

**To be sold by retail on the prescription of a Registered Medical Practitioner (RMP) only.**

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**TRUECEPROL OD**

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**1. Generic Name**

Oxaceprol Sustained Release Tablets 600 mg

**2. Qualitative and quantitative composition**

Each film coated sustained release tablet contains :

Oxaceprol .....600 mg

Colour: Titanium Dioxide I.P.

The excipients used are Mat SR Base-1, PVP K-30, Carbopol 71G, Magnesium Stearate, Colloidal Silicon Dioxide, Super Coat (Film), Talcum, Titanium Dioxide, Metolose 90SH, Microcrystalline Cellulose and Lactose.

**3. Dosage form and strength**

Dosage Form: Film coated sustained release tablets

Strength: 600 mg

**4. Clinical particulars**

**4.1 Therapeutic indication**

For the treatment of pain associated with osteoarthritis in adult patients.

**4.2 Posology and method of administration**

**Posology:** The general recommended dose of the Oxaceprol SR Tablets 600 mg is one tablet once daily. Patients can safely use Oxaceprol SR Tablets 600 mg up to 42 days. Patient must consult the physician for further treatment with Oxaceprol SR Tablets 600 mg.

**Method of administration:** For oral use

Oxaceprol SR Tablets 600 mg should be taken before meals.

**4.3 Contraindications**

- Hypersensitivity to the active substance or to any of the excipients
- Pregnancy & Lactation
- Anticoagulant therapy with Vitamin K antagonists
- Hepatic impairment
- Renal impairment

**4.4 Special warnings and precautions for use**

**Anticoagulant Therapy**

Patients taking anticoagulants from the vitamin K antagonist group may not completely exclude the effect of Oxaceprol on blood coagulation. Therefore, when taking this medicine at the same time regular monitoring of prothrombin time is recommended.

### **Duration of the treatment**

Patients can safely use Oxaceprol SR Tablets 600 mg up to 42 days. Patient must consult the physician for further treatment with Oxaceprol SR Tablets 600 mg.

### **Renal impairment**

The safety and efficacy of Oxaceprol SR Tablets 600 mg in renal impairment patients has not been established.

### **Hepatic impairment**

The safety and efficacy of Oxaceprol SR Tablets 600 mg in hepatic impairment patients has not been established

## **4.5 Drugs interactions**

Patients taking anticoagulants from the vitamin K antagonist group may not completely exclude the effect of Oxaceprol on blood coagulation. Therefore, when taking Oxaceprol at the same time regular monitoring of prothrombin time is recommended.

## **4.6 Use in special populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)**

### **Pregnancy**

There are limited data on the use of Oxaceprol in pregnant women. So far no adverse effect has been observed.

Animal studies do not indicate direct or indirect teratogenic or embryo-fetotoxic effects of administration of Oxaceprol. The significance of these findings for human risk assessment is not clear. As a precaution, it is recommended to avoid using Oxaceprol during pregnancy and is justified exceptionally if the potential benefit to the mother far outweighs the potential risk to the foetus.

### **Breastfeeding**

It is unknown whether Oxaceprol is excreted in human breast milk. Therefore, the use of Oxaceprol is not recommended during breastfeeding.

## **4.7 Effects on ability to drive and use machines**

Oxaceprol has no or negligible influence on the ability to drive and use machines.

## **4.8 Undesirable effects**

### **Clinical Trial Experience (unpublished data)**

A total of 102 patients were evaluated for safety when treated with Oxaceprol SR Tablets 600 mg once daily. This includes all 102 patients treated for six weeks.

Treatment with Oxaceprol SR Tablets 600 mg once daily was well-tolerated.

The adverse events in Oxaceprol SR Tablets 600 mg once daily were abdominal pain (1.96% - 2/102), nausea (1.96% - 2/102), diarrhea (0.98% - 1/102), dizziness (0.98% - 1/102) and itching in skin (1.96% - 2/102).

