VOTREX® Inj

(Diclofenac sodium)

ACTION

The solution in Votrex ampoules contains the sodium salt of diclofenac, a non-steroidal agent with pronounced antirheumatic, anti-inflammatory, analgesic and antipyretic activity.
Inhibition of prostaglandin biosynthesis by diclofenac has been demonstrated experimentally and this is considered fundamental to its mechanism of action. Prostaglandins play major role in causing inflammation, pain and fever.
In vitro, at concentrations equivalent to those attained in humans, Votrex does not suppress proteoglycan biosynthesis in cartilage.

Clinical efficacy

In rheumatic diseases, the anti-inflammatory and analgesic properties of diclofenac elicit a clinical response characterized by marked relief of signs and symptoms such as pain at rest, pain on movement, morning stiffness and swelling of the joints, and by improved function.
In post-traumatic and postoperative inflammatory conditions, Votrex rapidly relieves both spontaneous pain and pain on movement, and reduces inflammatory swelling and wound oedema.
When used concomitantly with opioids for the management of postoperative pain, Votrex significantly reduces the need for opioids.
In clinical trials Votrex has also been found to exert a pronounced analgesic effect in moderate and severe pain of non-rheumatic origin. This effect sets in within 15-30 minutes.
Votrex has also been shown to have a beneficial effect on symptoms in migraine attacks.
Votrex ampoules are particularly suitable for use in the initial treatment of inflammatory and degenerative rheumatic diseases, as well as for treatment of painful conditions due to inflammation of nonrheumatic origin.

INDICATIONS

Intramuscular injection

Initial treatment of:
- Exacerbation of inflammatory or degenerative forms of rheumatism: rheumatoid arthritis, ankylosing spondylitis, arthrosis, spondylarthritis, painful syndromes of the vertebral column, non-articular rheumatism.
- Acute attacks of gout.
- Renal and biliary colic.
- Post-traumatic and postoperative pain, inflammation and swelling.
- Severe migraine attacks.

Intravenous infusion

Treatment or prevention of postoperative pain in hospitalized patients.

DOSAGE AND ADMINISTRATION

Adults

Treatment with Votrex ampoules should not be given for more than 2 days. If necessary, treatment may be continued with Votrex tablets or suppositories.

Intramuscular injection

The following instructions for i.m. injection must be followed in order to avoid damage to a nerve or other tissue at the injection site.
The usual dosage is one 75 mg ampoule daily, given by deep intragluteal injection into the upper outer quadrant. In severe cases (e.g. colic) the daily dose may exceptionally be increased to two 75 mg ampoules (one given into each buttock), separated by an interval of a few hours. However, one 75 mg ampoule can also be combined with other dosage forms of Votrex (tablets, suppositories) up to a daily maximum of 150 mg.
In the treatment of migraine attacks, clinical experience is limited to the following approach: Administration of one 75 mg ampoule as soon as possible followed on the same day by suppositories up to 100 mg if required. The total dose on the first day should not exceed 175 mg. No data are available on the use of Votrex to treat migraine attacks lasting longer than one day. Should it be necessary to continue treatment on the following days, the maximum daily dose should be limited to 150 mg (given in divided doses in the form of suppositories).

Intravenous infusion

Votrex must not be given by intravenous bolus injection.
Immediately before the infusion, the contents of the Votrex ampoule must be diluted in a 0.9% saline or 5% glucose solution, buffered in either case with sodium bicarbonate.
Two alternative dosage regimens are recommended:
For the treatment of moderate to severe post-operative pain, 75 mg should be infused continuously over a period of 30 minutes to 2 hours. If necessary, this may be repeated after an interval of a few hours. No more than 150 mg may be given within a 24 hour period, however, for the prevention of post-operative pain, a loading dose of 25-50 mg should be infused after surgery over a period of 15 minutes to 1 hour, followed by a continuous infusion of about 5 mg/hour up to a maximum daily dosage of 150 mg.

Children

Votrex ampoules are contraindicated in children.

Instructions for use

The contents of Votrex ampoules may be administered either i.m. by deep gluteal injection in the upper outer quadrant or i.v. by slow infusion following dilution in accordance with the following instructions: Depending on the intended duration of infusion, mix 100-500 ml of isotonic saline (0.9%) or 5% glucose solution with sodium bicarbonate solution for injection taken from a freshly opened container (0.5 ml of an 8.4% solution, 1 ml of a 4.2% solution or a corresponding volume of solution at a different concentration). Add the contents of one Votrex ampoule to this solution. Only clear solutions should be used. Do not use the solution if crystals or precipitates are visible.

