

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Vostar

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 g emulgel contains

11,6 mg diclofenac diethylammonium equivalent to 10,0 mg diclofenac sodium.

Diclofenac sodium $C_{14}H_{10}C_{12}NNaO_2$

Diclofenac sodium

Sodium 2 - [(2,6-dichlorophenyl) amino] phenyl] acetate

3. PHARMACEUTICAL FORM

Emulgel

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

Vostar emulgel is potentially effective for the topical treatment of :

- * traumatogenic inflammation of the tendons, ligaments, muscles and joints, e.g. due to sprains, strains and bruises.
- * localised forms of soft tissue rheumatism (tenosynovitis, scalenus syndrome, thylacitis and periarthritis).
- * localised indication of degenerated arthropathy (osteoarthritis of peripheral joints and spine).

Treatment should not be continued for more than two weeks.

4.2. Posology and method of administration

Adults: Apply a small quantity of the emulgel on the suffering area three or four times daily unless otherwise prescribed by your physician. Massage gently. The quantity of emulgel required varies depending on the extent of the suffering area. For example 2-4 g of the emulgel (quantity between the size of a cherry and the size of a walnut) shall be sufficient for the treatment of a 400-800 cm² area.

Wash your hands after using Vostar emulgel, unless your hands are the treated area.

Duration of treatment depends on the indication and response. It is suggested to terminate treatment after 2 weeks.

Children: No dosage schemes and indications have been determined for children, and its use is not indicated in this category.

4.3. Contraindications

Vostar emulgel is contra-indicated in patients:

- known to be hypersensitive to diclofenac, acetylsalicylic acid and other NSAIDs, propylene glycol, isopropanol or other components of Vostar emulgel.
- In which crises of asthma, urticaria, acute rhinitis are caused by acetylsalicylic acid or other NSAIDs.

4.4. Special warnings and special precautions for use

Warnings

The possibility of systemic adverse reactions occurrence following topical treatment with Vostar emulgel is low compared to the frequency of adverse reactions occurrence with oral administration of diclofenac. However, when Vostar emulgel is applied to quite extended areas and for suggested time-periods, or if dosage exceeds by far the determined limit, the possibility of systemic adverse reactions cannot be excluded. Therefore, cautious administration is suggested in cases of renal and hepatic insufficiency, severe hypo-proteinemia, arterial hypertension, ischaemic cardiopathy, diabetes mellitus, epilepsy, parkinsonism, psychotic disorders, latent or not infections. In cases of similar use one should consult the general information of diclofenac.

Precautions

Vostar emulgel should be used only on healthy and intact skin parts (without open wounds or injuries). No impermeable bandage should be used and contact with the eyes and mucous membranes should be avoided. It should not be taken orally.

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

Diclofenac inhibits the thrombocyte's agglutination. Concomitant administration with orally taken anticoagulants requires close monitoring of blood coagulability and suitable anticoagulant dose adjustment.

It may increase toxicity of methotrexate, digoxine, and ciclosporine. It increases the levels and possibility of lithium toxic effect.

It may affect insulin action and orally administered antidiabetic agents, and concomitant administration requires close monitoring of the patient's glycaemia.

It blocks the action of diuretics and concomitant administration increases the risk of nephrotoxicity. Concomitant administration with potassium-sparing diuretics may cause or increase hyperkalemia. Similarly, concomitant administration with converting enzyme inhibitor increases the risk of nephrotoxicity and hyperkalemia. It may decrease the antihypertensive effect of β -inhibitors and converting enzyme inhibitors. With quinolones it may cause convulsions. Concomitant administration with corticoids increases the risk of gastro-intestinal bleedings.

Acetylsalicylic acid displaces diclofenac from binding positions and concomitant use is contra-indicated, as well as the concomitant administration of other NSAIDs, as it increases the risk of adverse reactions. Cholestyramine and cholestipole decrease the bioavailability of orally administered diclofenac. Misoprostole administered in high doses possibly decreases the AUC of diclofenac and increases the frequency and severity of its side-effects in the gastro-intestinal tract.

4.6. **Pregnancy and Lactation.**

Pregnancy: As there is not efficient experience in diclofenac administration in pregnant women, it is not recommended to use VOSTAR[®] emulgel during pregnancy.

Lactation: It is not expected to trace a detectable quantity of diclofenac in breast milk. However, as there is no experience in lactating women, it is not recommended to use VOSTAR[®] emulgel during lactation.

4.7. **Effects in driving ability and in ability to operating machines**

None known. Yet, when administered in relatively large skin areas for prolonged period of time, systemic effects cannot be excluded. Therefore, patients suffering from vertigo or other disorders of the Central Nervous System should avoid driving and operating machines.

4.8. **Adverse reactions**

Topical reactions

Occasionally: allergic or non-allergic contact dermatitis (with symptoms and signs such as pruritus, erythema, oedema, papules, vesicles, bullae burning or scaling of skin, rash), photosensitivity.

Systemic reactions:

In isolated cases: generalized skin rash, hypersensitivity reactions (e.g. asthmatic attacks, angio-oedema), photosensitivity reactions.

