OLSAR CH

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

Abbreviated Prescribing information for OLSAR CH [Chlorthalidone 6.25 mg and Olmesartan Medoxomil 20 mg]

[Please refer the complete prescribing information available at www.torrentpharma.com]

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: ***Chlorthalidone:*** Thiazide and thiazide-like diuretics act primarily on the distal renal tubule (early convoluted part), inhibiting $NaCl^-$ reabsorption (by antagonising the $Na+Cl^-$ cotransporter) and promoting Ca++ reabsorption (by an unknown mechanism). The enhanced delivery of Na+ and water to the cortical collection tubule and/or the increased flow rate leads to increased secretion and excretion of K+ and H+. ***Olmesartan Medoxomil***: Olmesartan medoxomil is a potent, orally active, selective angiotensin II receptor (type AT1) antagonist. It is expected to block all actions of angiotensin II mediated by the AT1 receptor, regardless of the source or route of synthesis of angiotensin II. The selective antagonism of the angiotensin II (AT1) receptors results in increases in plasma renin levels and angiotensin I and II concentrations, and some decrease in plasma aldosterone concentrations.

INDICATIONS: Treatment of essential hypertension.

DOSAGE AND ADMINISTRATION: Dosage: As directed by the Physician

CONTRAINDICATION: Known hypersensitivity to chlortalidone or any of the excipients. Anuria, severe hepatic or renal failure (creatinine clearance < 30 ml/min), hypersensitivity to chlortalidone and sulphonamide derivatives, refractory hypokalemia, hyponatremia and hypercalcemia, symptomatic hyperuricaemia (history of gout or uric acid calculi), hypertension during pregnancy, untreated addison's disease and concomitant lithium therapy. Biliary obstruction and the concomitant use of Olmesartan medoxomil with aliskiren containing products is contraindicated in patient with diabetes mellitus or renal impairment.

WARNINGS & PRECAUTIONS: ***Chlorthalidone:*** Chlortalidone should be used with caution in patients with impaired hepatic function or progressive liver disease since minor changes in the fluid and electrolyte balance due to thiazide diuretics may precipitate hepatic coma, especially in patients with liver cirrhosis. Chlortalidone should also be used with caution in patients with severe renal disease. Thiazides may precipitate azotaemia in such patients, and the effects of repeated administration may be cumulative. Treatment with thiazide diuretics has been associated with electrolyte disturbances such as hypokalaemia, hypomagnesaemia, hyperglycaemia and hyponatraemia. Since the excretion of electrolytes is increased, a very strict low-salt diet should be avoided. Hypokalaemia can sensitise the heart or exaggerate its response to the toxic effects of digitalis. Like all thiazide diuretics, kaluresis induced by Chlortalidone is dose dependent and varies in extent from one subject to another. With 25 to 50mg/day, the decrease in serum potassium concentrations averages 0.5mmol/l. ***Olmesartan Medoxomil:*** Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting. In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or Page 4 of 29 underlying renal disease, including renal artery stenosis), treatment with other drugs that affect this system has been associated with acute hypotension, azotaemia, oliguria or, rarely, acute renal failure. There is an increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicinal products that affect the renin-angiotensin-aldosterone system. When olmesartan medoxomil is used in patients with impaired renal function, periodic monitoring of serum potassium and creatinine levels is recommended. Use of olmesartan medoxomil is not recommended in patients with severe renal impairment (creatinine clearance < 20 mL/min). There is no experience in patients with severe hepatic impairment and therefore use of olmesartan medoxomil in this patient group is not recommended.

DRUG INTERACTIONS: ***Chlorthalidone:*** Diuretics potentiate the action of curare derivatives and antihypertensive drugs. The hypokalaemic effect of diuretics may be potentiated by corticosteroids, ACTH, ß2 – agonists, amphotericin and carbenoxolone. It may prove necessary to adjust the dosage of insulin and oral anti-diabetic agents. Thiazide-induced hypokalaemia or hypomagnesaemia may favour the occurrence of digitalis induced cardiac arrhythmias. Concomitant administration of certain non-steroidal anti-inflammatory drugs (e.g. indometacin) may reduce the diuretic and antihypertensive activity of Chlortalidone; there have been isolated reports of a deterioration in renal function in predisposed patients. The bioavailability of thiazide-type diuretics may be increased by anticholinergic agents (eg atropine, biperiden), apparently due to a decrease in gastrointestinal motility and stomachemptying rate. Absorption of thiazide diuretics is impaired in the presence of anionic exchange resins such as colestyramine. Concurrent administration of thiazide diuretics may increase the incidence of hypersensitivity

reactions to allopurinol, increase the risk of adverse effects caused by amantadine, enhance the hyperglycaemic effect of diazoxide, and reduce renal excretion of cytotoxic agents (eg cyclophosphamide, methotrexate) and potentiate their myelosuppressive effects. ***Olmesartan Medoxomil:*** The blood pressure lowering effect of Olmesartan medoxomil can be increased by concomitant use of other antihypertensive medications. Clinical trial data has shown that dual blockade of the renin-angiotensin-aldosterone-system (RAAS) through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is associated with a higher frequency of adverse events such as hypotension, hyperkalaemia and decreased renal function. Based on experience with the use of other drugs that affect the renin-angiotensin system, concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other drugs that may increase serum potassium levels.

ADVERSE REACTIONS: ***Chlorthalidone:*** hypokalaemia, hyperuricaemia, rise in blood lipids, hyponatraemia, hypomagnesaemia, hyperglycaemia, gout, hypercalcaemia, glycosuria, worsening of diabetic metabolic state, hypochloraemic alkalosis, urticaria, other forms of skin rash, photosensitization, intrahepatic cholestasis, jaundice, postural hypotension, cardiac arrhythmias, Dizziness, paraesthesia, headache, loss of appetite and minor gastrointestinal distress, mild nausea and vomiting, gastric pain, constipation and diarrhoea, pancreatitis, Thrombocytopenia, leucopenia, agranulocytosis, eosinophilia, impotence, Idiosyncratic pulmonary oedema, allergic interstitial nephritis. ***Olmesartan Medoxomil:*** headache, influenza-like symptoms, dizziness, hypertriglyceridaemia, creatine phosphokinase, Thrombocytopenia, Anaphylactic reaction, Hypertriglyceridaemia, Hyperuricaemia, Hyperkalaemia, Vertigo, Angina pectoris, Hypotension, Bronchitis, Pharyngitis, Cough, Rhinitis, Gastroenteritis, Diarrhoea, Abdominal pain, Nausea, Dyspepsia, Vomiting, Sprue-like enteropathy, Exanthema, Allergic dermatitis, Urticaria, Rash, Pruritus, Angioedema, Arthritis, Back pain, Skeletal pain, Myalgia, Muscle spasm, Haematuria, Urinary tract infection, Acute renal failure, Renal insufficiency, Peripheral oedema, Face oedema, Asthenia, Malaise, Lethargy, Hepatic enzymes increased, Blood urea increased, Blood creatine phosphokinase increased, and Blood creatinine increased

MARKETED BY:

Torrent Pharmaceuticals Limited.

IN/ OLSAR CH 6.25 +20, 12.5 + 20 and 12.5 + 40 mg/Feb-21/01/PI

(Additional information is available on request)