To be sold by retail on the prescription of Registered Medical Practitioner only.

PRESCRIBING INFORMATION

MYOTOP DSR

1. Generic name

Tolperisone Hydrochloride and Diclofenac Sodium

2. Qualitative and quantitative composition

Each film coated bilayered extended release tablet contains

Tolperisone Hydrochloride…….. 450 mg

Diclofenac Sodium IP…….. 100 mg

Excipients…… q.s

3. Dosage form and strength

Film coated bilayered extended release tablet

4. Clinical particulars

4.1 Therapeutic Indication

For the treatment of Patients with acute muscle/musculoskeletal spasm in adult

4.2 Posology and method of administration

In adults, the recommended dosage is one tablet of Myotop-DSR once daily.

Method of administration: Oral

4.3 Contraindications

- Myotop-DSR is contraindicated in patients with history of hypersensitivity to any component of the product
- In patients suffering from myasthenia gravis
- Pregnancy and lactation

4.4 Special warnings and precautions for use

Precautions

- Close monitoring of renal parameters in patients with advanced renal disease is advisable.
- Myotop-DSR should be used with caution in patients with peptic ulcer disease, gastrointestinal perforation or bleeding, impaired renal or liver functions, blood dyscrasias, and hypersensitivity to aspirin or other NSAIDs.

- Caution should be exercised when administering this combination in patients chronically treated with NSAIDs.
- Precautions have to be taken when Myotop-DSR is used together with other muscle relaxants.
- Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible.

Warning

- Rarely, hypersensitivity reactions can occur (pruritis, erythema, exanthema, dyspnea, angioneurotic edema and in single cases anaphylactic shock).

4.5 Drugs interactions

- Concomitant use of Myotop DSR with aspirin, methotrexate, digoxin, cyclosporin, ACE inhibitors, diuretics, lithium and warfarin is not advocated due to possibility of drug interactions with diclofenac.
- Tolperisone (in Myotop DSR) may enhance the effects of other neuromuscular blocking agents.

4.6 Use in special populations

Pregnancy and lactation

Myotop DSR should not be given during pregnancy and lactation

4.7 Effects on ability to drive and use machines

Undesirable effects such as dizziness, drowsiness, fatigue and visual disturbances are possible. If affected, patients should not drive or operate machinery.

4.8 Undesirable effects

Most common side effects include gastrointestinal (GI) upset with abdominal pain, heartburn, nausea, vomiting, diarrhea, dyspepsia, flatulence, GI ulcers, bleeding / perforation and dryness of mouth.

Other less common ADRs are abnormal renal function, edema, elevated liver enzymes, anemia, headaches, fatigue, muscle weakness or transient physical asthenia, dizziness, increased bleeding time, pruritus, rashes, arterial hypotension, hypersensitivity and other skin allergic reactions like skin rash, hives.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation 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 email to: **medico@zuventus.com**

Website: http://www.zuventus.co.in/safety.aspx

4.9 Overdose

Symptoms: Symptoms include headache, nausea, vomiting, epigastric pain, gastro-intestinal bleeding, diarrhea, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, and occasionally convulsions. In cases of significant poisoning acute renal failure and liver damage are possible.

Therapeutic Measures: Patients should be treated symptomatically as required. Frequent or prolonged convulsions should be treated with intravenous diazepam. Activated charcoal/gastric lavage should be considered within one hour of ingestion of a potentially toxic amount. Renal and liver function should be closely monitored. Patients should be observed for at least four hours after ingestion of potentially toxic amounts. Other measures may be indicated by the patient's clinical condition.

5. Pharmacological properties

5.1 Mechanism of Action

Being, centrally acting muscle relaxant, tolperisone acts at the level of spinal cord by blocking sodium channels and calcium channels.

Diclofenac is a non-steroidal anti-inflammatory drug (NSAID) that exhibits anti-inflammatory, analgesic, and antipyretic activities. The mechanism of action of Diclofenac, like that of other NSAIDs, is related to prostaglandin synthesis inhibition.

