NOVARTIS

Drug Regulatory Affairs

GLYVENOL®

(tribenosid)

200 mg Coated Tablets and 400 mg Capsules

Basic Prescribing Information

NOTICE

The Basic Prescribing Information (BPI) is the Novartis Core Data Sheet. It displays the company's current position on important characteristics of the product, including the Core Safety Information according to ICH E2C.

National Prescribing Information is based on the BPI. However, because regulatory requirements and medical practices vary between countries, National Prescribing Information (incl. US Package Insert or European SPCs) may differ in several respects, including but not limited to the characterisation of risk and benefits.

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Name of the medicinal product

GLYVENOL®

Qualitative and quantitative composition

Ethyl-3, 5, 6-tri-O-benzyl-D-glucofuranoside (= tribenosid), a synthetic active substance belonging to the category of the glucofuranosides.

The active substance is tribenosid.

For a full list of excipients, see section List of excipients.

Pharmaceutical form

Capsules of 400 mg.

Coated tablets of 200 mg.

Information might differ in some countries.

Clinical particulars

Therapeutic indications

Venous circulatory disorders: feelings of tiredness, heaviness, and tension in the legs, swelling and painful sensations in the legs experienced after prolonged standing or sitting.

Varicose syndrome: symptoms due to varicose veins, static oedema, and phlebalgia.

Haemorrhoids.

As an adjuvant in the treatment of phlebitis, periphlebitis, and post-thrombotic syndrome, as well as before and after sclerosing therapy.

Posology and method of administration

a) 1 capsule of 400 mg twice daily, to be taken during or after meals.

b) 1 tablet of 200 mg 3 to 4 times daily, to be taken during or after meals.

The recommended dose of 800 mg daily should not be exceeded, because raising the dose above this level achieves no further increase in the therapeutic effect.

Glyvenol® should be given for several weeks, even in cases where the symptoms rapidly subside.

It may be advisable to repeat the treatment from time to time, e.g. in housewives and other patients whose occupations entail prolonged exposure of the legs to chronic strain, especially at warmer times of the year.

Contraindications

Known hypersensitivity to tribenosid or or to any of the excipients.

Interaction with other medicinal products and other forms of interaction

Pharmacodynamic interactions

Although its active substance is derived from sugar, Glyvenol has not been found to interfere with carbohydrate metabolism, even in diabetics.

Pregnancy and lactation

Pregnancy

As in the case of any form of drug therapy, Glyvenol should be employed with caution during pregnancy, especially in the first 3 months.

Lactation

It is not known whether the active substance passes in to the breast milk. The benefits for the mother must be weighed against the risks for the child.

Undesirable effects

Skin disorders

Skin rashes may occur; these are usually of a harmless nature and disappear spontaneously when the medication is withdrawn. In rare cases of a more serious kind, it is advisable to resort to appropriate symptomatic measures. A relationship exists between the frequency of such side effects and the level of the dosage.

During post-marketing use of Glyvenol there have been reports of erythema multiforme and Stevens-Johnson syndrome.

Immune system disorders

Very rare cases of systemic anaphylaxis, including urticaria, angioedema, shortness of breath and circulatory distress, were reported.

Gastro-intestinal disorders

Gastrointestinal upsets may occur; these are usually of a harmless nature and disappear spontaneously when the medication is withdrawn. In rare cases of a more serious kind, it is advisable to resort to appropriate symptomatic measures. A relationship exists between the frequency of such side effects and the level of the dosage.

Overdose

Signs and symptoms

No cases of acute overdosage have yet been reported. In all probability, severe signs of poisoning would be unlikely to occur.

Pharmacological properties

Pharmacodynamic properties

Pharmacotherapeutic group: Other capillary stabilizing agents, ATC code: C05CX01.

Glyvenol reduces capillary permeability, thereby combating oedema.

It antagonises a variety of endogenous substances which play an important role as mediators in inflammatory processes and in the causation of pain. Glyvenol thus serves to counteract pathological processes occurring in the capillary beds, in the veins themselves, and in the paravenous tissues.

Pharmacokinetic properties

Tribenoside, the active substance of Glyvenol, is rapidly absorbed almost in its entirety and is intensively metabolised. Peak plasma concentrations of 9-18 micrograms/mL (tribenoside + metabolites) are recorded 1 hour after ingestion of tribenoside in a dosage of 10 mg/kg.

Tribenoside displays a varying affinity for different tissues and organs; in the walls of the blood vessels, for example, it attains relatively high concentrations.

Its elimination from the plasma shows a biphasic pattern.

The half-life (^{t}50 %alpha) for the first rapid phase is 2 hours. Once the plasma concentration has dropped below 2 micrograms/mL (i.e. approx. 8 hours after ingestion), the second, slower phase sets in, the half-life for which (^{t}50 %beta) is 20 hours. No accumulation of tribenoside occurs in the body, even in response to repeated daily doses. The active substance is excreted only in the form of metabolites and almost exclusively in the urine. The pharmacological activity of the main metabolites corresponds at the most to only half that of tribenoside, and 20 % of the dose administered is eliminated as hippuric acid. The excretion rate works out at 77-93 % of the dose in 9 hours and 93-100 % in 72 hours.

Pharmaceutical particulars

List of excipients

Tablets: Silica aerogel, cellulose microcryst., magnesium stearate, magnesium trisilicate, polyvinylpyrrolidone K 25, talc, wheat starch.

Capsules content: ethanol.

Capsule shell: canthaxanthin 10%, sodium salt of ethylparaben, gelatin, glycerin 85%, sodium salt of propylparaben.

Information might differ in some countries.

Incompatibilities

Not applicable.

Shelf life

Tablets: 3 years.

Capsules: 4 years.

Information might differ in some countries.

Special precautions for storage

Protect from heat and moisture. Do not store above 30°C.

Information might differ in some countries.

Glyvenol must be kept out of the reach and sight of children.

Nature and contents of container

20 capsules of 400 mg.

20 coated tablets of 200 mg.

Country specific.