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DOXIUM 500

OM Pharma

1. Trade name of the medicinal product

DOXIUM 500

2. Qualitative and quantitative composition

1 capsule contains:

Active principle: Calcium dobesilate monohydrate 500 mg.

Colour (E 132), excipients for capsule.

3. Pharmaceutical form

Capsules.

4. Clinical particulars

4.1. Therapeutic indications

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.

4.2. Posology and method of administration

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.

4.3. Contra-indications

Hypersensitivity towards calcium dobesilate.

4.4. Special warnings and special precautions for use

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 a hypersensitivity 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.

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

No interaction is known up to now.

At therapeutic doses, calcium dobesilate may interfere with creatinine assay by giving lower values.

4.6. Pregnancy and lactation

Pregnancy 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 the potential benefit justifies the potential risk to the foetus.

Calcium dobesilate enters the maternal milk in very low quantities (0,4 µg/ml after intake of 3x500 mg). As a precaution, either the treatment or the breastfeeding should be stopped.

4.7. Effects on ability to drive and use machines

Doxium 500 has no effect upon driving capacity and managing of machines.

4.8. Undesirable effects

The side effects are classified according to the MedDRA convention by system organ class and by frequency as follows:

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)

Gastrointestinal disorders

Rare : nausea, diarrhoea, vomiting.

Skin and subcutaneous tissue disorders
Rare: pruritus,rash.

General disorders and administration site conditions
Rare: fever,chills.

Musculoskeletal disorders
Rare : arthralgia.

Cardiac disorders
Uncommon: tachycardia.

Blood and lymphatic system disorders
Isolated cases of agranulocytosis have been reported mainly in elderly patients and in combination with other drugs.

These reactions are generally reversible when stopping treatment course.

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 hypersensitivity reactions.

5. Pharmacological data

ATC code: C05BX01 Other sclerosing agents

5.1. Pharmacodynamic properties

Regulator of capillary functions.

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.

5.2. Pharmacokinetic properties

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 urine 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”).

5.3. Preclinical safety data

Acute and chronic toxicity studies, foetotoxicity and mutagenicity studies on calcium dobesilate have not revealed any toxic effect.

6. Pharmaceutical particulars

6.1. List of excipients

1 capsule contains:
Magnesium stearate, maize starch, gelatin, yellow ferric oxide (E 172), indigotine (E 132), titanium dioxide (E 171).

6.2. Physical and chemical incompatibilities

No known up to now.

6.3. Shelf-life

The medication should not be used after the expiration date printed on the package together with the mention “EXP”.

6.4. Special precautions for storage

The medication should be stored protected from heat (below 30ºC).

Store in the original package.

6.5. Nature and contents of container
Boxes containing blister-packs of 10 capsules.
(Aluminium foil lacquered with PVDC-PVC/PVDC foil)

6.6. Instructions for use
No special instructions.

7. Marketing authorization holder
OM PHARMA, 22, rue du Bois-du-Lan, 1217 Meyrin 2/Geneva (Switzerland)