ÆSCULAPIUS
FARMACEUTICI

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ANGIOFLUX "600 LRU/2 ML INJECTABLE SOLUTION"
ANGIOFLUX "250 LRU SOFT CAPSULES"

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

ANGIOFLUX 600 LRU/2 ml injectable solution
One vial contains:
Active substance:
- Sulodexide LRU 600

ANGIOFLUX 250 LRU soft capsules
One capsule contains:
Active substance:
- Sulodexide LRU 250

For excipients, see 6.1

3. PHARMACEUTICAL FORM

- Injectable solution
- Soft capsules

4. CLINICAL INFORMATION

4.1. Therapeutic indications

Chronic venous ulcers

4.2 Posology and method of administration

Soft capsules: 1 capsule 2 times per day, away from meals.
Vial: 1 vial per day i.m. or i.v.
We mainly recommend starting therapy with the vials and, after 15 – 20 days, continuing with the capsules for 30 – 40 days.
The complete therapeutic cycle should be continued at least twice a year. Depending on the doctor's opinion, the quantity and frequency of the dose may be varied.

4.3 Contraindications

Hypersensitivity to the active substance or to one of the excipients.
As the molecular structure is similar to heparin, do not administer ANGIOFLUX to patients hypersensitive to heparin and heparinoids. Hemorrhagic diathesis.

4.4. Special warnings and special precautions for use

Patients should consult their doctors for instructions as to the correct way of administering the drug.
In all cases, where treatment is in progress with anti-coagulants, we recommend periodically controlling the haemo-coagulation parameters.

4.5. Interactions with other medicinal products and other forms of interaction

As sulodexide is a heparin-similar molecule, it may increase the anti-coagulation effects of heparin and of oral anti-coagulants if administered at the same time.

4.6. Pregnancy and lactation

In pregnant women and very early infancy, the product should be administered in cases of effective need, under the direct control of a doctor.
For cautionary reasons, we advise against use during pregnancy, even if the foetal toxicity studies have nor demonstrated any embryo-foetus toxicity.

4.7. Effects on ability to drive vehicles and use machines

ANGIOFLUX does not influence the ability to drive vehicles or to use machinery.

4.8. Undesirable effects

Occasional reports of:
Soft capsules: disturbances of the gastro-enteric apparatus with nausea, vomiting and epigastralgia.
Vial: pain, burning and haematoma at the injection site.

4.9. Overdose

Hemorrhagic accident is the only effect obtainable from an overdose. In case of hemorrhage it is necessary to inject Protamine sulphate at 1% (3 ml i.v. = 30mg) as adopted for “heparinic hemorrhage”.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

Pharmacotherapeutic category: Anti-thrombotic/Heparinic, ATC Code: B01AB11
Action mechanism:
The action mechanism depends on the complementary action of its constituents: the drug exerts an anti-thrombosis action mainly due to the inhibition of the activated coagulation factor (X). It also decreases haematic viscosity, has a fibrinolytic effect due to the release of the tissue plasminogen activator of the vessel wall (t-PA) and reduces the haematic levels of the plasminogen inhibitor activator (PAI).

5.2. Pharmacokinetic properties

The plasmatic kinetics of sulodexide has been studied in rat for years for the administration methods foreseen in therapy; in other words parenteral and oral administration. The parenteral administration of sulodexide proves to be characterised by a rapid distribution phase in organs and tissues and successive bi-phase elimination according to a double-compartmental criterion.
When administered orally, the absorption appeared less rapid and more gradual, with a maximum haematic concentration after 60' instead of after 5 – 15'. The kinetics for oral administration can be interpreted by a mono-compartmental model. On the basis of the respective AUC, the bio-availability of Sulodexide taken orally proves on average to be 50% of that for intramuscular administration. Sulodexide is mainly excreted in urine. The minimum recovery in the first 24 hours corresponds to around 50% and reaches 67% after 48 hours.

5.3. Preclinical safety data

The pre-clinical data proves an absence of risk in man on the basis of conventional pharmacological safety studies: toxicity from repeated administration, genotoxicity, cancerogenic potential, reproduction toxicity studies.

6. PHARMACEUTICAL INFORMATIONS

6.1. List of excipients

Injectable solution:
Sodium chloride, Water for injectable solutions.
Soft capsules:
Migliol 812, Sodium laurylsulphate, Precipitated silica.

- **Additional notes:**

Injectable solution.
The product contains less than 1 mmol of sodium in each dose, it is essentially "sodium-free".

6.2. Incompatibilities

As Sulodexide is an acid polysaccharide, if it is administered in extemporaneous associations, it may react by bonding with all the basic substances. Incompatible substances commonly used in extemporaneous associations for drips are: vitamin K, B complex vitamins, hydrocortisone, hyaluronidase, calcium gluconate, quaternary ammonia salts, cloramphenicol, tetracycline, streptomycin.

6.3. Validity period

3 years

6.4. Special precautions for storage

Storage:
250 LRU Soft capsules: store at a temperature not higher than 30°C.

600 LRU/2ml injectable solution: this medicine does not require any particular conservation conditions.

6.5. Nature and content of the container

Vial

type I neutral white glass vial of 2 ml, containing an in injectable solution.
600 LRU/2ml injectable solution – 10 vials of 2 ml

Soft capsules

Aluminium and PVC blister containing 50 soft capsules.
250 LRU Soft capsules - 50 Capsules

6.6 Use instructions

Unused product and refuse derived from this medicine must be disposed of in conformity with local laws.

7. MARKETING AUTHORISATION HOLDER

Aesculapius Farmaceutici S.r.l.
Via Cefalonia, 70 - 25124 Brescia.

8. MARKETING AUTHORISATION NUMBERS

ANGIOFLUX 600 LRU/2 ml Injectable solution – 10 vials of 2 ml A.I.C. no. 027932019
ANGIOFLUX 250 LRU Soft capsules – 50 capsules A.I.C. no. 027932021

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Renewal date: May 2008

10. DATE OF REVISION OF THE TEXT

March 2017