

TRITELSAR

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

Abbreviated Prescribing information for TRITELSAR (Chlorthalidone, Amlodipine & Telmisartan Tablets) [Please refer the complete prescribing information for details].

PHARMACOLOGICAL PROPERTIES:

Mechanism of Action: *Chlorthalidone:* is a benzothiadiazine (thiazide)-related diuretic with a long duration of action. 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^+ . *Amlodipine:* is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle. The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle. *Telmisartan:* Telmisartan is an orally active and specific angiotensin II receptor (type AT1) antagonist. Telmisartan displaces angiotensin II with very high affinity from its binding site at the AT1 receptor subtype, which is responsible for the known actions of angiotensin II.

INDICATIONS: For the treatment of essential hypertension in adults.

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

CONTRAINDICATION: • Hypersensitivity to dihydropyridine derivatives, amlodipine, chlorthalidone and other sulphonamide derivatives, or to any of the excipients, Severe hypotension, Shock (including cardiogenic shock), Obstruction of the outflow tract of the left ventricle

WARNINGS & PRECAUTIONS: *Chlorthalidone:* 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. Like all thiazide diuretics, kaluresis induced by Chlorthalidone 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. Periodic serum electrolyte determinations should be carried out, particularly in digitalised patients. Combined treatment consamlodipineg of Chlorthalidone and a potassium salt or a potassium-sparing diuretic should be avoided in patients also receiving ACE inhibitors. For nephrotic syndrome, Chlorthalidone should be used only under close control in normokalaemic patients with no signs of volume depletion *Telmisartan:* *Fetal Toxicity, Pregnancy Category D* Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue Telmisartan as soon as possible. *Amlodipine:* *Calcium channel blockers*, including amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality. Amlodipine should be initiated at the lower end of the dosing range and caution should be used, both on initial treatment and when increasing the dose. Slow dose titration and careful monitoring may be required in patients with *severe hepatic impairment*. In the elderly increase of the dosage should take place with care.

DRUG INTERACTIONS: *Telmisartan:* *Aliskiren:* Do not co-administer aliskiren with Telmisartan in patients with diabetes. Avoid use of aliskiren with Telmisartan in patients with renal impairment (GFR <60 mL/min). *Chlorthalidone:* Thiazide-induced hypokalaemia or hypomagnesaemia may favour the occurrence of digitalis-induced cardiac arrhythmias. 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. **Amlodipine:** *CYP3A4 inhibitors* Concomitant use of amlodipine with strong or moderate CYP3A4 inhibitors (protease inhibitors,azole antifungals, macrolides like erythromycin or clarithromycin, verapamil or diltiazem) may give rise to significant increase in amlodipine exposure resulting in an increased risk of hypotension.

ADVERSE REACTIONS: **Amlodipine:** Leukocytopenia, thrombocytopenia, Allergic reactions, Hyperglycaemia, Depression, mood changes (including anxiety), insomnia, Confusion, Somnolence, dizziness, headache (especially at the beginning of the treatment), Tremor, dysgeusia, syncope, hypoaesthesia, paraesthesia, Hypertonia, peripheral neuropathy, Visual disturbance (including diplopia), Tinnitus, Palpitations, Arrhythmia (including bradycardia, ventricular tachycardia and atrial fibrillation), Myocardial infarction, Flushing, Hypotension, Vasculitis, Dyspnoea, Cough, rhinitis, Abdominal pain, nausea, dyspepsia, altered bowel habits (including diarrhoea and constipation), Vomiting, dry mouth, Pancreatitis, gastritis, gingival hyperplasia, Hepatitis, jaundice, hepatic enzyme increased, Alopecia, purpura, skin discolouration, hyperhidrosis, pruritus, rash, exanthema, urticarial, Angioedema, erythema multiforme, exfoliative dermatitis, Stevens-Johnson syndrome, Quincke oedema, photosensitivity, Toxic epidermal necrolysis, Ankle swelling, muscle cramps, Arthralgia, myalgia, back pain Micturition, disorder, nocturia, increased urinary frequency, Impotence, gynaecomastia, Oedema, Fatigue, asthenia, Chest pain, pain, malaise, Weight increased, weight decreased. **Telmisartan:** Urinary tract infection including cystitis, upper respiratory tract infection including pharyngitis and sinusitis, Sepsis including fatal outcome, Blood and the lymphatic system disorders, Anaemia, Eosinophilia, thrombocytopenia, Immune system disorders, Anaphylactic reaction, hypersensitivity, Metabolism and nutrition disorders. Hyperkalaemia, Hypoglycaemia (in diabetic patients), Insomnia, depression, Anxiety, Syncope, Somnolence, Visual disturbance, Vertigo, Bradycardia, Tachycardia, Hypotension, orthostatic hypotension, Respiratory, thoracic and mediastinal disorders, Dyspnoea, cough, Interstitial lung disease⁴, Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting, Dry mouth, stomach discomfort, dysgeusia, Hepatic function abnormal/liver disorder, Skin and subcutaneous tissue disorders, Pruritus, hyperhidrosis, rash, Angioedema (also with fatal outcome), eczema, erythema, urticaria, drug eruption, toxic skin eruption, Musculoskeletal and connective tissue disorders, Back pain (e.g. sciatica), muscle spasms, myalgia, Arthralgia, pain in extremity, tendon pain (tendinitis like symptoms), Renal impairment including acute renal failure, General disorders and administration site conditions, Chest pain, asthenia (weakness), Influenza-like illness, Blood creatinine increased, Haemoglobin decreased, blood uric acid increased, hepatic enzyme increased, blood creatine phosphokinase increased. **Chlorthalidone:** hypokalaemia, hyperuricaemia, and rise in blood lipids, hyponatraemia, hypomagnesaemia and hyperglycaemia., gout, hypercalcaemia, glycosuria, worsening of diabetic metabolic state., hypochloraemic alkalosis, urticaria and other forms of skin rash, photosensitisation., cholestasis or jaundice, postural hypotension, cardiac arrhythmias, Dizziness, paraesthesia, headache, loss of appetite and minor gastrointestinal distress, mild nausea and vomiting, gastric pain, constipation and diarrhea, pancreatitis, Thrombocytopenia, leucopenia, agranulocytosis and eosinophilia, impotence, Idiosyncratic pulmonary oedema (respiratory disorders), allergic interstitial nephritis.

MARKETED BY:



TORRENT PHARMACEUTICALS LTD.

Torrent House, Off Ashram Road,
Ahmedabad-380 009, INDIA

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(Additional information is available on request)