Tilcotil®
Roche

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oral/rektal
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Antirheumatic and antiinflammatory agent

Composition
Active ingredient: tenoxicam. Tenoxicam is a thienothiazine derivative belonging to the chemical class of oxicams. Tablets and suppositories 20 mg.

Properties and effects
Tenoxicam has antiinflammatory, analgesic, antipyretic properties and also inhibits platelet aggregation. Tenoxicam is a potent inhibitor of prostaglandin biosynthesis, both in vitro (sheep seminal vesicles) and in vivo (protection of arachidonic acid-induced toxicity in mice). In-vitro tests of leukocyte peroxydase suggest that tenoxicam may act as a scavenger for active oxygen at the site of inflammation. These pharmacological effects explain, at least in part, the successful use of Tilcotil in the treatment of painful inflammatory and degenerative disorders of the musculoskeletal system. Tenoxicam showed no mutagenic, carcinogenic or teratogenic effects in animals.
As with other prostaglandin inhibitors, renal and gastrointestinal effects, increased incidence of dystocia and delayed parturition were observed in animal safety studies.

Pharmacokinetics
Absorption
On extravascular administration tenoxicam is absorbed in unchanged form: on oral administration it is absorbed completely, whereas absorption after rectal administration is approximately 80%. Peak plasma concentrations following oral or rectal administration are reached within two hours in fasting subjects. If tenoxicam is taken orally with a meal, it is absorbed to the same extent but at a somewhat slower rate.

Distribution
In the blood over 99% of the drug is bound to albumin. Tenoxicam penetrates well into the synovial fluid, but peak concentrations are reached later than in plasma.
With the recommended dosage regimen of 20 mg once daily, steady-state conditions are reached within 10 to 15 days without unexpected accumulation. Maximum steady-state concentrations in the plasma amount to 10–15 µg/ml (29.7–44.5 µmol/l) and did not change even on treatment for up to two years.

Metabolism
The major part of tenoxicam is converted to the inactive metabolite 5-hydroxypyridyl. Other metabolites occur in the form of glucuronidated compounds.

Elimination
Tenoxicam is eliminated with an average half-life of 72 hours (range: 42–98 hours). Up to two thirds of an oral dose is excreted in the urine (mainly as the inactive 5-hydroxy-pyridyl metabolite) and the rest via the bile (a significant portion in the form of glucuronidated compounds).

failure, or to patients with increased risk of bleeding, because of an increased risk of acute renal failure and possibly of impaired hemostasis.
Concurrent treatment with salicylates or other NSAIDs should be avoided because of the increased risk of gastrointestinal adverse reactions.

Precautions
As with other NSAIDs simultaneous treatment with anticoagulants and/or oral antidiabetics should be avoided unless the patient can be closely monitored.
Prostaglandin synthetase inhibition may have an adverse effect on renal function. As with other NSAIDs, therefore, with Tilcotil it is necessary to adequately monitor renal function (BUN, creatinine, development of edema, weight gain, etc.), when giving an NSAID to the elderly or to patients with conditions that could increase their risk of developing renal failure, such as:
- preexisting renal disease;
- impaired renal function in diabetics;
- hepatic cirrhosis;
- congestive heart failure;
- volume depletion;
- concomitant treatment with diuretics;
- concomitant treatment with drugs of known nephrotoxic potential.

Pregnancy, nursing mothers
No teratogenic effects were seen in animal studies, but no controlled trials have so far been carried out in pregnant women. The suitability of using Tilcotil during pregnancy or lactation has not, therefore, been established.

Undesirable effects
During clinical trials lasting from two weeks to one year, Tilcotil proved to be generally well tolerated in the recommended daily dose of 20 mg. The proportion of patients with undesirable clinical or laboratory effects was found to be around 12.5%. Usually these effects were mild and transient, and resolved even when treatment was continued. Only in about 1% of all patients did these effects necessitate interruption of treatment with Tilcotil at a dosage of 20 mg daily. Based on these trials, the following incidences of undesirable effects can be estimated:
In treatment lasting several weeks to three months:
11%: gastrointestinal tract (gastralgia, heartburn, nausea, diarrhea, constipation; rarely: hemorrhage, ulcers, perforation);
3%: central nervous system (dizziness and headache);
1–2%: skin (itching – also in the anal region after rectal administration – rash, erythema, urticaria). As with other NSAIDs, in rare instances severe skin reactions such as Stevens-Johnson syndrome and Lyell syndrome may occur;
1–2%: urinary tract and kidneys (increase in BUN or creatinine);
1–2%: liver and biliary tract (increase in SGOT, SGPT, γ-GT, bilirubin).
Rare miscellaneous effects include decreased hemoglobin, granulocytopenia, slight edema and photodermatosis.
Long-term studies (12–48 months) have not revealed any increase in the frequency of side effects.