All adverse reactions were mild and transient in nature.

### **Reporting of side effects**

If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of Torrent Pharma available at:

[http://www.torrentpharma.com/Index.php/site/info/adverse\\_event\\_reporting](http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting).

## 4.9 Overdose

Oxaceprol exhibits very low toxicity. There is no specific antidote.

In animal studies, toxic effects of oral administration were observed only 500 to 1000 times higher doses than recommended doses for use in humans, i.e. at doses  $\geq 10$  mg / kg body weight (sedation, ptosis, piloerection).

## 5. Pharmacological properties

### 5.1 Mechanism of Action

Oxaceprol prevents leukocyte infiltration into the joints, thus inhibiting an early step of inflammatory cascade and presenting a novel class of anti-inflammatory agents.

### 5.2 Pharmacodynamic properties

Oxaceprol is an amino acid derivative and acts like analgesic and anti-inflammatory, which has been used for decades for the symptomatic treatment of degenerative and inflammatory joint disease in Europe<sup>3</sup>. Its anti-inflammatory and analgesic efficacy is comparable to the conventional non-steroidal anti-inflammatory drugs (NSAIDs) like Diclofenac, but has a different mode of action. Instead of inhibiting the synthesis of prostaglandins, Oxaceprol prevents leukocyte infiltration into the joints, thus inhibiting an early step of inflammatory cascade and presenting a novel class of anti-inflammatory agents.

#### Clinical studies (unpublished data)

A randomized, open label, active-controlled, multicentre, prospective, comparative, phase III clinical study was conducted on 204 patients aged 30 to 65 years clinically diagnosed with sign and symptoms of osteoarthritis of knee in India (only grade 1 to 3 according to Kellgren and Lawrence grading scale & VAS score 40 mm or above included). The study consists of two arms i.e., Oxaceprol SR Tablets 600 mg once daily and Oxaceprol Tablets 200 mg three times daily for 42 days of treatment.

Oxaceprol SR Tablets 600 mg once daily produces statistically significant improvement in Western Ontario and McMasters (WOMAC) individual osteoarthritis (OA) indices and Composite Index (for pain, stiffness and physical function) & Visual analog scale (VAS) from baseline to end of the study (Day 42) and the improvements between both the arms were non-significant and comparable. The results of the study were mentioned as below;

Treatment Arms	Improvement in WOMAC Score		Improvement in VAS Score	
	Mean Value at Baseline	Mean Value at Day 42	Mean Value at Baseline	Mean Value at Day 42
Oxaceprol SR Tablets 600 mg	62.45 (17.93)	36.23 (12.51)	7.27 (1.29)	4.80 (1.64)
Oxaceprol Tablets 200 mg	62.29 (17.27)	33.75 (11.88)	7.21 (1.14)	4.50 (1.48)
P Value	0.9493	0.1496	0.7048	0.1850

Mean (SD), VAS score represented in cms

### 5.3 Pharmacokinetic properties

#### Absorption

An oral bioavailability study of Oxaceprol SR Tablets 600 mg was conducted on 23 healthy adult human subjects under fasting conditions and the pharmacokinetic parameters were mentioned as below;

Pharmacokinetic Parameter	C <sub>max</sub> (ng/mL)	AUC <sub>0-t</sub> (ng.hr/mL)	AUC <sub>0-∞</sub> (ng.hr/mL)	t <sub>max</sub> (hr)	t <sub>1/2</sub> (hr)
Observations	1058.44±686.11	8771.81±3453.19	9145.76±3494.68	4.23±1.43	5.38±3.63

Mean±SD

An oral bioavailability study of Oxaceprol SR Tablets 600 mg was conducted on 21 healthy adult human subjects under fed conditions and the pharmacokinetic parameters were mentioned as below;

Pharmacokinetic Parameter	C <sub>max</sub> (ng/mL)	AUC <sub>0-t</sub> (ng.hr/mL)	AUC <sub>0-∞</sub> (ng.hr/mL)	t <sub>max</sub> (hr)	t <sub>1/2</sub> (hr)
Observations	876.97±270.60	8982.87±4006.10	9456.84±4189.53	5.07±1.16	5.81±3.38

Mean±SD

### Distribution

Due to its aqueous solubility, Oxaceprol is distributed in the body. It permeates into the synovial fluid. No plasma-protein bond has been proved. There are no indications of accumulation.

