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

Biocon

℞

Telmisartan 40mg & Chlorthalidone 12.5mg Tablets

TELMISAT® CT 40 टेलमिसेट सीटी ४०

COMPOSITION
TELMISAT®CT 40
Each uncoated bilayered tablet contains:

Telmisartan IP	40 mg
Chlorthalidone IP	12.5 mg
Excipients	q.s.

Colour: Lake Sunset Yellow

PHARMACEUTICAL FORM
Tablets

PHARMACOLOGICAL PROPERTIES
Pharmacodynamic Properties
Pharmacotherapeutic group: Angiotensin II antagonists and diuretics
ATC code: C09DA07

TELMISAT® CT 40 tablets are a combination of angiotensin II receptor blockers (ARBs), telmisartan, and a thiazide-like diuretic, chlorthalidone. The combination of these ingredients has an additive antihypertensive effect, reducing blood pressure to considerable extent than either component alone.

Mechanism of Action
Telmisartan
Telmisartan is an orally effective and specific angiotensin II receptor subtype 1 (AT1) antagonist. Angiotensin II is the principal pressor agent of the renin-angiotensin system (RAS), with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium. Telmisartan blocks the vasoconstrictor and aldosterone secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the AT1 receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Its action is therefore independent of the pathways for angiotensin II synthesis. Unlike angiotensin converting enzyme (ACE) inhibitors, telmisartan does not affect the response to bradykinin. Telmisartan does not bind to or block other hormone receptors or ion channels known to be important in cardiovascular regulation.
Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on renin secretion, but the resulting increased plasma renin activity and angiotensin II circulating levels do not overcome the effect of telmisartan on blood pressure.
In addition to blocking the RAS, telmisartan acts as a selective modulator of peroxisome proliferator-activated receptor gamma (PPAR-γ), a central regulator of insulin and glucose metabolism. It is believed that telmisartan, due to its dual mode of action, may provide protective benefits against the vascular and renal damage caused by diabetes and cardiovascular disease.

Chlorthalidone
Chlorthalidone is a benxothiadiazine, thiazide-like diuretic, with a long duration of action. Chlorthalidone produces diuresis with increased excretion of sodium and chloride (decreased Na+Cl- reabsorption), and promoting Calcium reabsorption. The site of action appears to be the cortical diluting segment of the ascending limb of Henle's loop of the nephron. The diuretic effects of chlorthalidone lead to decreased extracellular fluid volume, plasma volume, cardiac output, total exchangeable sodium, glomerular filtration rate, and renal plasma flow. Although the mechanism of action of chlorthalidone and related drugs is not wholly clear, sodium and water depletion appear to provide a basis for its antihypertensive effect

Pharmacokinetic Properties
Telmisartan
Absorption
Following oral administration, peak concentrations of telmisartan are reached in 0.5 to 1.5 hours after dosing. The absolute bioavailability of telmisartan at 40 mg and 160 mg was 42% and 58%, respectively. Food slightly reduces the bioavailability of telmisartan with a reduction in the area under the plasma concentration time curve (AUC) of about 6% with 40 mg and about 19% with 160 mg dose. Three hours after administration plasma concentrations are similar, whether telmisartan is taken fasting or with food. The pharmacokinetics of orally administered telmisartan is non-linear over doses from 20 mg to 160 mg with greater than proportional increases of plasma concentrations (C_{max} and AUC) with increasing doses. Telmisartan shows bi-exponential decay kinetics with a terminal elimination half life of approximately 24 hours. Trough plasma concentrations of telmisartan with once daily dosing are about 10% to 25% of peak plasma concentrations. Telmisartan has an accumulation index in plasma of 1.5 to 2.0 upon repeated once daily dosing.

Distribution
Telmisartan is highly bound to plasma proteins (>99.5%), mainly albumin and α1-acid glycoprotein. The volume of distribution for telmisartan is approximately 500 L, indicating additional tissue binding.
Plasma protein binding is constant over the concentration range achieved with recommended doses.

Metabolism and Excretion
Following either intravenous or oral administration of ^{14}C-labeled telmisartan, most of the administered dose (>97%) was eliminated unchanged in feces via biliary excretion; only small amounts were found in the urine.
Telmisartan is metabolized by conjugation to form a pharmacologically inactive acylglucuronide; the glucuronide of the parent compound is the only metabolite that has been identified in human plasma and urine. After a single dose, the glucuronide represents approximately 11% of the measured radioactivity in plasma. The cytochrome P_{450} isoenzymes are not involved in the metabolism of telmisartan. Total plasma clearance of telmisartan is greater than 800 mL/min. Terminal half-life and total clearance appear to be independent of dose.

