a history of severe or chronic constipation, intestinal obstruction or stricture, toxic megacolon, or gastrointestinal perforation or adhesions. It is also contra-indicated in patients with a history of ischaemic colitis, impaired intestinal circulation, thrombophlebitis, or hypercoagulable state, and those with current or previous inflammatory bowel disease or diverticulitis.

Alosetron should not be used in those with severe hepatic impairment or a history thereof; it should be used with caution in patients with mild to moderate hepatic impairment. Elderly patients may be at increased risk of severe complications if constipation develops.

Interactions

Plasma concentrations of alosetron are markedly increased, and its half-life prolonged roughly threefold, when given with fluvoxamine; such a combination should be avoided. Licensed product information recommends that use with other more moderate inhibitors of cytochrome P450 isoenzyme CYP1A2 (such as quinolone antibacterials and cimetidine) should be avoided unless clinically necessary, because of the risk of similar interactions. Ketoconazole also increases plasma alosetron concentrations; care should be taken if alosetron is used with this or other potent inhibitors of the CYP3A4 isoenzyme (including clarithromycin, telithromycin, HIV-protease inhibitors, voriconazole, and itraconazole).

Pharmacokinetics

Alosetron is rapidly absorbed from the gastrointestinal tract; peak plasma concentrations are reached about 1 hour after an oral dose. Plasma concentrations are 30 to 50% lower in men than in women given the same oral dose; clearance is lower in women. Bioavailability is about 60%; the extent and rate of absorption are slightly reduced by food. Plasma protein binding is about 82%. Alosetron is extensively metabolised via cytochrome P450 isoenzymes, particularly CYP1A2, although CYP2C9 and CYP3A4 also play a role. Numerous metabolites are excreted in the urine and faeces; only 6% of a dose is recovered unchanged from the urine. The terminal elimination half-life of alosetron is reported to be about 1.5 hours.

◊ References.

1. Koch KM, *et al.* Sex and age differences in the pharmacokinetics of alosetron. *Br J Clin Pharmacol* 2002; **53:** 238–42.

Uses and Administration

Alosetron is a 5-HT_3 antagonist used in the treatment of severe diarrhoea-predominant irritable bowel syndrome (p.1699) in women who have not responded to conventional therapy; effectiveness in men has not been established. It is given orally as the hydrochloride but doses are expressed in terms of the base; alosetron hydrochloride 1.12 mg is equivalent to about 1 mg of alosetron.

The initial dose is the equivalent of alosetron 500 micrograms twice daily for 4 weeks; if tolerated, the dose may then be increased if necessary to 1 mg twice daily. If symptoms are not adequately controlled after 4 weeks of treatment with the higher dose, alosetron should be stopped.

◊ References.

1. Lembo A, *et al.* Alosetron in irritable bowel syndrome: strategies for its use in a common gastrointestinal disorder. *Drugs* 2003; **63:** 1895–1905.
2. Mayer EA, Bradesi S. Alosetron and irritable bowel syndrome. *Expert Opin Pharmacother* 2003; **4:** 2089–98.
3. Cremonini F, *et al.* Efficacy of alosetron in irritable bowel syndrome: a meta-analysis of randomized controlled trials. *Neurogastroenterol Motil* 2003; **15:** 79–86.
4. Andresen V, Hollerbach S. Reassessing the benefits and risks of alosetron: what is its place in the treatment of irritable bowel syndrome? *Drug Safety* 2004; **27:** 283–92.
5. Lembo AJ, *et al.* Effect of alosetron on bowel urgency and global symptoms in women with severe, diarrhea-predominant irritable bowel syndrome: analysis of two controlled trials. *Clin Gastroenterol Hepatol* 2004; **2:** 675–82.
6. Chey WD, *et al.* Long-term safety and efficacy of alosetron in women with severe diarrhea-predominant irritable bowel syndrome. *Am J Gastroenterol* 2004; **99:** 2195–2203.
7. Chang L, *et al.* A dose-ranging, phase II study of the efficacy and safety of alosetron in men with diarrhea-predominant IBS. *Am J Gastroenterol* 2005; **100:** 115–23.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Lotronex†; ***Mex.:*** Liminos†; ***USA:*** Lotronex.

