TRIOLSAR

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

Abbreviated Prescribing information for TRIOLSAR [Olmesartan Medoxomil, Amlodipine and Chlorthalidone Tablets]

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

PHARMACOLOGICAL PROPERTIES:

MECHANISM OF ACTION: ***Olmesartan Medoxomil-*** 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. ***Amlodipine-*** The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle. Amlodipine dilates peripheral arterioles and thus, reduces the total peripheral resistance (afterload) against which the heart works. ***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+.

INDICATIONS: It is indicated for Hypertension**.**

DOSAGE AND ADMINISTRATION: As directed by the Physician.

CONTRAINDICATION: • Second and third trimesters of pregnancy. •Biliary obstruction. •The concomitant use of olmesartan medoxomil with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m2). • Hypersensitivity to dihydropyridine derivatives, amlodipine or to any of the excipients • Severe hypotension. Page 3 of 37 • Shock (including cardiogenic shock). • Obstruction of the outflow tract of the left ventricle (e.g., high grade aortic stenosis). • Haemodynamically unstable heart failure after acute myocardial infarction. • Known hypersensitivity to Chlorthalidone or any of the excipients. Anuria, severe hepatic or renal failure (creatinine clearance).

WARNINGS & PRECAUTIONS: ***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, and diarrhoea or vomiting. Such conditions should be corrected before the administration of Olmesartan medoxomil. 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. 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). The use of medicinal products that affect the renin-angiotensin-aldosterone system may cause hyperkalaemia. The risk, that may be fatal, is increased in elderly people, in patients with renal insufficiency and in diabetic patients, in patients concomitantly treated with other medicinal products that may increase potassium levels. the combination of lithium and Olmesartan medoxomil is not recommended. special caution is indicated in patients suffering from aortic or mitral valve stenosis, or obstructive hypertrophic cardiomyopathy. se of olmesartan medoxomil is not recommended in patients with primary aldosteronism. In very rare cases severe, chronic diarrhoea with substantial weight loss has been reported in patients taking olmesartan few months to years after drug initiation, possibly caused by a localised delayed hypersensitivity reaction. Angiotensin II receptor antagonists should not be initiated during pregnancy. When pregnancy is diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately and, if appropriate, alternative therapy should be started. ***Amlodipine-*** Patients with heart failure should be treated with caution. It should therefore be initiated at the lower end of the dosing range and caution should be used. In the elderly increase of the dosage should take place with care. ***Chlorthalidone-*** Chlorthalidone should be used with caution in patients with impaired hepatic

function or progressive liver disease. Chlorthalidone should also be used with caution in patients with severe renal disease as it 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. Chlorthalidone should not be used as a first-line drug for long-term treatment in patients with overt diabetes mellitus or in subjects receiving therapy for hypercholesterolaemia.

DRUG INTERACTIONS: ***Olmesartan Medoxomil*** The blood pressure lowering effect of olmesartan medoxomil can be increased by concomitant use of other antihypertensive medications. NSAIDs (including acetylsalicylic acid at doses >3 g/day and COX-2 inhibitors) and angiotensin-II receptor antagonists may act synergistically by decreasing glomerular filtration. Concurrent administration of the bile acid sequestering agent colesevelam hydrochloride reduces the systemic exposure and peak plasma concentration of Olmesartan. Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium. ***Amlodipine-*** There is a risk of increased tacrolimus blood levels when co-administered with amlodipine. ***Chlorthalidone-*** The hypokalaemic effect of diuretics may be potentiated by corticosteroids, ACTH, ß2 – agonists, amphotericin and carbenoxolone. 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. Concomitant treatment with cyclosporin may increase the risk of hyperuricaemia and gout-type complications.

ADVERSE REACTIONS: Headache, influenza-like symptoms, dizziness, 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, renal and urinary disorders haematuria common urinary tract infection, acute renal failure renal insufficiency, pain, chest pain, peripheral oedema, fatigue, 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/ TRIOLSAR 20, 40, 6.25, 12.5, 5 mg/JUL-20/01/ABPI

(Additional information is available on request)