OXALTOR

For the use of a Registered Medical Practitioner or a Hospital or a Laboratory Only

Abbreviated Prescribing information for **OXALTOR**

(Oxaliplatin Injection I.P. 50 mg/10 ml and 100 mg/20 ml.) [Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

Mechanism of Action: Oxaliplatin is an antineoplastic active substance belonging to a new class of platinum-based compounds in which the platinum atom is complexed with 1,2-diaminocyclohexane ("DACH") and an oxalate group. Oxaliplatin is a single enantiomer, (SP-4-2)-[(1R,2R)-Cyclohexane-1,2-diamine-kN, kN'] [ethanedioato(2-)-kO1, kO2] platinum. Oxaliplatin exhibits a wide spectrum of both in vitro cytotoxicity and in vivo anti-tumour activity in a variety of tumour model systems including human colorectal cancer models. Oxaliplatin also demonstrates in vitro and in vivo activity in various cisplatin resistant models. A synergistic cytotoxic action has been observed in combination with 5-fluorouracil both in vitro and in vivo. Reported studies on the mechanism of action of oxaliplatin, although not completely elucidated, show that the aqua-derivatives resulting from the biotransformation of oxaliplatin, interact with DNA to form both inter and intra-strand cross-links, resulting in the disruption of DNA synthesis leading to cytotoxic and anti-tumour effects.

INDICATIONS: It is indicated for the treatment of advanced colorectal cancer

DOSAGE AND ADMINISTRATION: As directed by the Physician. Tablets should be taken orally.

CONTRAINDICATION: Oxaliplatin is contraindicated in patients who:

- have a known history of hypersensitivity to the active substance or to any of the excipients.
- are breast feeding
- have myelosuppression prior to starting first course, as evidenced by baseline neutrophils <2x109/l and/or platelet count of <100x109l
- have a peripheral sensitive neuropathy with functional impairment prior to first course
- have a severely impaired renal function (creatinine clearance less than 30 ml/min)

WARNINGS & PRECAUTIONS: *Renal impairmen:* Patients with mild to moderate renal impairment should be closely monitored for adverse reactions and the dose adjusted according to toxicity. *Hypersensitivity reactions*: Special surveillance should be ensured for patients with a history of allergic manifestations to other products containing platinum. *Neurological symptoms*: Neurological toxicity of oxaliplatin should be carefully monitored, especially if co-administered with other edicinal products with specific neurological toxicity. *Peripheral neuropathy*: If neurological symptoms (paraesthesia, dysaesthesia) occur, the following recommended oxaliplatin dosage adjustment should be based on the duration and severity of these symptoms:- if symptoms last longer than seven days and are troublesome, the subsequent oxaliplatin dose should be reduced from 85 to 65 mg/m2 (metastatic setting) or 75 mg/m2 (adjuvant setting)- if paraesthesia without functional impairment persists until the next cycle, the subsequent oxaliplatin dose should be reduced from 85 to 65 mg/m2 (metastatic setting) or 75 mg/m2 (adjuvant setting)- if paraesthesia with functional impairment persists until the next cycle, oxaliplatin should be discontinued. *Reversible Posterior Leukoencephalopathy Syndrome (RPLS)*: Cases of Reversible Posterior Leukoencephalopathy Syndrome (RPLS also known as PRES, Posterior Reversible Encephalopathy Syndrome) have been reported in patients receiving oxaliplatin in combination chemotherapy. RPLS is a rare, reversible, rapidly evolving neurological condition, which can include seizure, hypertension, headache, confusion, blindness, and other visual and neurological disturbances.

Diagnosis of RPLS is based upon confirmation by brain imaging, preferably MRI (Magnetic Resonance Imaging). *Pulmonary:* In the case of unexplained respiratory symptoms such as non-productive cough, dyspnoea, crackles or radiological pulmonary infiltrates, oxaliplatin should be discontinued until further pulmonary investigations exclude an interstitial lung disease or pulmonary fibrosis. *Blood disorders:* Haemolytic-uraemic syndrome (HUS) is a life-threatening side effect (frequency not known). Oxaliplatin should be discontinued at the first signs of any evidence of microangiopathic haemolytic anaemia, such as rapidly falling haemoglobin with concomitant thrombocytopenia, elevation of serum bilirubin, serum creatinine, blood urea nitrogen, or LDH. *QT prolongation:* QT prolongation may lead to an increased risk for ventricular arrhythmias including Torsade de Pointes, which can be fatal. The QT interval should be closely monitored on a regular basis before and after administration of oxaliplatin. *Rhabdomyolysis*: Rhabdomyolysis has been reported in patients treated with oxaliplatin, including fatal outcomes. In case of muscle pain and swelling, in combination with weakness, fever or darkened urine, oxaliplatin treatment should be discontinued. If rhabdomyolysis is confirmed, appropriate measures should be taken. *Gastrointestinal ulcer/ Gastrointestinal haemorrhage and perforation:* Oxaliplatin treatment can cause gastrointestinal ulcer and potential complications, such as gastrointestinal haemorrhage and perforation, which can be fatal. In case of gastrointestinal ulcer, oxaliplatin treatment should be discontinued and appropriate measures taken. *Hepatic:* In case of abnormal liver function test results or portal hypertension which does not obviously result from liver metastases, very rare cases of drug-induced hepatic vascular disorders should be considered.

DRUG INTERACTIONS: In patients who have received a single dose of 85 mg/m² of oxaliplatin, immediately before administration of 5-fluorouracil, no change in the level of exposure to 5-fluorouracil has been observed. In vitro, no significant displacement of oxaliplatin binding to plasma proteins has been observed with the following agents: erythromycin, salicylates, granisetron, paclitaxel, and sodium valproate. Caution is advised when oxaliplatin treatment is co-administered with other medicinal products known to cause QT interval prolongation. In case of combination with such medicinal products, the QT interval should be closely monitored. Caution is advised when oxaliplatin treatment is administered concomitantly with other medicinal products known to be associated with rhabdomyolysis.

ADVERSE REACTIONS:

Very common: allergies/allergic reactions, stomatitis / *mucositis*, low platelet count, abnormal bruising (thrombocytopenia). *Common:* neutropenic sepsis, febrile neutropenia, *Uncommon:* sepsis, blockage or swelling of the bowel, difficulty in hearing, vertigo, ringing in ears. *Rare:* disseminated intravascular coagulation, abnormal bruising, persistent or severe diarrhoea or vomiting, reversible short-term loss of vision, headache, altered mental functioning, extreme tiredness. *Very rare:* symptoms of acute renal failure, symptoms include abdominal pain and swelling, weight gain and tissue swelling of the feet, ankles or other parts of the body

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.
Torrent House, Off Ashram Road,
Ahmedabad-380 009, INDIA

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(Additional information is available on request)