THEORIL®
(Thiocolchicoside)

تھیورِل

COMPOSITION
Each capsule contains:
Thiocolchicoside ……. 4 mg
(As per innovator's specs.)

DESCRIPTION
Thiocolchicoside is a semi-synthetic derivative of the colchicine, a natural anti-inflammatory glycoside. It is a muscle relaxant with anti-inflammatory and analgesic effects.

CLINICAL PHARMACOLOGY

Mechanism of action
Thiocholchicoside is a muscle relaxing agent that works through selective binding to the GABA-A receptor. It prevents muscle contractions by activating the GABA inhibitory motor pathway. This medication acts as a competitive GABA receptor antagonist and inhibits glycine receptors with similar potency as nicotinic acetylcholine receptors. In one study, thiocolchicoside inhibited the function of recombinant human strychnine-sensitive glycine receptors composed of the alpha1 subunit with a potency (median inhibitory concentration of 47 microM) lower than that apparent with recombinant GABA(A) receptors.

Pharmacokinetics
Absorption
After oral administration, no thiocolchicoside is detected in plasma. Only two metabolites are observed: The pharmacologically active metabolite SL18.0740 and an inactive metabolite SL59.0955. For both metabolites, maximum plasma concentrations occur 1hour after thiocolchicoside administration. After a single oral dose of 8 mg of thiocolchicoside the Cmax and AUC of SL18.0740 are about 60 ng/mL and 130 ng.h/mL respectively. For SL59.0955 these values are much lower: Cmax around 13 ng/mL and AUC ranging from 15.5 ng.h/mL (until 3h) to 39.7 ng.h/mL (until 24h).

Metabolism
After oral administration, thiocolchicoside is first metabolized in the aglycon 3-demethylthiocolchicine or SL59.0955. This step mainly occurs by intestinal metabolism explaining the lack of circulating unchanged thiocolchicoside by this route of administration.
SL59.0955 is then glucuroconjugated into SL18.0740 which has equipotent pharmacological activity to thiocolchicoside and thus supports the pharmacological activity after oral administration of thiocolchicoside. SL59.0955 is also demethylated into didemethyl-thiocolchicine.

Distribution
In humans, the binding of thiocolchicoside to human serum proteins is low (13%) and not dependent on the therapeutic concentration of thiocolchicoside. Serum albumin is mainly involved in protein binding.

Elimination
Thiocolchicoside is not eliminated unchanged, rather as one of three metabolites found in either feces (~79 %) or in urine 20%. SL18.0740 and SL59.0955 are found in urine and feces while the didemethyl-thiocolchicine is only recovered in feces. After oral administration of thiocolchicoside, the SL18.0740 metabolite is eliminated with an apparent t1/2 ranging from 3.2 to 7 hours and the metabolite SL59.0955 has a t1/2 averaging 0.8h.

INDICATIONS
Adjuvant treatment of painful muscle contractures in acute spinal pathology in adults and adolescents from 16 years onwards.

DOSAGE AND ADMINISTRATION
The recommended dose is two 4 mg capsules bid and the maximum recommended dose is 16 mg per day. The treatment duration is limited to 7 consecutive days.

CONTRAINDICATIONS
Thiocolchicoside must not be used
- in patients hypersensitive to the active substance or to any of the excipients
- during the entire pregnancy period
- during lactation
- in women of childbearing potential not using contraception.

WARNINGS AND PRECAUTIONS

• In preclinical studies, one of thiocolchicoside metabolites (SL59.0955) induced aneuploidy at concentrations close to human exposure observed at doses 8 mg twice daily per os. Aneuploidy is reported as a risk factor for teratogenicity, embryo/foeto-toxicity, spontaneous abortion, cancer, and impaired male fertility. As a precautionary measure, use of the product at doses exceeding the recommended dose or long term use should be avoided.

• Thiocolchicoside may precipitate seizures, especially in patients with epilepsy or those at risk for seizures.

• Postmarketing cases of cytolytic and cholestatic hepatitis have been reported. Severe cases in patients concomitantly taking NSAIDs or paracetamol. Patients should be advised to stop treatment and report any sign of liver toxicity.
• Patients should be carefully informed about the potential risk of a possible pregnancy and about effective contraceptive measures to be followed.

• Reduce the dosage, as necessary, in case of diarrhea.

Effects on ability to drive and use machines: There is no data available on the effect on driving vehicles and using machines. Somnolence may occur commonly and that has to be taken into account when driving vehicles and operating machines.

ADVERSE REACTIONS
Very common (≥ 10%) and common (≥1 and <10%) adverse reactions are somnolence, diarrhoea, gastralgia. Rare cases of gastrointestinal disorders, cutaneous allergic reactions, anaphylactic reactions, hypotension or anaphylactic shock and drowsiness have been reported.

DRUG INTERACTIONS
Not known

USE IN SPECIAL POPULATIONS

Pregnancy
The use of thiocolchicoside is contraindicated in pregnancy and in women of child bearing potential who are not using effective contraceptive.

Lactation
Since it passes into the mother's milk, the use of thiocolchicoside is contraindicated during breastfeeding.

Pediatrics
Thiocolchicoside should not be used in children and adolescents under 16 years of age because of safety concerns.

PRESENTATION
Thewril 4mg ……. Pack of 20 Capsules

INSTRUCTIONS
Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, email us at
reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

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