5.2 Pharmacodynamic properties

Tolperisone exerts its spinal reflex inhibitory action predominantly via a pre synaptic inhibition of the transmitter release from the primary afferent endings via a combined action on voltage-gated sodium and calcium channels. Tolperisone increases the blood supply to skeletal muscles; this action is noteworthy since a muscle contracture may compress the small blood vessels and induce ischemia leading to release of pain stimulating compounds. Tolperisone causes preferential antinociceptive activity against thermal stimulation that is likely to be attributed to its local anesthetic action. Tolperisone causes muscle relaxation by its action on central nervous system. It also leads to membrane stabilization & has analgesic activity. This muscle relaxation is dose dependant.

Diclofenac reduces inflammation and by extension reduces nociceptive pain and combats fever**.**

5.3 Pharmacokinetic properties

Parameters	**Tolperisone**	**Diclofenac**
T_{max}	3.8 hr	5.3 hr
Plasma protein binding	60-75%	99.7%
Half life ($T_{1/2}$)	6.5 hrs	2.3 hrs

Metabolism	Mainly metabolised by p450-mediated CYP2D6 metabolic pathway into its active metabolite hydroxymethyl tolperisone.	Undergoes hepatic metabolism by CYP3A4
Excretion	Mainly in urine	60% in urine, 30% in faeces

6. Nonclinical properties

6.1 Animal Toxicology or Pharmacology

Tolperisone

Tolperisone is a central myorelaxant with solid non-clinical pharmacological and toxicological background. The non-clinical data support the clinical use of tolperisone in the currently approved indication and posology.

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.

Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use. Embryo toxic variations were observed in rats at 500 mg/kg body weight and in rabbits at 250 mg/kg body weight oral doses. These doses are several times higher than the human dose-range.

Diclofenac

Carcinogenesis

Long-term carcinogenicity studies in rats given diclofenac sodium up to 2 mg/kg/day (approximately 0.2 times the maximum recommended human dose [MRHD] of Diclofenac Capsules based on body surface area [BSA] comparison) have revealed no significant increase in tumor incidence. A 2-year carcinogenicity study conducted in mice employing diclofenac sodium at doses up to 0.3 mg/kg/day (approximately 0.014 times the MRHD based on BSA comparison) in males and 1 mg/kg/day (approximately 0.04 times the MRHD based on BSA comparison) in females did not reveal any oncogenic potential.

Mutagenesis

Diclofenac sodium did not show mutagenic activity in in vitro point mutation assays in mammalian (mouse lymphoma) and microbial (yeast, Ames) test systems and was nonmutagenic in several mammalian in vitro and in vivo tests, including dominant lethal and male germinal epithelial chromosomal aberration studies in Chinese hamsters.

Impairment of Fertility

Diclofenac sodium administered to male and female rats at 4 mg/kg/day (approximately 0.4 times the MRHD based on BSA comparison) did not affect fertility.

7. Description

Myotop-DSR is a fixed dose combination of a Tolperisone (centrally acting muscle relaxant) and Diclofenac (NSAID).

8. Pharmaceutical particulars

8.1 Incompatibilities

8.2 Shelf-life

8.3 Packaging information

8.4 Storage and handing instructions

9. Patient Counselling Information

- Advice patients not to take this medicine, if they are allergic to Tolperisone Hydrochloride and Diclofenac Sodium
- Signs of an allergic reaction include a rash, itching or shortness of breath.
- Pregnancy: Tell female patients Myotop DSR should not be given during pregnancy and lactation.
- Discuss treatment options with women planning to become pregnant. Tell patients to report pregnancies to their physicians as soon as possible.
- Tell the patients if they get any side effects, talk to the doctor or pharmacist. This includes any possible side effects not listed in this leaflet.
- Advice patients if they have any further questions, ask the doctor or pharmacist.

10.Details of manufacturer

11.Details of permission or licence number with date

12. Date of revision

22/01/2021