Special Populations
Pediatrics
Telmisartan pharmacokinetics have not been investigated in patients <18 years of age.

Geriatrics
The pharmacokinetics of telmisartan does not differ between the elderly and those younger than 65 years (see **Posology and Method of Administration** section).

Gender
Plasma concentrations of telmisartan are generally 2 to 3 times higher in females than in males. In clinical trials, however, no significant increases in blood pressure response or in the incidence of orthostatic hypotension were found in women. No dosage adjustment is necessary (see **Posology and Method of Administration** section).

Renal Impairment
Renal excretion does not contribute to the clearance of telmisartan. Based on modest experience in patients with mild-to-moderate renal impairment (creatinine clearance of 30 to 80 mL/min, mean clearance approximately 50 mL/min), no dosage adjustment is necessary in patients with decreased renal function. Telmisartan is not removed from blood by hemofiltration (see **Posology and Method of Administration** section).

Hepatic Impairment
In patients with hepatic insufficiency, plasma concentrations of telmisartan are increased, and absolute bio availability approaches 100% (see **Posology and Method of Administration** section).

Chlorthalidone
Absorption
The bioavailability of an oral dose of 50 mg is approximately 64%, peak blood concentrations (C_{max}) being attained after 8 to 12 hours.

Distribution
About 75% of chlorthalidone is bound to plasma proteins in the blood, mostly albumin.

Metabolism and Excretion
The mean plasma half-life of chlorthalidone is about 40 to 60 hours. It is eliminated primarily as unchanged drug in the urine. Non-renal routes of elimination have yet to be clarified.

Special Populations
Renal Impairment
Renal dysfunction does not alter the pharmacokinetics of chlorthalidone, the rate-limiting factor in the elimination of the drug from blood or plasma being most probably the affinity of the drug to the carbonic anhydrase of erythrocytes. No dosage adjustment is needed in patients with impaired renal function (see **Posology and Method of Administration** section).

Geriatrics
In elderly patients, the elimination of chlorthalidone is slower than in healthy young adults, although absorption is the same. Therefore, close medical observation is indicated when treating patients of advanced age with chlorthalidone.

Pediatrics
The safety and efficacy in children have not been established.

Preclinical Safety Data
Telmisartan
Telmisartan showed no evidence of mutagenicity and relevant clastogenic activity in *in vitro* studies and no evidence of carcinogenicity in rats and mice. No clear evidence of a teratogenic effect was observed, however at toxic dose levels of telmisartan an effect on the postnatal development of the off-springs such as lower body weight and delayed eye opening was observed.

Chlorthalidone
There is no clinically relevant preclinical safety data available.

CLINICAL PARTICULARS
Therapeutic Indications
TELMISAT®CT 40 is indicated for the treatment of hypertension.

Posology and Method of Administration
Telmisartan
The usual starting recommended dose is 40 mg once a day. In cases where the target blood pressure is not achieved, telmisartan dose can be increased to a maximum of 80 mg once daily.

Chlorthalidone
Therapy should be initiated with the lowest possible dose, and then titrated according to individual patient response. The usual recommended dose is 12.5 mg to 25 mg, preferably taken as a single dose in morning.

Method of Administration
TELMISAT®CT 40 is for once-daily oral administration and should be taken with water, with or without food.
Telmisartan and chlorthalidone tablets should be kept in the sealed blister due to the hygroscopic property of the tablets. Tablets should be taken out of the blister shortly before administration (see **Special Precautions for Disposal and Other Handling** section).

Special Populations
Pediatrics
The safety and efficacy in children is not established. Therefore, this combination is not recommended in children.
Geriatrics
No dose adjustment is necessary. But, close medical observation is indicated when treating patients of advanced age with chlorthalidone (see **Pharmacokinetic Properties** section).

Renal Impairment
Dosage adjustment is necessary in patients with mild or moderate renal impairment. The lowest possible dose is recommended in such patients. In patients with more severe renal impairment, loop diuretics are preferred, so telmisartan and chlorthalidone tablets are not recommended in such type of population. Periodic monitoring of renal function is advised (see **Pharmacokinetic Properties** and **Special Warnings and Precautions for Use** section).