Basic Aluminium Carbonate

Aluminium Hydroxycarbonate; Aluminum Carbonate, Basic *(USAN)*; Carbonato básico de aluminio.

Основный Углекислый Алюминий

Profile

Basic aluminium carbonate is a combination of aluminium hydroxide and aluminium carbonate. It is an antacid with general properties similar to those of aluminium hydroxide (below).

Basic aluminium carbonate has also been given orally as a phosphate binder in the treatment of hyperphosphataemia. For a discussion of the choice of phosphate binders, see Renal Osteodystrophy, p.1086.

Preparations

Proprietary Preparations (details are given in Part 3)
Multi-ingredient: ***Port.:*** Gastropensan.

Aluminium Formate

Aluminium Triformate.

Муравьинокислый Алюминий; Формиат Алюминия

$Al(CHO_2)_3.3H_2O$ = 216.1.

CAS — 7360-53-4 (anhydrous aluminium formate).

Profile

Aluminium formate has astringent properties and has been used in topical preparations for mouth disorders.

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Dynexan Zahnfleischtropfen.

Multi-ingredient: ***Austria:*** Cional; Dynexan; Methyment; ***S.Afr.:*** Dynexan.

Aluminium Glycinate

Aluminio, glicinato de; Basic Aluminium Aminoacetate; Dihydroxyaluminum Aminoacetate. (Glycinato-*N*,*O*)dihydroxyaluminium hydrate.

Алюминия Глицинат

$C_2H_6AlNO_4(+xH_2O)$ = 135.1 (anhydrous).

CAS — 13682-92-3 (anhydrous aluminium glycinate); 41354-48-7 (aluminium glycinate hydrate).

ATC — A02AB07.

ATC Vet — QA02AB07.

Pharmacopoeias. In *Br.* and *US.*

BP 2008 (Aluminium Glycinate). A white or almost white, odourless or almost odourless, powder. It contains 34.5 to 38.5% of Al_2O_3 calculated on the dried substance, and not more than 12% loss of weight on drying. Practically insoluble in water and in organic solvents; it dissolves in dilute mineral acids and in aqueous solutions of alkali hydroxides. A 4% suspension in water has a pH of 6.5 to 7.5.

USP 31 (Dihydroxyaluminum Aminoacetate). A white, odourless, powder. It may contain small amounts of aluminium oxide and aminoacetic acid. It loses not more than 14.5% of its weight on drying. Insoluble in water and in organic solvents; soluble in dilute mineral acids and in solutions of fixed alkalis. A 4% suspension in water has a pH of 6.5 to 7.5.

Profile

Aluminium glycinate is an antacid with general properties similar to those of aluminium hydroxide (below). It has been given in doses of up to 1 g by mouth.

Preparations

USP 31: Dihydroxyaluminum Aminoacetate Magma.

Proprietary Preparations (details are given in Part 3)
Denm.: Almin.

Multi-ingredient: ***Arg.:*** Dafne; ***Austria:*** Gastripan; ***Belg.:*** Alucid; ***Chile:*** Sinacid; ***Denm.:*** Alminox; ***Fr.:*** Acidrine; ***Ger.:*** Acidrine†; ***Gr.:*** Novalox; ***Indon.:*** Acidrine; ***Ital.:*** Acidrine; ***Pol.:*** Proacid; ***Spain:*** Gastroglutal†; Meteori; Natrocitral; Secrepat.

Used as an adjunct in: ***Austria:*** Ambene N; Indobene; ***Braz.:*** Reumix†; Somalgin; ***Chile:*** Butartrol; Flexono; ***Ger.:*** Indomet-ratiopharm m†; ***Ital.:*** Aspirina 03; ***Switz.:*** Bonidon; ***USA:*** Buffex.

Aluminium Hydroxide

Aliuminio hidroksidas; Alumiinihydroksidi; Aluminii Hydroxidum; Aluminii oxidum hydricum; Aluminium Oxidum Hydricum; Aluminium (oxyde d') hydraté; Aluminiumhydroxid; Aluminum Hydroxide; Alüminyum Hidroksit; Glinu wodorotlenek; Hidróxido de aluminio; Hydroxid hlinitý; Wasserhaltiges Aluminiumoxid.

Алюминий Гидроксид

CAS — 21645-51-2 [$Al(OH)_3$].

ATC — A02AB01.

ATC Vet — QA02AB01.