Systemic absorbance of VOSTAR[®] emulgel is low compared to plasma levels obtained following administration of oral forms of diclofenac. However, when the emulgel is applied to relatively large areas of skin, and over a prolonged period or if dosage exceeds limits by far, the possibility of systemic side-effects cannot be completely excluded. Such side-effects include:

Gastro-intestinal tract: diarrhoea, dyspepsia, nausea, vomit, constipation, flatulence, ulcer, haemorrhage, increase of hepatic enzymes. Rarely aphthous stomatitis, oesophagitis, mucous xerosis, hepatitis, hepatic necrosis, pancreatitis, colitis, rectitis due to suppository usage.

Nervous system: Dizziness, vertigo. More rarely insomnia, depression, diplopia, , anxiety, irritability, sterile meningitis, and rarely paraesthesia, memory disorders, nightmares, tremor, muscle asynergy, convulsions, disorientation, psychotic reactions.

Skin: Rash, pruritus. More rarely alopecia, urticaria, eczema, face flush, dermatitis, pustules, allergic porphyria, erythema multiform, angioedema, Stevens-Jhonson syndrome, necrotic epidermolysis, and rarely perspiration and dermatitis exfoliativa. Topical treatment may cause photosensitivity.

Cardiovascular system: Rarely hypertension, cardiac insufficiency, palpitations, tachycardia, supraventricular exceptional contractions, myocardium infraction.

Blood: Rarely decrease of haemoglobin level, leucopenia, thrombocytopenia, haemolytic anaemia, agranulocytosis, porphyria.

Senses: Rarely blurred vision, taste disorders, invertible hearing loss, skotodinia.

Urinary track – kidney: Rarely nephrotic syndrome, proteinurea, oligurea, fibrous nephritis, necrosis of renal papillae, azotemia, acute renal insufficiency, frequent uresis, nocturea, haematuria, impotence, vagina haemorrhage.

Respiratory tract: Rarely epistaxis, asthma, larynx or pharynx oedema, dyspnea, hyperpnea.

General: Abdominal pain or gripes, headache, retention of fluids, abdominal dilation, and more rarely, tongue and lips oedema, malaise, photosensitivity, anaphylactoid reactions, anaphylaxis, thoracalgia.

4.9. **Overdosage**

Low systemic absorption of topically applied diclofenac makes overdosage highly unlikely.

5. **PHARMACOLOGICAL PROPERTIES**

5.1. **Pharmacodynamic properties**

Pharmacotherapeutic group

Non-steroid anti-inflammatory drugs (NSAIDs).

Action mechanism

Inhibition of prostaglandin biosynthesis by diclofenac has been proved by experiments and is regarded an important aspect of its action mechanism.

Pharmacodynamic effects

In inflammations of traumatic or rheumatic cause, diclofenac emulgel has been proved to comfort pain, diminish oedema and decrease recovery time.

5.2. **Pharmacokinetic properties**

Absorption

The portion of diclofenac absorbed through the skin is proportional to the duration of contact and the area of the skin where the emulgel is applied, and it depends on the total topical dose and skin hydration. About 6% of the dose applied is absorbed after topical application of 2,5 g emulgel on a 500 cm² skin area, as determined by urinary excretion compared to diclofenac tablets. Obliteration for a 10-hour period leads to a threefold increase of absorbed diclofenac.

Distribution

After topical application of diclofenac emulgel in hand and knee joints diclofenac can be measured in plasma, synovial tissue and synovial fluid. Maximal diclofenac plasma levels following topical application are about 100 times lower than following oral administration of diclofenac tablets. 99,7% of diclofenac is bound to blood proteins, mainly albumin (99,4%).

Biotransformation

It is metabolised in the liver by a P450 cytochrome enzyme of the CYP2c group to 4-hydroxydiclofenac, which is the main metabolite, and to other hydroxylated forms. After glucuronidation and sulphunidation metabolites are excreted by 65% in the urine and 35% by the bile.

Elimination

The total systemic clearance of diclofenac in plasma is 263 ± 56 ml/min (mean value \pm SD). The terminal half life in plasma is 1-2 hours.

Four of the metabolites, including the two active ones, also have short plasma half-lives of 1-3 hours. One metabolite, 3-hydroxy-4-methoxy-diclofenac has a far greater plasma half-life. However, this metabolite is practically inactive. Diclofenac and its metabolites are mainly excreted in the urine.

Characteristics in patients

In patients with impaired renal function no accumulation of diclofenac and its metabolites is expected. In patients with chronic hepatitis or non-decompensated cirrhosis, the kinetics and metabolism of diclofenac may be affected.

5.3. **Preclinical safety data**

Preclinical studies with diclofenac emulgel did not reveal any toxicological effects.

6. **PHARMACEUTICAL DATA**

6.1. **List of Excipients**

Diethylamine, Carbomer 934 P, Cetomacrogol 1000, Cetiol LC, Isopropanol, Paraffin liquid, Lavendar oil, Propylene glycol, Water purified.

6.2. **Incompatibilities**

None known.

6.3. **Shelf Life**

The product has a shelf life of 24 months under normal conditions in the market packaging.

6.4. Special precautions for storage

Vostar emulgel should be stored at room temperature ($\leq 25^{\circ}\text{C}$), away from the reach of children.

6.5. Nature and contents of container

Vostar is a white emulgel. It is supplied in aluminium tubes printed with the product's and manufacturer's characteristics containing 100 g emulgel.

A patient information leaflet is included in any package.

6.6. Instructions for use and handling

There are no special instructions.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

122/02201

9. DATE OF FIRST AUTHORISATION /RENEWAL:

To be advised

10. DATE OF REVISION OF TEXT:

February 2005