Composition:

Active principle: Calcium dobesilate.

Capsule: Calcium dobesilate 500 mg, colour (E132), excipients for capsule.

Properties/Effects:

Calcium dobesilate acts on the capillary walls by regulating its impaired physiological functions, increased permeability and decreased resistance. It increases erythrocyte flexibility, inhibits platelet hyperaggregation and in diabetic retinopathy, it reduces plasma and blood hyperviscosity, thus improving blood rheological properties and tissue irrigation. These effects allow to correct capillary dysfunctions either of functional origin or caused by constitutional or acquired metabolic disorders. Calcium dobesilate contributes to reduce oedema.

Pharmacokinetics:

After oral administration of 500 mg of calcium dobesilate, its blood level is above 6 µg/ml between the 3rd and 10th hour, with a maximum (C_{max}) of 8 µg/ml on the average after 6 hours (t_{max}). Twenty four hours after intake, blood level is about 3 µg/ml. The rate of protein-binding is 20-25%. In animals, calcium dobesilate does not cross the haematoencephalic or the placental barrier, but it is not known whether this is also the case in humans. Calcium dobesilate enters the maternal milk in very low quantities (0.4 µg/ml after intake of 1500 mg as observed in one study). Calcium dobesilate does not enter the enterohepatic cycle and is excreted mainly unchanged with only 10% being excreted as metabolites. About 50% of the orally administered dose are eliminated in the first 24-hour and about 50% in the faeces. Plasma half-life is around 5 hours.

Kinetics in particular clinical situations:

It is not known to what extent renal function disorders influence the pharmacokinetic properties of calcium dobesilate (see precautions)

Indications and usage:

Microangiopathies, in particular diabetic retinopathy.

Clinical signs of chronic venous insufficiency in the lower limbs (Pain, cramps, paresthesia, oedema, stasis, dermatosis), as adjuvant in superficial thrombophlebitis.

Haemorrhoidal syndrome, microcirculation disorders of arteriovenous origin.

Dosage:

Generally 500 to 1000 mg - 1 capsule once or twice a day - to be taken with the main meals.

Treatment duration, which is generally between a few weeks and several months, depends on the disease and its evolution.

Dosage should be adapted individually according to the severity of the case.

LIMITATIONS FOR USE

Contraindications:

Hypersensitivity towards calcium dobesilate.

Precautions:

Dosage should be reduced in case of severe renal insufficiency requiring dialysis.

In very rare cases (0.32/million patients), incidence estimated on the basis of spontaneous reports, the intake of calcium dobesilate may induce agranulocytosis, probably linked to hyper-sensitivity reaction. This condition may be expressed by symptoms such as high fever, oral cavity infections, (Tonsillitis) sore throat, anogenital inflammation and accompanying symptoms, that are often signs of an infection. The patient should be told that by any sign of infection he/she must immediately inform his/her physician. In that case, it is essential to control without delay the blood formula and leucogram and to discontinue the treatment.

Pregnancy/Breast-feeding:

Pegnancy category C: Studies in pregnant women or animals are not available. As it is not known whether calcium dobesilate crosses the placental barrier in humans, the drug should only be administered if it was estimated that the anticipated therapeutic benefit outweigh the potential risk to the fetus. Calcium dobesilate enters the maternal milk in

very low quantities (0.4 µg/ml after intake of 3×500 mg). As a precaution either the treatment or the breast-feeding should be stopped.

Adverse effects:

Rarely gastrointestinal disorders including nausea and diarrhea, skin reactions, fever, articular pain and in very rare cases, agranulocytosis (see precautions) have been reported. These reactions are generally spontaneously reversible after treatment withdrawal. In case of gastrointestinal disorders, the dosage should be reduced or the treatment temporarily withdrawn. In case of skin reactions, fever, articular pain or change in blood formula, the treatment must be stopped and the treating physician informed as this may constitute allergic reactions.

Interactions:

No interaction is known up to now.

Overdosage:

The clinical signs of a possible overdosage are not known.

PARTICULAR REMARKS

Incompatibilities:

No incompatibility is known up to now.

Information:

At therapeutic doses, calcium dobesilate may interfere with the assay of creatinine (too low values).

Stability:

Doxium 500 should not be used after the expiration date printed on the package after "EXP".

Presentation:

Capsules (500 mg): 30 capsules.