Galsulfase *(BAN, USAN, rINN)*

BM-102; Galsulfasa; Galsulfasum; recombinant human arylsulfatase B; rhASB. *N*-Acetylgalactosamine 4-sulfatase.

Гальсульфас

CAS — 552858-79-4.

ATC — A16AB08.

ATC Vet — QA16AB08.

Profile

Galsulfase is recombinant human *N*-acetylgalactosamine 4-sulfatase used as enzyme replacement therapy in the treatment of mucopolysaccharidosis VI (see below). Galsulfase is given by intravenous infusion in a dose of 1 mg/kg once a week. Infusion reactions are common and patients should be pre-treated with antihistamines with or without antipyretics. Galsulfase should be reconstituted to a final volume of 250 mL in sodium chloride 0.9% and given using an infusion pump. The initial infusion rate should be 6 mL/hour for the first hour, which may then be increased to 80 mL/hour if well tolerated. The total infusion time should be at least 4 hours to minimise the risk of infusion reactions, but may be extended to up to 20 hours, or interrupted, if necessary, in the event of infusion reactions. Patients weighing 20 kg and under may be susceptible to fluid overload and a smaller infusion volume of 100 mL should be considered, in which case, the infusion rate should be decreased accordingly so that the total infusion time is not less than 4 hours.

Adverse effects. References.

1. Kim KH, *et al.* Successful management of difficult infusion-associated reactions in a young patient with mucopolysaccharidosis type VI receiving recombinant human arylsulfatase B (galsulfase [Naglazyme]). Abstract: *Pediatrics* 2008; **121:** 609. Full version: http://pediatrics.aappublications.org/cgi/content/full/121/3/e714 (accessed 01/05/08)

Mucopolysaccharidosis VI. Mucopolysaccharidosis VI (Maroteaux-Lamy syndrome) is a rare progressive disorder characterised by inherited deficiency of the enzyme *N*-acetylgalactosamine 4-sulfatase, which is necessary to catalyse the hydrolysis of the sulfate moiety of the glycosaminoglycan, dermatan sulfate. This results in accumulation of dermatan sulfate in the lysosomes producing widespread irreversible cellular and tissue damage, and organ dysfunction. There is a rapidly advancing form of the disease that presents in the first year of life characterised by short stature, skeletal and joint deformities, dysmorphic facial features, upper airway obstruction requiring tracheostomy, and recurrent ear infections. There is also a more slowly advancing form that progresses over many decades. Both forms result in significant morbidity and functional problems with a reduced lifespan.[1]

Treatment is supportive and symptomatic involving many body systems; physical and occupational therapy is also necessary.[1] Haematopoietic stem-cell transplantation to supply the deficient enzyme is of benefit to some patients, although it is associated with significant morbidity and mortality.[1] Enzyme replacement therapy with galsulfase has been reported to confer benefit with an acceptable safety profile.[1,2]

1. Giugliani R, *et al.* Management guidelines for mucopolysaccharidosis VI. *Pediatrics* 2007; **120:** 405–18.
2. Harmatz P, *et al.* Enzyme replacement therapy for mucopolysaccharidosis VI: a phase 3, randomized, double-blind, placebo-controlled, multinational study of recombinant human *N*-acetylgalactosamine 4-sulfatase (recombinant human arylsulfatase B or rhASB) and follow-on, open-label extension study. *J Pediatr* 2006; **148:** 533–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Cz.: Naglazyme; ***Fr.:*** Naglazyme; ***Port.:*** Naglazyme; ***USA:*** Naglazyme.

Gamma-aminobutyric Acid

Ácido gamma-aminobutírico; Acidum Aminobutyricum Gamma; γ-Aminobutírico, ácido; Aminobutyric Acid; GABA; Gamma-aminosmörsyra; Gamma-aminovoihappo; Piperidic Acid. 4-Aminobutyric acid.

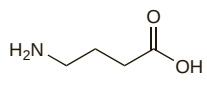
Гамма-аминобутировая Кислота

$C_4H_9NO_2$ = 103.1.

CAS — 56-12-2.

ATC — N03AG03.

ATC Vet — QN03AG03.



Profile

Gamma-aminobutyric acid is a principal inhibitory neurotransmitter in the CNS. It has been claimed to be of value in cerebral disorders and to have an antihypertensive effect.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Gammar; ***Hong Kong:*** Gammalon; ***Port.:*** Mielomade†; ***Thai.:*** Bainto; Gammalon.