Patients with hepatic impairment
Telmisartan and chlorthalidone tablets are not recommended for patients with severe hepatic impairment. Patients with biliary obstructive disorders or hepatic insufficiency should have treatment started under close medical supervision using the least dose of the combination (see **Pharmacokinetic Properties** and **Special Warnings and Precautions for Use** section).

Contraindications
Telmisartan and chlorthalidone tablets are contraindicated in the patients with following conditions:
- Hypersensitivity to any of the active substances (telmisartan, chlorthalidone) or to other sulphonamide-derived substances or to any of its excipients
- Second and third trimesters of pregnancy (see Special Warnings and Precautions for Use and Pregnancy and Lactation section)
- Cholestasis and biliary obstructive disorders
- Severe hepatic impairment
- Severe renal impairment (creatinine clearance <30 mL/min)
- Refractory hypokalemia, hyponatremia, symptomatic hyperuricemia, hypercalcemia
- Untreated Addison's disease
- Patients with anuria
- Co-administration of lithium therapy (see **Drug Interactions** section)
- Co-administration of telmisartan and chlorthalidone tablets with aliskiren in patients with diabetes (see **Drug Interactions** section).

Special Warnings and Precautions for Use
Fetal Toxicity
The use of ARBs is not recommended during the first trimester of pregnancy. The use of ARBs is contraindicated during the second and third trimesters of pregnancy (see **Special Warnings and Precautions for Use** and **Pregnancy and Lactation** sections).
The ARBs should not be initiated during pregnancy. When pregnancy is diagnosed, treatment with ARBs should be stopped immediately, and, if appropriate, alternative therapy should be started. Unless continued ARBs therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. If therapy with ARBs is found essential for the patient during her pregnancy, she should be apprised of the possible adverse effects to the fetus.

Hypotension in Volume-Depleted Patients
Intravascular hypovolemia
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 diarrhea or vomiting. Such conditions should be corrected before the administration of telmisartan and chlorthalidone tablets.

Other conditions with stimulation of the renin-angiotensin-aldosterone system
In patients whose vascular tone and renal function depend predominantly on the activity of the RAS (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with medicinal products that affect this system has been associated with acute hypotension, hyperazotemia, oliguria, or rarely acute renal failure (see **Undesirable Effects** section). In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) were observed.
If hypotension occurs, the patients should be placed in the supine position and, if necessary, given an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further treatment which usually can be continued without difficulty once the blood pressure has stabilized.

Hepatic Impairment
As the majority of telmisartan is eliminated by biliary excretion, patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. Thiazide diuretics should be used with caution in patients with impaired hepatic function or progressive liver disease, since minor alterations of fluid and electrolyte balance may precipitate hepatic coma. Telmisartan and chlorthalidone tablets should therefore be used with caution in these patients.

Renal Impairment
Telmisartan and chlorthalidone tablets should not be used in patients with severe renal impairment (creatinine clearance <30 mL/min, see **Contraindications** section). There is no experience regarding the administration of telmisartan and chlorthalidone tablets in patients with recent kidney transplantation. Experience with this combination is modest in patients with mild to moderate renal impairment, therefore periodic monitoring of potassium, creatinine and uric acid serum levels is recommended. Thiazide diuretic-associated azotemia may occur in patients with impaired renal function. Cumulative effects of the drug may develop in patients with impaired renal function.

Primary Aldosteronism
Patients with primary aldosteronism generally will not respond to antihypertensive medicinal products acting through inhibition of the RAS. Therefore, the use of telmisartan and chlorthalidone combination is not recommended.

Aortic and Mitral Valve Stenosis, Obstructive Hypertrophic Cardiomyopathy
As with other vasodilators, special caution is indicated in patients suffering from aortic or mitral stenosis, or obstructive hypertrophic cardiomyopathy.

Reno-vascular Hypertension
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 RAS.

Metabolic and Endocrine Effects
Chlorthalidone therapy may impair glucose tolerance whereas hypoglycemia may occur in diabetic patients under insulin or anti-diabetic therapy and telmisartan treatment. Therefore, in these patients blood glucose monitoring should be considered; a dose adjustment of insulin or anti-diabetics may be required, when indicated. Latent diabetes mellitus may become manifest during chlorthalidone therapy.
An increase in cholesterol and triglyceride levels has been associated with thiazide diuretic therapy; therefore chlorthalidone should be used with caution.
Hyperuricemia may occur or frank gout may be precipitated in some patients receiving chlorthalidone therapy.