NOTE. Algeldrate (*USAN*, *pINN*) is defined as a hydrated aluminium hydroxide with the general formula of $Al(OH)_3.xH_2O$. Compounded preparations of aluminium hydroxide may be represented by the following names:

- Co-magaldrox *x/y* (*BAN*)—where *x* and *y* are the strengths in milligrams of magnesium hydroxide and aluminium hydroxide respectively.

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

Ph. Eur. 6.2 (Aluminium Oxide, Hydrated; Dried Aluminium Hydroxide BP 2008). It contains the equivalent of 47 to 60% Al_2O_3. It is a white or almost white, amorphous powder. Practically insoluble in water; it dissolves in dilute mineral acids and in solutions of alkali hydroxides. Store in airtight containers at a temperature not exceeding 30°.

Ph. Eur. 6.2 (Aluminium Hydroxide, Hydrated, for Adsorption; Aluminii Hydroxidum Hydricum ad Adsorptionem). A white or almost white, translucent, viscous, colloidal gel. A supernatant may be formed upon standing. A clear or almost clear solution is obtained with alkali hydroxide solutions and with mineral acids. pH 5.5 to 8.5. Store at a temperature not exceeding 30°. Do not allow to freeze.

USP 31 (Aluminum Hydroxide Gel). A suspension of amorphous aluminium hydroxide in which there is a partial substitution of carbonate for hydroxide. It is a white viscous suspension from which small amounts of clear liquid may separate on standing. It has a pH of between 5.5 and 8.0. Store in airtight containers. Avoid freezing.

USP 31 (Dried Aluminum Hydroxide Gel). An amorphous form of aluminium hydroxide in which there is a partial substitution of carbonate for hydroxide. It contains the equivalent of not less than 76.5% of $Al(OH)_3$ and may contain varying quantities of basic aluminium carbonate and bicarbonate. The labelling requirements states that 1 g of dried aluminium hydroxide gel is equivalent to 765 mg of $Al(OH)_3$. It is a white, odourless, tasteless, amorphous powder. Insoluble in water and in alcohol; soluble in dilute mineral acids and in solutions of fixed alkali hydroxides. A 4% aqueous dispersion has a pH of not more than 10.0. Store in airtight containers.

Adverse Effects and Precautions

Aluminium hydroxide, like other aluminium compounds, is astringent and may cause constipation; large doses can cause intestinal obstruction.

Excessive doses, or even normal doses in patients with low-phosphate diets, may lead to phosphate depletion accompanied by increased bone resorption and hypercalciuria with the risk of osteomalacia.

Aluminium salts are not, in general, well absorbed from the gastrointestinal tract, and systemic effects are therefore rare in patients with normal renal function. However, care is necessary in patients with chronic renal impairment: osteomalacia or adynamic bone disease, encephalopathy, dementia, and microcytic hypochromic anaemia have been associated with aluminium accumulation in such patients given large doses of aluminium hydroxide as a phosphate-binding agent. Similar adverse effects have also been associated with the aluminium content of dialysis fluids.

Aluminium hydroxide used as an adjuvant in adsorbed vaccines has been associated with the formation of granulomas.

Children. For the suggestion that aluminium-containing antacids should not be used in infants, see Toxicity, below.

Porphyria. Aluminium hydroxide is considered by some to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *animals.*

UK licensed product information states that aluminium hydroxide may be unsafe in patients with porphyria undergoing haemodialysis.

Toxicity. References to aluminium toxicity in dialysis patients and the possible association between aluminium ingestion and Alzheimer's disease are included under Aluminium (see p.2254).

Aluminium accumulation does not generally appear to be significant in patients with normal renal function taking therapeutic doses of aluminium-containing antacids, and there is little evidence that such antacids are a risk factor for Alzheimer's disease.[1] Elevated plasma-aluminium concentrations have been reported in infants with normal renal function given aluminium-containing antacids but there were no obvious signs of toxicity.[2] There have, however, been reports of phosphate depletion and rickets in a few infants caused by the use of antacids containing magnesium and aluminium hydroxides. In these cases the antacid had been started within a few months of birth and continued for up to 8 months. In reports that described a total of 3 infants,[3,4] the authors suggested that the use of soya-based infant feeding formulas, the phytates of which can interfere with mineral ab-