### Elimination

The elimination occurs exclusively by renal route.

## 6. Nonclinical properties

### 6.1 Animal Toxicology or Pharmacology

#### Acute toxicity

When orally administered, the LD<sub>50</sub> in rats is 7,751 mg/kg of body weight, in mice 5,688 mg/kg of body weight, when intra muscularly administered in rats and mice, it was more than 4,000 mg/kg and 2921 mg/kg of body weight respectively.

#### Chronic toxicity

The toxicity after repeated administration was determined in rats and beagles. The animals were given on 29 and 28 respectively successive days 3 dosages of the agent (4.5; 36; 288 mg/kg of body weight). In rats, apart from local effects caused by the application (inflammatory processes at the injection site) no unwanted effects occurred. In dogs, with the two lower dosages no effects occurred. With the highest dosage, slight changes on cornea and renal tubules were observed, the pathological importance of which is not known. No cases of death occurred.

#### Mutagenicity

Oxaceprol was extensively tested with regard to mutagenic properties. No incidence of mutagenic potential was found.

#### Carcinogenicity

No incidence of tumorigenic potential was found.

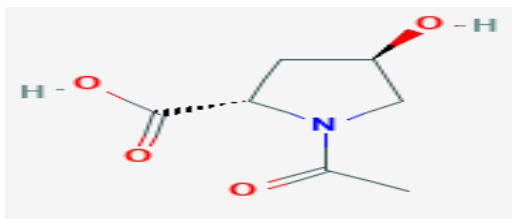
#### Reproductive toxicity

In a study conducted in pregnant female rabbits at a dose of 288 mg/kg/day, an increase was observed fetal resorption but the same effect was not observed in the repeated examination. Dose of 288 mg/kg/day in rabbits corresponds to a human dose 90 times the recommended therapeutic dose. In non-clinical trials, effects are observed only at dose exposures that are

significantly higher than the maximum allowed in humans, indicating their low relevance for clinical application.

## 7. Description

Oxaceprol is (2S,4R)-1-acetyl-4-hydroxypyrrolidine-2-carboxylic acid having molecular weight of 173.17 and molecular formula is C<sub>7</sub>H<sub>11</sub>NO<sub>4</sub> and chemical structure is:



Oxaceprol Sustained Release Tablets are white coloured elongated, biconvex, film coated tablets, scored on one side. The excipients used are Mat SR Base-1, PVP K-30, Carbopol 71G, Magnesium Stearate, Colloidal Silicon Dioxide, Super Coat (Film), Talcum, Titanium Dioxide, Metolose 90SH, Microcrystalline Cellulose and Lactose.

## 8. Pharmaceutical particulars

### 8.1 Incompatibilities

None stated

### 8.2 Shelf-life

Do not use later than the date of expiry.

### 8.3 Packaging information

TRUECEPROL OD is packed in strips of 10 tablets

### 8.4 Storage and handing instructions

Store below 30° C, protected from light & moisture.

Keep all medicines out of reach of children.

## 9. Patient counselling information

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.

- Keep this leaflet. You may need to read it again.
- Dosage will be as directed by the Physician
- Keep all medicines out of reach of children
- Direction for use: Tablets to be swallowed whole & not to be chewed, crushed or broken.
- If you have any further questions, ask your doctor or pharmacist.
- **This medicine has been prescribed for you only.** Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet.