Multi-ingredient: ***Arg.:*** Butineuron; Cadencial Plus; ***Braz.:*** Complevit; Gaba†; Gabax; Id Sedin†; ***Chile:*** Actebral; Gamalate B6; ***Spain:*** Cefabol; Gamalate B6.

Gamolenic Acid *(BAN, rINN)*

Acide Gamolénique; Ácido gamolénico; Acidum Gamolenicum; GLA; γ-Linolenic Acid. (*Z,Z,Z*)-Octadeca-6,9,12-trienoic acid.

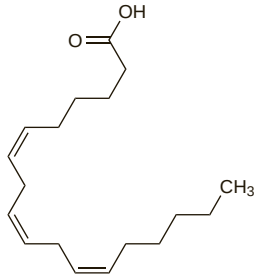
Гамоленовая Кислота

$C_{18}H_{30}O_2$ = 278.4.

CAS — 506-26-3.

ATC — D11AX02.

ATC Vet — QD11AX02.



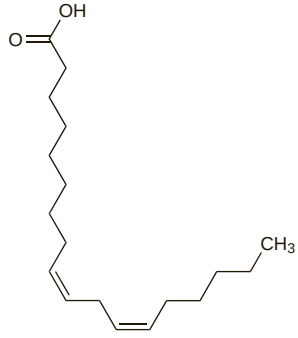
Linoleic Acid

Kwas linolowy; Linoleico, ácido; Linolic Acid; Linolsäure. (*Z,Z*)-Octadeca-9,12-dienoic acid.

Линолевая Кислота

$C_{18}H_{32}O_2$ = 280.4.

CAS — 60-33-3.



Adverse Effects and Precautions

Gamolenic and linoleic acids from evening primrose oil, and presumably other sources, can produce minor gastrointestinal disturbances and headache. They can precipitate symptoms of undiagnosed temporal lobe epilepsy, and should be used with caution in patients with a history of epilepsy or those taking epileptogenic drugs, in particular phenothiazines. Hypersensitivity reactions may also occur.

Uses and Administration

Gamolenic and linoleic acid are essential fatty acids of the omega-6 series that act as prostaglandin precursors. Endogenous gamolenic acid is derived from linoleic acid, which is present in many vegetable oils and is an essential constituent of the diet. The most widely-used source of these acids is evening primrose oil (see p.2302). Gamolenic and linoleic acids have been used in skin disorders and mastalgia, and have been investigated in other disorders including multiple sclerosis, rheumatoid arthritis, and the premenstrual syndrome.

Preparations containing essential fatty acids (formerly known collectively as vitamin F), including arachidonic acid, linoleic acid, linolenic acid (α-linolenic acid, p.1362), oleic acid, and their derivatives, have been used similarly. Conjugated linoleic acid (CLA), a mixture of isomers in which *cis*-9,*trans*-11-octadecadienoic acid and *trans*-10,*cis*-12-octadecadienoic acid predominate, has also been used.

Products containing gamolenic-acid rich plant oils are promoted in many countries as dietary supplements, often in combination with fish oils or other sources of omega-3 fatty acids (see p.1362).

A derivative of gamolenic acid, lithium gamolenate, has been investigated in pancreatic cancer.

Eczema. Atopic eczema (p.1579) may be due to a defect in essential fatty acid metabolism[1,2] and some beneficial symptomatic effects have been reported with evening primrose oil.[1,3] Meta-analysis of 9 studies involving 311 patients[4] has reported improvement in disease symptoms, especially itching, but a subsequent study in 123 patients found no therapeutic effect of evening primrose oil, alone or with fish oil.[5] Although the design and interpretation of this study has been criticised by the manufacturers of evening primrose oil,[6] the authors consider such criticism invalid,[7] and point out that an earlier large study yielded similar results.[8] No difference was found between placebo and evening primrose oil in a further study[9] in children with eczema, and there was also no effect on asthma symptoms in those patients suffering from both disorders. Studies[10,11] of borage oil (another source of gamolenic acid) also found no overall efficacy in adults or children with atopic eczema, although one study noted a suggestion of benefit in a subgroup of patients.[10] In a study[12] of a group of formula-fed infants with a high maternal familial risk of developing atopic eczema, borage oil supplementation did not prevent the expression of atopy, although it showed a tendency to alleviate the severity of the condition later in infancy.