Interactions

pounds).

Pharmacokinetics in special situations
Studies in elderly and in patients with renal insufficiency or liver cirrhosis suggest that no dose adjustment is necessary to achieve plasma concentrations similar to those in healthy subjects. Because of the high plasma protein binding of tenoxicam, caution is required when plasma albumin levels are markedly reduced (e.g. in nephrotic syndrome).

Indications and usage
Tilcotil is indicated for the symptomatic treatment of the following painful inflammatory and degenerative disorders of the musculoskeletal system:
- rheumatoid arthritis;
- osteoarthritis; arthrosis;
- ankylosing spondylitis;
- extraarticular disorders, e.g. tendinitis, bursitis, periarthritis of shoulders (shoulder-hand syndrome) or hips, strains and sprains;
- acute gout.

Interactions
No interaction has been found with concomitantly administered antacids, probenecid, cimetidine, glibornuride, tolbutamide, warfarin and phenprocoumon at the recommended dosages. As in the case of other NSAIDs, salicylate displaces tenoxicam from protein binding sites and thus increases clearance and volume of distribution of tenoxicam (see Restrictions on use). No clinically relevant interaction was found in the small number of patients receiving concomitant treatment with gold or penicillamine. No changes in blood pressure or heart rate were observed in patients being treated concomitantly with various antihypertensives. During clinical trials no interaction was reported for patients treated concomitantly with digitalis products. As with NSAIDs in general, Tilcotil should not be administered concurrently with potassiumsparing, dehydrating drugs (diuretics). Until further data are available, the possibility that the diuretic effect of other dehydrating drugs is reduced by Tilcotil cannot be ruled out.

acute gout.

Dosage and administration

Standard dosage

For all indications except gouty arthritis, a daily dosage of 20 mg should be given (1 tablet or 1 suppository) at the same time of day. Where indicated, treatment may be initiated with 1 vial of Tilcotil (20 mg) i.v. or i.m. daily for one to two days (see package insert of Tilcotil ampoules). The tablets should be taken with a glass of water.

Although the therapeutic effect of Tilcotil is evident early in treatment, there is a progressive increase in response over the first two weeks until the steady-state plasma level is reached.

Daily doses higher than 20 mg should be avoided, since this would increase the frequency and intensity of adverse reactions without significantly increasing efficacy. For patients needing longterm treatment a reduction to a daily dose of 10 mg (½ tablet) may be tried for maintenance.

For acute attacks of gouty arthritis, the recommended dose is 40 mg (2 tablets or 2 suppositories) once daily for two days followed by 20 mg (1 tablet or 1 suppository) once daily for a further five days.

Special dosage instructions

In principle, the above dosage recommendations also apply to elderly patients and to patients suffering from kidney or liver disease (see Restrictions on use). Because of lack of clinical experience, no dosage recommendations have so far been established for patients under 18 years of age.

Restrictions on use

Contraindications

Tilcotil should not be administered to patients known to be hypersensitive to the drug. Patients in whom salicylates or other nonsteroidal antiinflammatory drugs (NSAIDs) induce symptoms of asthma, rhinitis or urticaria should also be excluded. This also applies to patients who are suffering or have suffered from severe diseases of the upper gastrointestinal tract, including gastritis, gastric and duodenal ulcer. Before anesthesia or surgery, Tilcotil, like other NSAIDs, should not be given to elderly patients, to patients at risk of kidney

Overdosage

Although there is no experience of acute overdosage with tenoxicam, it may be expected that the signs and symptoms mentioned under Undesirable effects would be more pronounced.

In case of real or suspected overdosage the drug should be discontinued. No specific antidote is known at present. Overdosage should be countered by measures to reduce absorption and speed up elimination. Gastrointestinal disorders may be treated with antacids and H_2-receptor-blocking drugs. If necessary, the elimination of tenoxicam can be accelerated significantly by the administration of three 4 g doses of cholestyramine.

Stability

This medicine should not be used after the expiry date (EXP) shown on the pack.

Packs

Tablets (scored) 20 mg	30, 100
Suppositories 20 mg	10

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, 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.

Keep medicaments out of reach of children

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