## **What is in this leaflet?**

9.1. What TRUECEPROL OD is and what it is used for

9.2. What you need to know before you take TRUECEPROL OD

9.3. How to take TRUECEPROL OD

9.4. Possible side effects

9.5. How to store TRUECEPROL OD

9.6. Contents of the pack and other information

### **9.1 What TRUECEPROL OD is and what it is used for**

Oxaceprol is an amino acid derivative and acts like analgesic and anti-inflammatory medicine.

TRUECEPROL OD is used for the treatment of pain associated with osteoarthritis in adult patients.

### **9.2 What you need to know before you take TRUECEPROL OD**

#### **Do not take TRUECEPROL OD**

- If you are allergic to Oxaceprol or any of the other ingredients of this medicine

#### **Warnings and precautions**

- Talk to your doctor before taking Trueceprol OD
- Regular monitoring of prothrombin time is recommended, When patients taking anticoagulants from the vitamin K antagonist group.

#### **Infants**

- Safety and efficacy in infants less than 2 months of age have not been established.

#### **Other medicines and TRUECEPROL OD**

- Tell your doctor or pharmacist if you are taking or have recently taken or might take any other medicines.

#### **Pregnancy and breast-feeding**

- If you are pregnant or breastfeeding, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before taking this medicine.
- You should not stop your treatment without discussing this with your doctor.

#### **Driving and using machines**

- Oxaceprol has no or negligible influence on the ability to drive and use machines.

### **9.3 How to take TRUECEPROL OD**

Always take this medicine exactly as described in this leaflet or as your doctor or pharmacist have told you. Check with your doctor or pharmacist if you are not sure.

TRUECEPROL OD tablets should be administered orally before meals.

If you take more TRUECEPROL OD than you should contact your doctor if you took more tablets than you should. Your doctor will establish the best possible treatment of overdose.

**If you forget to take TRUECEPROL OD:**

Contact your doctor if you have missed one or more doses.

Do not take a double dose to make up for a forgotten tablet.

**If you stop taking TRUECEPROL OD**

Should your doctor decide to stop your TRUECEPROL OD treatment, he/she will instruct you about the gradual withdrawal of TRUECEPROL OD.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

**9.4 Possible side effects**

Like all medicines, this medicine can cause side effects, although not everybody gets them.

**Tell your doctor immediately or contact the casualty department at your nearest hospital, if you get any of the following serious side effects:**

- weakness, feel light-headed or dizzy or have difficulty breathing, as these may be signs of a serious allergic (anaphylactic) reaction
- abdominal pain, nausea, diarrhoea

**Reporting of side effects**

If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via any point of contact of **Torrent Pharma** available at: [http://www.torrentpharma.com/Index.php/site/info/adverse\\_event\\_reporting](http://www.torrentpharma.com/Index.php/site/info/adverse_event_reporting). By reporting side effects, you can help provide more information on the safety of this medicine.

**9.5 How to store TRUECEPROL OD**

Store below 30° C, protected from light & moisture.

Keep all medicines out of reach of children

**9.6 Contents of the pack and other information**

**What TRUECEPROL OD contains**

- The active substances are Oxaceprol .....600 mg

**The other ingredients are**

Mat SR Base-1, PVP K-30, Carbopol 71G, Magnesium Stearate, Colloidal Silicon Dioxide, Super Coat (Film), Talcum, Titanium Dioxide, Metolose 90SH, Microcrystalline Cellulose and Lactose.

**10. Details of manufacturer**

Synokem Pharmaceuticals Ltd.

Plot No. 56-57, Sector 6A, I.I.E (SIDCUL),  
Ranipur (BHEL), Hardiwar – 249403, Uttarakhand.

**11. Details of permission or licence number with date**

Mfg Lic No. 27/UA/2018 issued on 28.11.2018

**12. Date of revision**

Dec 2020

**MARKETED BY**



TORRENT PHARMACEUTICALS LTD.

**IN/ TRUECEPROL OD 600 mg/Dec 20/02/PI**