IZRA L

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

Abbreviated prescribing information for IZRA L (Enteric coated Esomeprazole 40 mg & Sustained Release Levosulpiride 75 mg Capsules.) [Please refer the complete prescribing information available at www.torrentpharma.com]

MECHANISM OF ACTION: *Esomeprazole* is a weak base and is concentrated and converted to the active form in the highly acidic environment of the secretory canaliculi of the parietal cell, where it inhibits the enzyme H +K + -ATPase – the acid pump and inhibits both basal and stimulated acid secretion. *Levosulpiride:* The medicine can induce extrapyramidal effects and sleep disorders, at higher doses and in patients sensitive to neuroleptics. In these cases it will be advisable to reduce the dosage or discontinue the treatment, according to the physician decision.

INDICATION: For short term therapy of Gastroeasophageal Reflux Disease (GERD) in patients who do not respond to PPI alone.

DOSAGE AND ADMINISTRATION: The dose of IZAR must be taken as prescribe by Physician. Administration: The tablets should be swallowed orally with liquid. The tablets should not be chewed or crushed.

CONTRAINDICATION: Hypersensitivity to the active substance, to substituted benzimidazoles or to any of the excipients. Hypersensitivity reactions may include anaphylaxis, anaphylactic shock, angioedema, bronchospasm, acute interstitial nephritis, and urticaria. Esomeprazole should not be used concomitantly with nelfinavir. Elderly people, Children less than 14 years of age, Parkinson disease, Severe renal or hepatic insufficiency, History of epilepsy, Porphyrias, Breast cancer, Alcohol intoxication, Certain tumors like phaeochromocytoma and pituitary prolactinoma , Hypokalemia, The drug should be used cautiously in pregnancy (only when it is expected to benefit the mother more than the possibility of risking the fetus). The drug is known to be secreted in breast milk, so, its use should be restricted in breastfeeding women.

WARNINGS & PRECAUTIONS*: Esomeprazole:* Long term use, Helicobacter pylori eradication, Gastrointestinal infections, Absorption of vitamin B12, Hypomagnesaemia, Risk of fracture, Subacute cutaneous lupus erythematosus (SCLE), Co-administration of esomeprazole with atazanavir is not recommended and Increased Chromogranin A (CgA) level may interfere with investigations for neuroendocrine tumours. To avoid this interference, esomeprazole treatment should be stopped for at least 5 days before CgA measurements. *Levosulpiride*: Extrapyramidal reactions, mainly akathisia, and for that dosage reduction warranted. Increased motor agitation at higher dosages. Neuroleptic malignant syndrome (NMS), a potentially fatal symptom complex, has been reported in association with other antipsychotic drugs. NMS is associated with hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatinine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. In such an event, or with unexplained high fever without additional clinical manifestations of NMS, all antipsychotic drugs must be discontinued. If resumption of treatment with antipsychotic drugs becomes essential, the patient should be carefully monitored. Levosulpiride should be used with caution in patients with manic states such as in the manic phase of manic depressive psychosis. Caution is advised when the drug is administered to patients with cerebrovascular events including risk factors for stroke. Caution is also advised when levosulpiride is given to patients with cardiac insufficiency. Levosulpiride should not be used when gastrointestinal stimulation of motility can be harmful, e.g., in presence of gastrointestinal hemorrhage, mechanical obstructions or perforations. Levosulpiride may cause drowsiness in some patients especially at higher doses, thus patients should be advised to exercise

caution when driving or operating machinery. Elderly patients are more susceptible to postural hypotension, sedation and extrapyramidal effects. The dose should be reduced if there is evidence of renal impairment. Caution is advised when there is prolongations of QTc interval or factors that may predispose QTc interval prolongation (Bradycardia, hypokalemia, congenital QTc prolongation, decreased intracardiac conduction) Clinical experience in children under 14 years of age is insufficient to permit specific recommendations.