CONTRAINDICATIONS

- Known hypersensitivity to the active substance or any of the excipients.
- History of allergic conditions (such as bronchospasm, acute rhinitis, nasal polyps, urticaria) following ingestion of acetylsalicylic acid or other non-steroidal anti-inflammatory drugs (NSAIDs).
- Administration during the third trimester of pregnancy.
- Active gastric and/or duodenal ulcers, or gastrointestinal bleeding.
- Inflammatory intestinal disease such as Crohn's disease or ulcerative colitis.
- Severe heart failure.
- Severe liver failure (Child-Pugh score C).
- Moderate or severe renal failure (creatinine clearance < 50 ml/min), hypovolaemia or dehydration.
- Patients at high risk for postoperative bleeding, anticoagulation, incomplete haemostasis, haemopoietic disturbances or cerebrovascular bleeding.
- Children under 14 years of age.

WARNINGS AND PRECAUTIONS

Patients with gastrointestinal disorders, impaired liver function or a history suggestive of gastric or intestinal ulcer should be given this product only if strictly indicated, and under close medical supervision.
Gastrointestinal bleeding or ulceration/perforation generally have more serious consequences in the elderly. They can occur at any time during treatment, without warning symptoms or a previous history.
In the rare event of gastrointestinal bleeding or ulceration in a patient receiving Votrex, the drug should be withdrawn.
Owing to the importance of prostaglandins in maintaining renal blood flow, particular caution is called for in patients with impaired cardiac or renal function, the elderly, patients being treated with diuretics, and patients with extracellular volume depletion of whatever cause (e.g. peri/post-operative phases of major surgery). Monitoring of renal function is recommended as a precautionary measure when using Votrex in such cases. Withdrawal of treatment is usually followed by a return to the pretreatment state.
Caution is indicated in elderly patients on basic medical grounds. In particular, it is recommended that the lowest effective dosage be used in frail elderly patients or those with a low bodyweight.
As with other NSAIDs, levels of one or more liver enzymes may increase during treatment with Votrex. Although this has been observed in clinical studies with diclofenac and may occur in around 15% of patients, it is rarely accompanied by symptoms and its clinical significance is unknown. Increases are border line in the majority of cases, and are occasionally (2.5%) moderate (≥ 3 - < 8 times the upper limit of normal); increases are marked (≥8 times the upper limit of normal) in around 1% of cases. Raised liver enzyme values were accompanied by clinically manifest liver damage in 0.5% of cases in the above-mentioned clinical studies. Values generally returned to normal after discontinuation of the drug.
As with other NSAIDs, long-term treatment with Votrex calls for regular checks on liver enzyme levels. Votrex should be discontinued if liver function disturbance persists or worsens, if clinical signs or symptoms consistent with liver disease (e.g. hepatitis) develop, or if other manifestations occur (e.g. eosinophilia, rash). In addition to raised liver enzyme values, there have been rare reports of severe hepatic reactions, including jaundice and, in isolated cases, fulminant hepatitis with fatal outcome.
Hepatitis may develop without prodromal symptoms. Caution is called for when using Votrex in patients with hepatic porphyria, since it may trigger an attack. As with other NSAIDs, complete blood counts are recommended during prolonged treatment with Votrex.
Like other NSAIDs, Votrex may temporarily inhibit platelet aggregation. Patients with coagulation disorders should be closely supervised. Particular caution is required when administering Votrex parenterally to patients with bronchial asthma, as the symptoms may be aggravated.
As with other NSAIDs, allergic reactions - including anaphylactic/anaphylactoid reactions - can even occur in the absence of previous exposure.
The sodium metabisulphite contained in the ampoule solution may also cause hypersensitivity reactions in isolated cases. Its pharmacodynamic properties mean that, like other NSAIDs, Votrex may mask the signs and symptoms of infection.

DRUG INTERACTIONS (Including interactions reported for other dosage forms of Diclofenac sodium)

Lithium, digoxin

Diclofenac sodium may increase plasma concentrations of concomitantly administered lithium or digoxin.

Diuretics

Like other NSAIDs, diclofenac sodium may reduce the efficacy of diuretics. Furthermore, concomitant treatment with a potassium-sparing diuretic may be associated-with increased serum potassium levels, which should therefore be checked at regular intervals.

NSAIDs

Concomitant administration of systemic NSAIDs may increase the frequency of adverse effects.

Anticoagulants

Although clinical studies do not seem to indicate that diclofenac sodium affects the action of anticoagulants, there have been isolated reports of an increased risk of haemorrhage in patients receiving diclofenac sodium and anticoagulants concomitantly. Close monitoring of such patients is therefore recommended.

Antidiabetic agents

Clinical studies have shown that diclofenac sodium can be given together with oral antidiabetic agents without influencing their clinical effect. However, there have been isolated reports of both hypoglycaemic and hyperglycaemic effects following administration of diclofenac sodium, necessitating changes in the antidiabetic dosage.

