INFORMATION FOR PROFESSIONALS

DOXIUM 500

COMPOSITION
Active substance: Calcium dobesilate monohydrate
Excipients: colouring: Indigo carmine (E132), magnesium stearate, maize starch, gelatine, yellow iron oxide (E172), titanium dioxide (E171), water

GALENIC FORM AND QUANTITY OF ACTIVE SUBSTANCE PER UNIT
Capsule
Each capsule contains 500 mg of calcium dobesilate monohydrate.

INDICATIONS/POSSIBILITIES FOR USE
Microangiopathies, in particular diabetic retinopathy.
Clinical symptoms of chronic venous insufficiency of the legs (pains, cramps, paraesthesia, oedemas, stasis dermatitis), superficial thrombophlebitis in adjuvant treatment.
Haemorrhoidal syndrome, post-thrombotic syndrome, microcirculatory disorders of arteriovenous origin.

POSOLOGY/INSTRUCTIONS FOR USE
Posology
For adults only
In general 500 to 2000 mg (1 to 2 capsules, once or twice a day) Doxium must be taken during or immediately after meals, in order to minimise any gastric discomfort.
The dose should be adapted depending on the severity of the individual case.
The duration of treatment, in general a few weeks to several months, depends on the illness and its progression.

Kidney failure
The safety and efficacy of calcium dobesilate have not been studied in patients with kidney disorders. As the medication is excreted in the urine, care must be taken in the case of kidney failure. Consequently, the dose may be reduced for the administration of Doxium to such patients, in particular in patients with severe kidney failure requiring dialysis.

Liver failure
The safety and efficacy of calcium dobesilate have not been studied in patients with liver failure. Precautions should therefore be taken with the administration of Doxium to such patients. It is recommended that the benefit of the treatment be reassessed in the event of a significant increase in liver values.

Children
No trials have been conducted to study the use of calcium dobesilate in children.

CONTRAINDICATIONS
Hypersensitivity to calcium dobesilate or to one of the excipients according to the composition.

WARNINGS AND PRECAUTIONS

In the case of severe kidney failure requiring dialysis, the dose may be reduced.
In very rare cases, the administration of calcium dobesilate can cause agranulocytosis (see section entitled "Undesirable effects"). In this case, symptoms can include: high fever, infections of the oral cavity (tonsillitis), sore throat, inflammation of the anus and genitals and other symptoms that are common signs of infection .The patient must be informed that at the slightest sign of infection, they must inform their doctor as soon as possible. In such cases, it is essential to carry out a blood count and leukocyte differential as soon as possible and stop the medication.
Doxium can trigger severe hypersensitivity reactions (anaphylactic shock or reaction). In the event of a hypersensitivty reaction, treatment must be stopped.

INTERACTIONS

No interactions with other medications are known to date.
At therapeutic doses, calcium dobesilate can interfere with creatinine enzyme measurements resulting in lower values than expected.

During treatment with Doxium, the taking of a sample (e.g. a blood sample) required for laboratory tests must be done before the first administration of the medication in order to minimise any potential interaction between Doxium and the laboratory tests.

PREGNANCY, LACTATION

Pregnancy
Data on the use of calcium dobesilate in pregnant women is limited.
Studies conducted in animals have not shown any direct or indirect harmful effect with regard to reproductive toxicity.

As a precaution, the medication should not be administered during pregnancy unless absolutely necessary.

Breast-feeding
Calcium dobesilate passes into breast milk in very low quantities (0.4 µg/mL after taking 3 x 500 mg). The administration of Doxium is not indicated during breast-feeding. As a precaution, either treatment or breast-feeding should be suspended.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

No relevant studies have been conducted. Taking Doxium can cause undesirable effects such as nausea, headaches and fatigue. This is why care is recommended when driving and operating machines (see "Undesirable effects").

UNDESIRABLE EFFECTS

Undesirable effects are presented by MedDRA 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)
Unknown frequency (cannot be estimated from the available data)

Blood and lymphatic system disorders
Very rare: agranulocytosis (see section "warnings and precautions")
Unknown: neutropenia, leucopenia

Immune system disorders
Uncommon: hypersensitivity (rash, allergic dermatitis, pruritus, urticaria, facial oedema; see section "warnings and precautions")
Very rare: anaphylactic reaction (see section "warnings and precautions")

Nervous system disorders
Common: headache

Gastrointestinal disorders
Common: abdominal pain, nausea, diarrhoea, vomiting

Hepatobiliary disorders
Common: increased alanine aminotransferase

Musculoskeletal and connective tissue disorders
Common: joint pain, muscle pain

General disorders and administration site conditions
Uncommon: pyrexia, shivering, asthenia, fatigue

These reactions are generally reversible once treatment has been stopped.

In the event of gastrointestinal disorders, reduce the dose or temporarily suspend treatment. In the event of rashes and fever, joint pains or changes in blood count, treatment must be stopped immediately, as it might be a case of hypersensitivity reactions.

OVERDOSE
No cases of overdose have been reported and the clinical signs of overdose are not known. Overdose must be treated in accordance with standard medical practice.

PROPERTIES/EFFECTS
ATC code: C05BX01 – Other vasoprotective agent.
Calcium dobesilate acts at the level of the capillary walls, where it regularises disturbed physiological functions – permeability and reduced resistance. It increases erythrocyte flexibility, inhibits platelet hyperaggregation and, in diabetic retinopathy, reduces blood and plasma hyperviscosity, thus improving the rheological properties of the blood and tissue irrigation.

These effects help to correct capillary dysfunctions, whether they are functional or linked to constitutional or acquired metabolic disorders.
Furthermore, calcium dobesilate helps to reduce swelling.

PHARMACOKINETICS
After oral absorption of a dose of 500 mg of calcium dobesilate, blood levels are greater than 6 μg/mL between the third and tenth hours, with a maximum (Cmax) of 8 μg/mL on average after 6 hours (Tmax). 24 hours after administration, blood levels are of the order of 3 μg/mL. The plasma protein binding rate is 20–25%.

In animals, calcium dobesilate does not cross the haematoencephalic barrier, but it is not known whether this is the case in humans. Calcium dobesilate passes into breast milk in very low quantities (results observed in one study: 0.4 μg/mL after taking 1500 mg).

Calcium dobesilate does not enter the enterohepatic cycle and is mainly eliminated in unchanged form and only 10% is eliminated in the form of metabolites.

In the first 24 hours, around 50% of the dose administered orally is eliminated in the urine and around 10% in the faeces.
The plasma half-life is around 5 hours.

Kinetics in special clinical situations
It is not known to what extent kidney function disorders influence the pharmacokinetic properties of calcium dobesilate (see sections "Posology/Instructions for use" and "Warnings and precautions").

PRECLINICAL DATA
Preclinical studies have not shown any mutagenic effect of calcium dobesilate.

SPECIAL COMMENTS
Incompatibilities
None known at present.

Influence on diagnostic methods
At therapeutic doses, calcium dobesilate can interfere with creatinine measurements, resulting in lower values than expected.

Stability
The medication should not be used after the date shown after "EXP" on the container.

Comments on storage
Store at room temperature (15–25°C) in its original packaging to protect it from moisture and out of the reach of children.

AUTHORISATION NUMBER (Swissmedic)
39217 (Swissmedic)

PRESENTATIONS
In pharmacies with a medical prescription (B).
Box of 30 or 60 capsules

AUTHORISATION HOLDER
OM Pharma SA- Meyrin, Switzerland

REVISION OF INFORMATION

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