SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

X-VEN 500 mg capsules

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance

Calcium dobesilate monohydrate 500 mg

Excipients

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Capsule

White to almost white powder in the opaque hard gelatine capsules.

4. KLİNİK ÖZELLİKLER

4.1. Therapeutic indications

It is indicated for:

- Microangiopathy (particularly diabetic retinopathy)
- Venous insufficiency with pain, cramps and inactivity.

Additionally, it is used for adjuvant treatment of circulation disorders of arteriovenous origin and hemorrhoidal disorders.

4.2. Posology and method of administration

Posology:

The dosage and duration of treatment should be determined by the physician based on the disease to be treated.

Frequency and duration of administration:

For adult use only.

Generally, 1 or 2 capsules should be taken once or twice a day with some water.

Method of administration:

It is only for oral use.

Capsules should be ingested whole, with food.

Additional information on special populations:

Renal/Liver Failure: Dose should be reduced in dialysis patients with serious renal failure.

Paediatric population: There is currently insufficient data to recommend a dosage regimen for routine use in children.

Geriatric population: Use in elderly is exactly the same as in adults.

4.3. Contraindications

It is contraindicated in subjects who are hypersensitive to calcium dobesilate.

4.4. Special warnings and precautions for use

Dose should be reduced in dialysis patients with serious renal failure.

Rarely, spontaneous agranulocytosis cases (0,32/million patients) have been reported due to hypersensitivity reactions following calcium dobesilate administration. This condition may present with fever, oral cavity infections (tonsillitis), sore throat, anogenital area inflammation and accompanying symptoms. These symptoms are typical signs of an infection. Patients should inform their doctor immediately if any infection symptom is present. In that case, blood values should be assessed and treatment should be stopped without any delay.

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

No data has yet been obtained on the interaction of X-VEN with other drugs.

4.6. Pregnancy and lactation

General recommendation

Pregnancy category is C.

Women with Childbearing Potential/Birth control (Contraception)

There are no adequate data from the use of X-VEN in pregnant women.

Animal studies are insufficient with respect to effects on pregnancy /and-or/ embryonal/foetal development/ and-or/ parturition/ and-or/ postnatal development (see 5.3). The potential risk for humans is unknown

X-VEN should not be used during pregnancy unless clearly necessary

Pregnancy

It is not known whether calcium dobesilate crosses the placental barrier; therefore, the drug should be used in pregnancy only if the potential benefits to the mother outweigh the potential risks to the foetus.

Lactation

Calcium dobesilate is excreted into the breast milk in low quantities. Therefore, either the treatment or breastfeeding should be discontinued.

Reproduction / Fertility

It has no effect on reproduction.

4.7. Effects on ability to drive and use machines

There are no reported adverse events suggesting any impairment of the ability to drive and use machines in patients receiving calcium dobesilate.

4.8. Undesirable effects

X-VEN is well tolerated even in long-term treatments.

The frequency is defined as follows: very common (≥ 1/10); common (≥ 1/100 to< 1/10); uncommon (≥ 1/1000 to < 1/100); rare (≥ 1/10.000 to < 1/1000); very rare (< 1/10.000), not known (cannot be estimated from available data).

Blood and lymphatic system disorders

Very rare: Isolated agranulocytosis cases have been reported in elderly patients and when used with other medicines

Gastrointestinal disorders

Rare: Nausea, diarrhoea, vomiting

Skin and subcutaneous tissue disorders

Rare: Skin rash, itching

Musculoskeletal, connective tissue and bone disorders

Rare: Joint pain

General disorders and administration site conditions

Rare: Fever, chill-shivering

These side effects are usually resolved with discontinuation of therapy.

In gastrointestinal disorders, the dose should be reduced or treatment should be temporarily stopped.

Treatment should be terminated when there are skin rash, fever, joint paint and changes in blood values.

Reporting of suspected adverse reaction

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via Turkish Pharmacovigilance Center (TÜFAM). (www.titck.gov.tr; e-mail: tufam@titck.gov.tr; tel.: 800 314 00 08; fax: 0 312 218 35 99)

4.9. Overdose

No cases of overdose have been reported to date.

5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic Properties

Pharmacotherapeutic group: Vasoprotectives

ATC Code: C05BX01

Mechanism of action:

X-VEN is a capillary function regulator.

Calcium dobesilate acts on the capillary walls by regulating impaired physiological functions such as increased permeability and decreased resistance. It increases erythrocyte flexibility, inhibits platelet hyperaggregation and reduces blood and plasma hyperviscosity in diabetic retinopathy. These provide restoration of blood properties and blood supply to tissues. These effects correct capillary dysfunctions, either of functional origin or caused by structural or acquired metabolic disorders. Calcium dobesilate contributes to reduction of edema.

5.2. Pharmacokinetic properties

General properties

Absorption

After oral administration of 500 mg of calcium dobesilate, its blood levels rise over 6µg/ml between 3rd and 10th hours. Maximum blood concentration (Cmax) is 8 µg/ml and occurs after averagely 6 hours (t_{max}). Blood concentration at 24 hours after intake is about 3 µg/ml.

Distribution

Protein-binding ratio is 20-25%. Calcium dobesilate does not cross the blood-brain barrier and placental barrier in animals but information on this issue is not available for humans. Calcium dobesilate is excreted into the breast milk in low quantities (one study found 0,4 µg/ml of mother milk after intake of 1500 mg)

Elimination

Calcium dobesilate does not enter the enterohepatic circulation and is excreted mainly unchanged. Only 10% of the administered dose is in form of its metabolites. Fifty percent of the orally administered dose is excreted in the urine and 50% in the faeces within 24 hours. Plasma half-life is approximately 5 hours.

Kinetics in particular clinical situations:

The effects of renal function impairments on the pharmacokinetic properties of calcium dobesilate is not known.

5.3. Preclinical safety data

Oral LD50 levels in mice and rats was found over 4000 mg/kg, which is 120 times higher than the dosage administered in humans.

Target organ specific toxicity, reproductive toxicity or mutagenic activity were not observed with preclinical toxicity evaluation of calcium dobesilate.

6. PHARMACEUTICAL PROPERTIES

6.1. List of excipients

Maize starch

Magnesium stearate

Colloidal silicon dioxide

Gelatine

Titanium dioxide (E171)

6.2. Incompatibilities

There is no evidence that X-VEN is incompatible with any drug or substance.

6.3. Shelf life

24 months

6.4. Special precautions for storage

Store at room temperature below 25ºC.

6.5. Nature and contents of container

Aluminium folio-PVC/PVDC blister.

Available in blister packs of 30 or 60 capsules.

6.6. Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with "Directive on Control of Medical Waste" and "Directive on the Control of Packaging and Packaging Waste".

7. MARKETING AUTHORIZATION HOLDER

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8. MARKETING AUTHORISATION NUMBER(S)

2016/238

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorization: 30.03.2016
Date of latest renewal:

10. DATE OF REVISION OF THE TEXT