Methotrexate

Caution is called for if NSAIDs are administered less than 24 hours before or after treatment with methotrexate because blood levels of methotrexate rise and methotrexate toxicity may increase.

Ciclosporin

The effects of NSAIDs on renal prostaglandins may increase the nephrotoxicity of ciclosporin.

Quinolone antibiotics

There have been isolated reports of convulsions that may have been due to concomitant use of quinolones and NSAIDs.

PREGNANCY AND LACTATION

First and second trimesters: No controlled data involving pregnant women are available.
Animal studies have not shown any direct or indirect toxicity affecting pregnancy, embryonic development, fetal development and/or postnatal development. During pregnancy, diclofenac sodium should be given only if absolutely essential and only at the lowest effective dose.
Third trimester: Diclofenac sodium is contraindicated owing to the possibility of uterine inertia and premature closure of the ductus arteriosus.
Following oral doses of 50 mg every 8 hours, the amount of active substance excreted in breast milk is so small that adverse effects on the infant are unlikely.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Patients experiencing dizziness or other central nervous system disturbances - including disturbances of vision - should not drive or use machines.

SIDE EFFECTS

(Including adverse effects reported for other dosage forms of diclofenac sodium)

Frequency

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).

Blood

Very rare: Thrombocytopenia, leucopenia, agranulocytosis, haemolytic anaemia, aplastic anaemia.

Immune system

Rare: Hypersensitivity reactions such as asthma and systemic anaphylactic/anaphylactoid reactions with loss of blood pressure.
Very rare: Vasculitis, pneumonitis.

Nervous system

Uncommon: Headache, light-headedness, dizziness.
Rare: Fatigue.
Very rare: Sensory disturbances, including paraesthesia; memory disturbances, disorientation, insomnia, irritability, convulsions, depression, anxiety, nightmares, tremor, psychotic reactions, aseptic meningitis.

Eye disorders

Very rare: Disturbances of vision (impaired visual acuity, diplopia).

Ear disorders

Very rare: Impaired hearing, tinnitus.

Heart

Very rare: Palpitations, chest pain, hypertension, heart failure.

Gastrointestinal disorders

Uncommon: Epigastric pain, other gastrointestinal reactions such as nausea, vomiting, diarrhoea, abdominal cramps, dyspepsia, flatulence and loss of appetite.
Rare: Gastrointestinal bleeding (haematemesis, melaena, bloody diarrhoea), gastric or intestinal ulceration with or without bleeding or perforation.
Very rare: Aphthous stomatitis, glossitis, dysgeusia, oesophageal lesions, diaphragm-like intestinal strictures; lower gastrointestinal tract disorders, such as non-specific haemorrhagic colitis, exacerbation of ulcerative colitis or Crohn's disease; constipation, pancreatitis.

Liver

Common: Increase in serum aminotransferase enzyme (SGOT, SGPT) levels, occasionally moderate (≥ 3 times the upper limit of normal) or marked (≤ 8 times the upper limit of normal).
Rare: Hepatitis, with or without jaundice; fulminant in isolated cases.

Skin

Uncommon: Rash.
Rare: Urticaria.
Very rare: Bullous eruptions, eczema, erythema multiforme, stevens-Johnson syndrome, lyell's syndrome (toxic epidermal necrolysis), erythroderma (exfoliative dermatitis), hair loss, photosensitivity, purpura (including allergic purpura).

Kidneys

Rare: Oedema.
Very rare: Acute renal insufficiency, haematuria, proteinuria, interstitial nephritis, nephrotic syndrome, papillary necrosis.

Reactions at the site of administration

Uncommon: Local reactions at the site of i.m. injection (e.g. pain and induration).
Very rare: Local abscesses and necrosis at the site of i.m. injection.

OVERDOSE

Management of acute poisoning with NSAIDs consists essentially of supportive and symptomatic measures. There is no known typical clinical picture associated with an overdosage. of diclofenac.
The following therapeutic measures should be taken: Supportive and symptomatic measures to combat hypotension, renal insufficiency, convulsions, gastrointestinal irritation and respiratory depression. Specific measures such as forced diuresis, dialysis or haemoperfusion are unlikely to be helpful in accelerating the elimination of NSAIDs because of their high protein-binding and extensive metabolism.

STORAGE

Store between 15-25°C, away from light.

PRESENTATION

Ampoules:

VOTREX: Diclofenac sodium 75 mg/ 3 ml

Excipients: Benzyl alcohol, propylene glycol, sodium metabisulphite, sodium hydroxide, water for injection.

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

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hikma.

Keep medicament out of the reach of children
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