Dual Blockade of the Renin-Angiotensin System
As a consequence of inhibiting the RAS, changes in renal function (including acute renal failure) have been reported. Dual blockade of the RAS (e.g. by adding an ACE-inhibitor to an angiotensin II receptor antagonist) should include close monitoring of renal function. Concomitant use of telmisartan and ramipril is not recommended (see **Drug Interactions** section).

Electrolyte Imbalance
As for any patient receiving diuretic therapy, periodic determination of serum electrolytes should be performed at appropriate intervals.
Thiazides/thiazide-like diuretics, including chlorthalidone, can cause fluid or electrolyte imbalance (including hypokalemia, hyponatremia and hypochloremic alkalosis). Warning signs of fluid or electrolyte imbalance are dryness of mouth, thirst, asthenia, lethargy, drowsiness, restlessness, muscle pain or cramps, muscular fatigue, hypotension, oliguria, tachycardia, and gastrointestinal disturbances such as nausea or vomiting. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity.

Hypokalemia
Although hypokalemia may develop with the use of thiazide diuretics, concurrent therapy with telmisartan may reduce diuretic-induced hypokalemia. The risk of hypokalemia is greater in patients with cirrhosis of liver, in patients experiencing brisk diuresis, in patients who are receiving inadequate oral intake of electrolytes and in patients receiving concomitant therapy with corticosteroids or adrenocorticotropic hormone [ACTH] (see **Drug Interactions** section).

Hyperkalemia
Conversely, due to the antagonism of the angiotensin II (AT1) receptors by telmisartan, hyperkalemia might occur. Although clinically significant hyperkalemia is not anticipated with telmisartan and chlorthalidone combination, risk factors for the development of hyperkalemia include renal insufficiency and/or heart failure, and diabetes mellitus. Potassium-sparing diuretics, potassium supplements or potassium-containing salt substitutes should be co-administered cautiously with telmisartan and chlorthalidone tablets (see **Drug Interactions** section).

Hyponatremia and hypochloremic alkalosis
There is no evidence that telmisartan and chlorthalidone combination would reduce or prevent diuretic-induced hyponatremia. Chloride deficit is generally mild and usually does not require treatment.

Hypercalcemia
Thiazides may decrease urinary calcium excretion and cause an intermittent and slight elevation of serum calcium in the absence of known disorders of calcium metabolism. Marked hypercalcemia may be evidence of hidden hyperparathyroidism. Thiazides/thiazide-like diuretics should be discontinued before carrying out tests for parathyroid function.

Hypomagnesemia
Thiazide diuretics have been shown to increase the urinary excretion of magnesium, which may result in hypomagnesemia.

Hyperuricemia
Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving chlorthalidone.

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Others
The antihypertensive effect of ACE inhibitors is potentiated by agents that increase plasma renin activity (diuretics). It is recommended that the diuretic be reduced in dosage or withdrawn for 2 to 3 days and/or that the ACE inhibitor therapy is started with a low initial dose of the ACE inhibitor. Patients should be monitored for several hours after the first dose.

Drug Interactions
Telmisartan
Aliskiren
Do not co-administer aliskiren with telmisartan and chlorthalidone tablets in patients with diabetes (see **Contraindications** section). Avoid use of aliskiren with this combination drugs in patients with renal impairment (glomerular filtration rate [GFR] <60 mL/min).

Digoxin
When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. It is, therefore, recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing telmisartan to avoid possible over- or under-digitalization.
Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors. Cases have also been reported with ARBs including telmisartan. Because lithium should not be used with diuretics, the use of lithium with telmisartan and chlorthalidone tablets is not recommended.

Non-steroidal Anti-inflammatory Agents including Selective Cyclooxygenase-2 Inhibitors
In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, co-administration of non-steroidal anti-inflammatory drugs (NSAIDs), including selective cyclooxygenase-2 (COX-2) inhibitors, with ARBs including telmisartan, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. Monitor renal function periodically in patients receiving telmisartan and NSAID therapy. The antihypertensive effect of ARBs, including telmisartan may be attenuated by NSAIDs including selective COX-2 inhibitors.

Ramipril and Ramiprilat
Co-administration of telmisartan and ramipril/ramiprilat may increase the antihypertensive effect because of the possibly additive pharmacodynamic effects of the combined drugs, and also because of the increased exposure to ramipril and ramiprilat in the presence of telmisartan (see **Special Warnings and Precautions for Use** section).

