FLUXUM®

Low molecular weight heparin Sodium salt (INN: Parnaparin)

FLUXUM (Parnaparin) is a low molecular weight glycosaminoglycan with mean molecular weight of 4,500 Daltons obtained using an original patented heparin fragmentation and purification process.
FLUXUM, unlike heparin, has the property of keeping its antithrombotic activity separate from its anticoagulant activity. In fact, differently from heparin, the ratio between its antithrombotic activity, measured by activated factor X (Xa) assay, and its anticoagulant activity, represented by activated thromboplastin time (aPTT) and thrombin time (TT) values, is higher than 4. This ratio may be considered as a therapeutic or safety index.
FLUXUM is an antithrombotic agent with a quick onset and longer duration of activity and is active in venous thrombo-embolic disease prophylaxis.
On an average, FLUXUM shows its maximum anti-Xa activity plasma peak 3 hours after subcutaneous administration and has a plasma half-life of about 6 hours. The anti-Xa activity persists in the blood for about 20 hours after a single injection; these characteristics make a single daily dose possible.
FLUXUM, unlike heparin, has no platelet pro-aggregant activity. It is virtually devoid of acute and chronic toxicity and mutagenic activity, and does not interfere with the reproductive function and embryonal development in experimental models.

INDICATIONS
Prophylaxis of deep venous thrombosis (DVT) in general and orthopaedic surgery.

CONTRAINDICATIONS
History of thrombocytopenia with FLUXUM (also see «Precautions»).
Occurrence or tendencies towards haemorrhagies linked with haemostasis disturbances, with the exception of consumption coagulopathy not related to heparin.
Organ injuries with risk of bleeding.
Acute bacterial endocarditis (with the exception of those relating to mechanical prostheses).
Haemorrhagic cerebrovascular accidents.
Allergy to the product.
Relative contraindications: co-administration with ticlopidine, salicylates or NSAIDs, antiplatelet agents as dipyridamole, sulphinpyrazone, etc..

ADVERSE REACTIONS
Slight haemorrhagic manifestations mainly linked with preexistent risk factors, such as organic lesions with haemorrhagic tendencies, or iatrogenic effects (see «Contraindications» and «Drug Interactions»).
Rare cases of thrombocytopenia, occasionally severe (see «Precautions»).
Rare cases of cutaneous necrosis, normally localized at the injection site, which are observed both with classical heparins and low molecular weight heparins.
These phenomena are preceded by the occurrence of purpura or infiltrated and painful erythematous plaques with or without general symptoms. In these cases it is necessary to stop the treatment immediately.
In some cases, slight haematomas occur at the injection site.
Rare occurrences of cutaneous or general allergy.
In some cases it has been necessary to interrupt the treatment.
Increase in transaminases has been reported.

PRECAUTIONS
FLUXUM must not be administered intramuscularly.
Biological monitoring: perform a platelet count before the treatment and then twice a week; if prolonged treatment is foreseen, this frequency of monitoring must be kept up for at least the first month, after which the monitoring can be less frequent.
If there are records of thrombocytopenia as a consequence of treatment with another heparin, particular attention must be paid to the clinical state and the platelet count should be carried out every day.
If thrombocytopenia arises with classical heparin (unfractionated), substitution with a low molecular weight heparin is a possible solution. In this case daily monitoring of platelet count is necessary and the treatment must be interrupted as soon as possible. In fact there have been reports of cases where the initial thrombocytopenia has persisted with low molecular weight heparin. In vitro platelet aggregation tests are only of indicative value. It is advisable to get in contact with a specialized team.
FLUXUM should be used with caution in case of liver failure, renal failure, arterial hypertension, medical history of gastrointestinal ulcer or any other organic lesions which are susceptible to bleeding, or chorioretinal vascular diseases.
FLUXUM should be used with caution during the postoperative period after brain or spinal cord surgery.
Low molecular weight heparins differ in production method, molecular weight and their specific activity. It is therefore not advisable to change from one proprietary product to another during treatment. For prudential reasons its use is not recommended during pregnancy and lactation even if foetal toxicity studies have not shown any embryo-foetal toxic effects.
KEEP OUT OF REACH OF CHILDREN

DRUG INTERACTIONS
Unadvisable co-administrations
— *Acetylsalicylic acid and other salicylates* (systemic route)
Increase in risk of haemorrhage (inhibition of platelet function and injury to the gastroduodenal mucosa caused by salicylates).
Use other analgesic or antipyretic agents.
— *NSAIDs* (systemic route)
Increase in risk of haemorrhage (inhibition of platelet function and injury to the gastroduodenal mucosa caused by non-steroidal anti-inflammatory drugs).
If it is not possible to avoid the co-administration, careful clinical and biological monitoring is necessary.
— *Antiplatelet agents (ticlopidine, dipyridamole, sulphinpyrazone, etc.)*
Increase in risk of haemorrhage (inhibition of platelet function).
— *Heparin*
The co-administration with high doses of heparin is not recommended.
Co-administrations which require precautions for use
— *Oral anticoagulant agents*
Potentiation of the anticoagulant effect. If it is not possible to avoid the co-administration, careful clinical and biological monitoring is necessary.
— *Glucocorticoids* (systemic route)
Worsening of the risk of haemorrhage characteristic of glucocorticoid therapy (gastric mucosa, vascular fragility) at high doses or in long term treatments of over ten days.
The co-administration should be justified; increase the clinical monitoring.
— *Dextran* (parenterally)
Increase in risk of haemorrhage (inhibition of platelet function).
Adjust the heparin posology so as not to exceed a hypocoagulability of 1.5 times the reference value both during the co-administration and after suspending the dextran.

DOSAGE AND ADMINISTRATION

Subcutaneous administration

In general surgery:

0.3 ml (3,200 I.U. aXa) subcutaneously 2 hours before the operation. Subsequently every 24 hours for at least 7 days. Haemocoagulation tests are not necessary.

Patients with a high thromboembolic risk and in orthopaedic surgery:

0.4-0.6 ml (4,250-6,400 I.U. aXa, depending on the thrombotic risk of the patients) subcutaneously 12 hours before and 12 hours after the operation, then one injection a day during the postoperative period.

The duration of the treatment is at least 10 days.

INJECTION TECHNIQUE

The injection must be made in the subcutaneous tissue of the upper outer quadrant of the gluteal region, alternating the right side with the left, or of the anterolateral and posterolateral abdominal girdle.

The needle must be inserted for its whole length perpendicularly (not tangentially) into the thickness of a cutaneous fold held between the operator's thumb and forefinger.

The fold must be held till the end of the injection.

OVERDOSAGE AND ANTIDOTE

The prefilled syringe containing FLUXUM makes an overdosage very unlikely; however should an overdosage occur accidentally, effects linked with its anticoagulant activity (bleeding) may occur, which are not normally present at therapeutic doses.

These effects can be neutralized by administering protamine sulphate i.v.; 0.6 ml of protamine sulphate is necessary in order to inhibit 0.1 ml of FLUXUM.

STORAGE CONDITIONS

Store below 30°.

PACKAGES

Box of two 0.3 ml prefilled syringes (3,200 I.U. aXa).
Box of six 0.3 ml prefilled syringes (3,200 I.U. aXa).
Box of two 0.4 ml prefilled syringes (4,250 I.U. aXa).
Box of six 0.4 ml prefilled syringes (4,250 I.U. aXa).
Box of two 0.6 ml prefilled syringes (6,400 I.U. aXa).
Box of six 0.6 ml prefilled syringes (6,400 I.U. aXa).

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