DRUG INTERACTIONS: Effects of esomeprazole on the pharmacokinetics of other drugs like Protease inhibitors, Methotrexate, Tacrolimus, Medicinal products metabolised by CYP2C19, Diazepam, Phenytoin, Voriconazole, Cilostazol, Cisapride, Warfarin, Clopidogrel, Amoxicillin and quinidine, Naproxen or rofecoxib, Medicinal products which inhibit CYP2C19 and/or CYP3A4 and Medicinal products which induce CYP2C19 and/or CYP3A4.

ADVERSE REACTIONS: These effects are rare and may affect up to 1 in 1,000 people. *Common (may affect up to 1 in 10 people):* Headache, Effects on your stomach or gut: diarrhoea, stomach pain, constipation, wind (flatulence), Feeling sick (nausea) or being sick (vomiting), Benign polyps in the stomach, ***Uncommon*** *(may affect up to 1 in 100 people);* Swelling of the feet and ankles, Disturbed sleep (insomnia), Dizziness, tingling feelings such as "pins and needles", feeling sleepy, Spinning feeling (vertigo), Dry mouth, Changes in blood tests that check how the liver is working, Skin rash, lumpy rash (hives) and itchy skin, Fracture of the hip, wrist or spine (if Esomeprazole is used in high doses and over long duration), ***Rare*** *(may affect up to 1 in 1,000 people):* Blood problems such as a reduced number of white cells or platelets. This can cause weakness, bruising or make infections more likely, Low levels of sodium in the blood. This may cause weakness, being sick (vomiting) and cramps, Feeling agitated, confused or depressed, Taste changes, Eyesight problems such as blurred vision, Suddenly feeling wheezy or short of breath (bronchospasm), An inflammation of the inside of the mouth, An infection called "thrush" which can affect the gut and is caused by a fungus, Liver problems, including jaundice which can cause yellow skin, dark urine, and tiredness, Hair loss (alopecia), Skin rash on exposure to sunshine. Joint pains (arthralgia) or muscle pains (myalgia). Generally feeling unwell and lacking energy. Increased sweating. Heart related diseases (eg. QT prolongation, Ventricular arrhythmias such as torsades de pointes, Ventricular tachycardia, Ventricular fibrillation, Cardiac arrest) ***Very rare*** *(may affect up to 1 in 10,000 people):* Changes in blood count including agranulocytosis (lack of white blood cells), Weight gain. Aggression, Seeing, feeling or hearing things that are not there (hallucinations), Psychological disease like Parkinsonism, disorders related to movement (eg. Dyskinesia, Tremor, Dystonia, Psychomotor agitation, Disorders of the autonomic nervous system, Severe liver problems leading to liver failure and inflammation of the brain, Sudden onset of a severe rash or blistering or peeling skin. This may be associated with a high fever and joint pains (Erythema multiforme, Stevens-Johnson syndrome, toxic epidermal necrolysis). Muscle weakness, Severe kidney problems, Acute kidney injury, Enlarged breasts in men, Sudden death. *Not known (frequency cannot be estimated from the available data):* If you are on IZRA-L for more than three months it is possible that the levels of magnesium in your blood may fall. Low levels of magnesium can be seen as fatigue, involuntary muscle contractions, disorientation, convulsions, dizziness or increased heart rate. If you get any of these symptoms, please tell your doctor promptly. Low levels of magnesium can also lead to a reduction in potassium or calcium levels in the blood. Your doctor may decide to perform regular blood tests to monitor your levels of magnesium. Inflammation in the gut (leading to diarrhoea). Rash, possibly with pain in the joints. Disease related to brain eg. Neuroleptic Malignant Syndrome, Abnormal absence of menstruation, Spontaneous flow of milk from the breast, unassociated with childbirth or nursing, Changes in sexual desire, Disorder related to blood clot (Thromboembolism), Disorders related to pregnancy and new borns (Neonatal withdrawal syndrome, Extrapyramidal symptoms),High levels of prolactin hormone in blood.

MARKETED BY:

TORRENT PHARMACEUTICALS LTD.

IN/IZRA-L 40,75mg/JUN-20/01/PI
(Additional information is available on request)