SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the Medicinal Product
ACTOVEGIN®

2. Qualitative and Quantitative Composition 1
coated tablet contains :

Tablet core: *active ingredient:* blood components – deproteinized calf blood derivative – 200.0 mg, as an Actovegin® granulate* – 345.0 mg

3. Pharmaceutical Form
Coated tablets
Description: Round biconvex bright greenish-yellow coated shiny tablets

4. Clinical Particulars 4.1
Therapeutic Indications As
part of combined therapy:

- Symptomatic treatment of cognitive impairment including post-stroke cognitive impairment and dementia;
- Symptomatic treatment of peripheral perfusion disorders and their sequelae; Symptomatic treatment of diabetic polyneuropathy (DPN).

4.2 Posology and Method of Administration
Orally, before food intake, without chewing, with a small amount of fluid. *Post-stroke cognitive impairment*

In acute period of ischemic stroke, beginning from 5 – 7day, 2000 mg per day intravenously dropwise up to 20 infusions with subsequent switching to 2 tablets 3 times a day (1200 mg/day). The overall duration of treatment is 6 months.

Dementia

2 tablets 3 times a day (1200 mg/day). The overall duration of treatment is 20 weeks. *Peripheral perfusion disorders and their sequelae*

1-2 tablets 3 times a day (600 – 1200 mg/day). The duration of treatment is 4 – 6 weeks.
Diabetic polyneuropathy
2000 mg a day intravenously dropwise 20 infusions with subsequent switch to 3 tablets 3 times a day (1800 mg/day). The duration is 4 – 5 months.

Use in pediatric patients
No data are currently available and usage is not recommended in pediatric patients.

4.3 Contraindications
- Hypersensitivity to Actovegin® and similar preparations or their excipients.
- Fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency.
- Age below 18 years.

Use with caution

Pregnancy and breastfeeding.

4.4 Special warnings and special precautions for use Clinical data

In multicentre, randomized, double blind, placebo-controlled trial ARTEMIDA (NCT01582854) aimed to examine the effect of Actovegin® treatment on cognitive impairment in 503 patients with acute ischemic stroke over six months, the overall incidence of serious adverse events and death was similar across the two treatments groups. Although the incidence of recurrent ischemic stroke was within the range expected in this patient population, a higher incidence was observed in the Actovegin group compared with the placebo, however this difference was not statistically significant. There was no established causal relationship between the adverse event and Actovegin®. As shown by the APOLLO study (NCT03469349), the purpose of which was to study the therapeutic effect of the drug Actovegin® in relation to the distance of pain-free walking in 366 patients with chronic obliterating diseases of the arteries of the lower extremities IIB stage according to the Fontaine classification, the therapeutic effect of the use of the drug persists for at least 3 more months. after discontinuation of the drug.

Excipients of Known Effect

Phenylalanine

This medicinal product contains phenylalanine. Phenylalanine may be harmful for patients with phenylketonuria (PKU).

4.5 Interaction with other medicinal products At present, no interactions have been reported.

4.6 Use during pregnancy and lactation

Actovegin® should only be used if the therapeutic benefits outweigh the potential risk for the fetus or child

4.7 Effects on ability to drive and use machines Not detected

4.8 Adverse reactions

The frequency of an adverse drug reaction (ADR) is determined according to the Council for International Organizations of Medical Sciences (CIOMS) classification: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to< 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data).

Immune system disorders

Rare: Allergic reactions (drug fever, shock symptoms).

Skin and subcutaneous tissue disorders Rare:

Urticaria, flush.

4.9 Overdose

There has been no experience of overdose with Actovegin®.

5. Pharmacological Properties

Pharmacotherapeutic group

stimulant of tissue regeneration.

ATC code: B06AB.

5.1 Pharmacodynamics
Actovegin® is an antihypoxant showing three main categories of effect: metabolic, neuroprotective and microcirculatory. Actovegin® improves oxygen utilization and uptake; Inositol phospho-oligosaccharides as part of the Actovegin® composition positively affect glucose transport and utilization, which result in energy metabolism improvement and reduction of lactate formation.

Several pathways are seen as being responsible for Actovegin´s neuroprotective mechanism of action:

Actovegin® prevents Aβ25-35 induced apoptosis.

Actovegin® modulates activity of nuclear factor kappa B (NF-KB) which plays wide-ranging roles within both the central and peripheral nervous systems.

Another important pathway is linked to the nuclear enzyme poly (ADP-ribose) polymerase (PARP). PARP has an important role in the detection of single-strand DNA breaks and repair, but excessive activation of the enzyme can trigger cellular death during such conditions as cerebrovascular diseases and diabetic polyneuropathy. Actovegin® is found to reduce PARP activity which results in a functional and morphological improvement of the central and peripheral nervous system.

Positive effects of Actovegin® affecting microcirculatory processes and endothelium are: increase in capillary blood flow rate, reduce of pericapillary zone and reduce of the myogenic tone of precapillary arterioles and capillary sphincters, decrease of arteriolo-venular shunting of blood flow with blood flowing largely to the capillary bed, and increase of endothelial oxide synthase function of the microvasculature.

Different studies showed an onset of the effect of Actovegin® 30 minutes at the latest after administration. The maximum effect is reached 3 hours after parenteral administration and 2-6 hours after oral administration.

5.2 Pharmacokinetics
Pharmacokinetic parameters of ACTOVEGIN® cannot be assessed by means of pharmacokinetic methods, because it contains only natural physiological components which are usually present in the body.
5.3 Preclinical safety data According to pre-clinical studies data Actovegin® does not show toxic effects even with doses up to 30-40 folds higher than a dose recommended for human use.
6 Pharmaceutical Particulars
6.1 List of Excipients
Tablet core: magnesium stearate – 2.0 mg, talc – 3.0 mg.

Coating: gum acacia – 6.8 mg, montan-glycol wax – 0.1 mg, hypromellose phthalate – 29.45 mg, diethylphthalate – 11.8 mg, quinoline yellow aluminium lake – 2.0 mg, macrogol-6000 – 2.95 mg, povidone-K30 – 1.54 mg, saccharose – 52.3 mg, talk – 42.2 mg, titanium dioxide – 0.86 mg.

*Actovegin® granulate consists of: *active ingredient:* blood components – deproteinized calf blood derivative – 200.0 mg, *excipients* – povidone-K90 – 10.0 mg, microcrystalline cellulose – 135.0 mg.

6.2 Incompatibilities
Not applicable

6.3 Shelf Life 3 years.

Do not use medicine when expiry date is over.

6.4 Storage conditions
Protected from light below 25°C.

Keep out of the reach of children!

6.5 Nature and Contents of Container
50 tablets in dark glass bottle with a screw neck and a tamper-evident screw aluminum cap. 1 bottle is placed in a carton along with a Patient Information Leaflet. Each pack has a transparent security round sticker with hologram and tamper-evident control.

6.6 Instructions for Use/Handling Rx
(a prescription-only drug).

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9. Date of last revision
09 Sep 2020