Benefit has been reported in infants with seborrhoeic dermatitis from local application of borage oil.[13]

1. Wright S. Essential fatty acids and the skin. *Br J Dermatol* 1991; **125:** 503–15.
2. Horrobin DF. Essential fatty acid metabolism and its modification in atopic eczema. *Am J Clin Nutr* 2000; **71** (suppl): 367S–372S.
3. Rustin MHA. Dermatology. *Postgrad Med J* 1990; **66:** 894–905.
4. Morse PF, *et al.* Meta-analysis of placebo-controlled studies of the efficacy of Epogam in the treatment of atopic eczema: relationship between plasma essential fatty acid changes and clinical response. *Br J Dermatol* 1989; **121:** 75–90.
5. Berth-Jones J, Graham-Brown RAC. Placebo-controlled trial of essential fatty acid supplementation in atopic dermatitis. *Lancet* 1993; **341:** 1557–60. Correction. *ibid.*; **342:** 564.
6. Shield MJ, *et al.* Essential fatty acid supplementation in atopic dermatitis. *Lancet* 1993; **342:** 377.
7. Berth-Jones J, *et al.* Essential fatty acid supplementation in atopic dermatitis. *Lancet* 1993; **342:** 377–8. Correction. *ibid.*; 752.
8. Bamford JTM, *et al.* Atopic eczema unresponsive to evening primrose oil (linoleic and gamma-linolenic acids). *J Am Acad Dermatol* 1985; **13:** 959–65.
9. Hederos C-A, Berg A. Epogam evening primrose oil treatment in atopic dermatitis and asthma. *Arch Dis Child* 1996; **75:** 494–7.
10. Henz BM, *et al.* Double-blind, multicentre analysis of the efficacy of borage oil in patients with atopic eczema. *Br J Dermatol* 1999; **140:** 685–8.
11. Takwale A, *et al.* Efficacy and tolerability of borage oil in adults and children with atopic eczema: randomised, double blind, placebo controlled, parallel group trial. *BMJ* 2003; **327:**1385–7.
12. van Gool CJ, *et al.* γ-Linolenic acid supplementation for prophylaxis of atopic dermatitis—a randomized controlled trial in infants at high familial risk. *Am J Clin Nutr* 2003; **77:** 943–51.
13. Tollesson A, Frithz A. Borage oil, an effective new treatment for infantile seborrhoeic dermatitis. *Br J Dermatol* 1993; **129:** 95.

Mastalgia. Gamolenic acid (usually given in the form of evening primrose oil) has fewer adverse effects than drugs such as danazol or bromocriptine and has been preferred for mastalgia (p.2092), especially in patients with less severe symptoms or those who require prolonged or repeated treatment. However, there is no clear evidence of efficacy.

Multiple sclerosis. There is some evidence that modifying the intake of dietary fats and supplementing the diet with omega-6 polyunsaturated fatty acids, such as linoleic acid, could influence the clinical course of multiple sclerosis (p.892) and many patients practise dietary modification, including taking evening primrose oil. One study[1] has shown a reduction in severity and duration of relapse in patients taking linoleic acid supplements (as sunflower oil), and another[2] has reported benefit in patients who limited their intake of dietary saturated fatty acids and supplemented their diet with polyunsaturated fatty acids. A systematic review[3] of the relationship between dietary interventions (including linoleic acid supplements) and MS concluded that there was insufficient evidence to determine their benefits or risks.

1. Millar JHD, *et al.* Double-blind trial of linoleate supplementation of the diet in multiple sclerosis. *BMJ* 1973; **1:** 765–8.
2. Swank RL, Dugan BB. Effect of low saturated fat diet in early and late cases of multiple sclerosis. *Lancet* 1990; **336:** 37–9.
3. Farinotti M, *et al.* Dietary interventions for multiple sclerosis. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 22/04/08).

Premenstrual syndrome. Progressive improvement in premenstrual syndrome (p.2099) was reported over 5 cycles in an open pilot study in 19 patients receiving evening primrose oil.[1] However, subsequent results have not shown any benefit.[2-4] Evening primrose oil has been considered for cyclical mastalgia (see above).

1. Larsson B, *et al.* Evening primrose oil in the treatment of premenstrual syndrome: a pilot study. *Curr Ther Res* 1989; **46:** 58–63.
2. Khoo SK, *et al.* Evening primrose oil and treatment of premenstrual syndrome. *Med J Aust* 1990; **153:** 189–92.
3. Collins A, *et al.* Essential fatty acids in the treatment of premenstrual syndrome. *Obstet Gynecol* 1993; **81:** 93–8.
4. Budeiri DJ, *et al.* Is evening primrose oil of value in the treatment of premenstrual syndrome? *Control Clin Trials* 1996; **17:** 60–8.