Warfarin
Telmisartan administered for 10 days slightly decreased the mean warfarin trough plasma concentration; this decrease did not result in a change in international normalized ratio (INR).

Other Drugs
Co-administration of telmisartan did not result in a clinically significant interaction with acetaminophen, amlodipine, glibenclamide, simvastatin, or ibuprofen. Telmisartan is not metabolized by the cytochrome P_{450} system and had no effects *in vitro* on cytochrome P_{450} enzymes, except for some inhibition of CYP2C19.

Chlorthalidone
When administered concurrently, the following drugs may interact with thiazide/thiazide-like diuretics.
Alcohol,barbiturates, or narcotics: potentiation of orthostatic hypotension may occur.

Anti-diabetic drugs (oral agents and insulin): dosage adjustment of the anti-diabetic drug may be required.

Other antihypertensive drugs: additive effect or potentiation of antihypertensive effect is observed.

Cholestyramine and colestipol resins: absorption of chlorthalidone is impaired in the presence of anionic exchange resins.

Corticosteroids, ACTH: intensified electrolyte depletion, particularly hypokalemia is observed. Thiazide-induced hypokalaemia or hypomagnesaemia may favour the occurrence of digitalis-induced cardiac arrhythmias (see **Special Warnings and Precautions for Use** section).

Pressor amines (e.g. norepinephrine): possible decreased response to pressor amines but not sufficient to preclude their use.

Anticholinergic agents: The bioavailability of thiazide-type diuretics may be increased by anticholinergic agents (e.g. atropine, biperiden), apparently due to a decrease in gastrointestinal motility and stomach-emptying rate.

Skeletal muscle relaxants, non-depolarizing (e.g. tubocurarine): possible increased responsiveness to the muscle relaxant.
Lithium: it should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of Lithium toxicity.

Non-steroidal anti-inflammatory drugs: in some patients, the administration of NSAID can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium sparing and thiazide diuretics. Therefore, when telmisartan and chlorthalidone tablets and NSAIDs are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

Cyclosporine: Concomitant treatment with may increase the risk of hyperuricemia and gout-type complications.

Calcium salts and vitamin D: The pharmacological effects of both calcium salts and vitamin D may be increased to clinically significant levels if given with thiazide diuretics. The resultant hypercalcemia is usually transient but may be persistent and symptomatic (weakness, fatigue, anorexia) in patients with hyperparathyroidism.

Others: 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 (e.g. cyclophosphamide, methotrexate) and potentiate their myelosuppressive effects.

Pregnancy and Lactation
Pregnancy category D
Use of drugs that act on the RAS 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 and chlorthalidone tablets as soon as possible.
In the unusual case that there is no appropriate alternative to therapy with drugs affecting the RAS for a particular patient, apprise the mother of the potential risk to the fetus. Perform serial ultrasound examinations to assess the intra-amniotic environment. If oligohydramnios is observed, discontinue telmisartan and chlorthalidone tablets, unless it is considered lifesaving for the mother. Fetal testing may be appropriate, based on the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. Closely observe infants with histories of in utero exposure to telmisartan and chlorthalidone tablets for hypotension, oliguria, and hyperkalemia (see **Special warnings and Precautions for Use** section). Thiazides cross the placental barrier and appear in cord blood, so there is a risk of fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions that have occurred in adults.

Lactation
As no information is available regarding the use of telmisartan and chlorthalidone tablets during breast-feeding, this combination is not recommended, and alternative treatments with better established safety profiles are preferable. Chlorthalidone is excreted in human milk in small amounts. Thiazides in high doses cause intense diuresis and can inhibit the milk production. Therefore, telmisartan and chlorthalidone tablets should be used during breast feeding only when there is no other appropriate alternative therapy available.

Effects on Ability to Drive and Use Machines
When driving vehicles or operating machinery it should be taken into account that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy (see **Undesirable Effects** section)

Undesirable Effects
Telmisartan
The common adverse effects observed in patients treated with telmisartan in clinical trials were fatigue, dizziness, diarrhea, nausea, sinusitis pain, headache, cough, urinary tract infection and upper respiratory tract infection.

Other adverse experiences that have been reported with Other adverse experiences that have been reported with telmisartan, without regard to causality, are listed below:

System	Adverse Effects
Autonomic nervous system	Impotence, increased sweating, flushing.
Body as a whole	Allergy, fever, leg pain, malaise, chest pain.
Cardiovascular	Palpitation, dependent edema, angina pectoris, leg edema, abnormal ECG, hypertension, peripheral edema.
Central nervous system	Insomnia, somnolence, migraine, vertigo, paresthesia, involuntary muscle contractions, hypoesthesia
Gastrointestinal	Flatulence, constipation, gastritis, drymouth, hemorrhoids, gastroenteritis, enteritis, gastroesophageal reflux, toothache, non-specific gastrointestinal disorders.
Metabolic	Gout, hypercholesterolemia, diabetes mellitus.
Musculoskeletal	Arthritis, arthralgia, leg cramps, myalgia.
Psychiatric	Anxiety, depression, nervousness.
Resistance mechanism	Infection, fungal infection, abscess, otitis media.
Respiratory system	Asthma, rhinitis, dyspnea, epistaxis.
Skin	Dermatitis, eczema, pruritus.
Urinary	Micturition frequency, cystitis.
Vascular	Cerebrovascular disorder.
Special senses	Abnormal vision, conjunctivitis, tinnitus, earache.

ECG: Electrocardiogram
A single case of angioedema was reported.
Post-marketing Experience
The adverse effects reported during post marketing experience is headache, dizziness, asthenia, coughing, nausea, fatigue, weakness, edema, face edema, lower limb edema, angioneurotic edema, urticaria, hypersensitivity, sweating increased, erythema, chest pain, atrial fibrillation, congestive heart failure, myocardial infarction, increased blood pressure, aggravated hypertension, hypotension (including postural hypotension), hyperkalemia, syncope, dyspepsia, diarrhea, pain, urinary tract infection, erectile dysfunction, back pain, abdominal pain, muscle cramps (including leg cramps), myalgia, bradycardia, eosinophilia, thrombocytopenia.
The other common adverse effects reported were increased uric acid, abnormal hepatic function/liver disorder, renal impairment including acute renal failure, anemia, increased creatinine phosphokinase (CPK), anaphylactic reaction, tendon pain (including tendonitis, tenosynovitis), drug eruption (toxic skin eruption mostly reported as toxicoderma, rash, and urticaria), hypoglycemia (in diabetic patients), and angioedema (with fatal outcome).
Rare cases of rhabdomyolysis have been reported in patients receiving ARB's, including telmisartan.

Chlorthalidone

The adverse reactions observed with use of chlorthalidone are mentioned in below table:

System	Adverse Effects
Gastrointestinal system	Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis.
Central nervous system	Dizziness, vertigo, paresthesias, headache, xanthopsia.
Hematologic	Leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia.
Dermatologic-hypersensitivity	Purpura, photosensitivity, rash, urticaria, necrotizing angiitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis).
Cardiovascular	Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics.
Other	Hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence.

Overdose
Telmisartan
The most likely manifestation of overdosage with telmisartan would be hypotension, dizziness and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted, the patient should be placed in a supine position, with salt and volume replacement given quickly. Telmisartan is not removed by hemodialysis. Suggested measures include induction of emesis and / or gastric lavage. Activated charcoal may be useful in the treatment of over dosage. Serum electrolytes and creatinine should be monitored frequently.

Chlorthalidone
In case of over dosage the following signs and symptoms may occur: dizziness, nausea, somnolence, hypovolemia, hypotension and electrolyte disturbances associated with cardiac arrhythmias and muscle spasms. There is no specific antidote to chlorthalidone. Gastric lavage, emesis or activated charcoal should be employed to reduce absorption. Blood pressure and fluid and electrolyte balance should be monitored and appropriate corrective measures taken. Intravenous fluid and electrolyte replacement may be indicated.

PHARMACEUTICAL PARTICULARS
Incompatibilities
Not applicable.

Shelf Life: Please refer to carton/strip

Storage and Precautions
Store below 25°C, protect from light and moisture.
Keep out of reach of children.

Special Precautions for Disposal and Other Handling
Telmisartan and Chlorthalidone tablets should be taken out of the strip shortly before administration due to their hygroscopic nature.
Any unused medicinal product should be disposed off in accordance with the local requirements.

Pack Presentation: Telmisat CT 40 are available in a strip pack.
Sales pack size: 10x10 Tablets.

Marketed by:
Biocon Biologics India Limited
Biocon House, Semicon Park,
Electronics City, Phase - II,
Bengaluru - 560 100, India.

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To report adverse events and/or product complaints visit our website **www.biocon.com** or call toll free number: **1800 102 9465** or e-mail us at **drugsafety@biocon.com**