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

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Telmisartan and Hydrochlorothiazide Tablets IP 40mg/12.5mg
Telmisartan and Hydrochlorothiazide Tablets IP 80mg/12.5mg

TELMISAT® H / TELMISAT® 80 H टेलमिसेट एच / टेलमिसेट ८०एच

COMPOSITION:
TELMISAT® H
Each uncoated bilayered tablet contains:
Telmisartan IP 40 mg
Hydrochlorothiazide IP 12.5 mg
Excipients q.s.
Colour: Lake Quinoline Yellow

TELMISAT® 80 H
Each uncoated bilayered tablet contains:
Telmisartan IP 80 mg
Hydrochlorothiazide IP 12.5 mg
Excipients q.s.
Colour: Lake Sunset Yellow

WARNING
AVOID USE IN PREGNANCY
When used in pregnancy, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, Telmisartan tablets should be discontinued as soon as possible.

Special Alerts:
ISSUE: A recently published study a meta-analysis combining cancer related findings from several clinical trials suggested use of angiotensin receptor blockers (ARBs) may be associated with a little increased risk of cancer

RECOMMENDATION: FDA has not concluded that ARBs increase the risk of cancer. The Agency is reviewing information related to this safety concern and will update the public when additional information is available. FDA believes the benefits of ARBs continue to outweigh their potential risks. For more information visit the FDA website.

PHARMACEUTICAL FORM
Tablets

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

TELMISAT® H/TELMISAT® 80 H is a combination of angiotensin I receptor blockers (ARBs), telmisartan, and a thiazide diuretic, hydrochlorothiazide. The combination of these ingredients has an additive antihypertensive effect, reducing blood pressure to a greater degree than either component alone. This combination, once daily produces effective and smooth reductions in blood pressure across the therapeutic dose range.

Mechanism of Action
Telmisartan
Telmisartan is an orally effective and specific angiotensin receptor subtype 1 (AT$_1$) 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.

Hydrochlorothiazide
Hydrochlorothiazide is a thiazide diuretic. Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium salt and chloride in approximately equivalent amounts. Indirectly, the diuretic action of hydrochlorothiazide reduces plasma volume, with consequent increases in plasma renin activity, increases in aldosterone secretion, increases in urinary potassium loss, and decreases in serum potassium. The renin-aldosterone link is mediated by angiotensin II, so co-administration of an angiotensin II receptor antagonist tends to reverse the potassium loss associated with these diuretics. The mechanism of the antihypertensive effect of thiazides is not fully understood.

Pharmacokinetic Properties
Concomitant administration of hydrochlorothiazide and telmisartan does not appear to affect the pharmacokinetics of either substance.

Absorption
Telmisartan
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 does not accumulate significantly in plasma on repeated administration.

Hydrochlorothiazide
Following oral administration peak plasma concentration of hydrochlorothiazide is reached in 1 to 3 hours.

Distribution
Telmisartan
Telmisartan is highly bound to plasma proteins (>99.5%), mainly albumin and 1-acid glycoprotein. The volume of distribution for telmisartan is approximately 500 L, indicating additional tissue binding.

Hydrochlorothiazide
Hydrochlorothiazide is 68 % protein bound in the plasma and its apparent volume of distribution is 0.83 to 1.14 L/kg. Hydrochlorothiazide crosses the placental but not the blood-brain barrier and is excreted in breast milk.

Metabolism and Excretion
Telmisartan
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 P450 isoenzymes are not involved in the metabolism of telmisartan. Total plasma clearance of telmisartan is >800 mL/min. Terminal half-life and total clearance appear to be independent of dose.

Hydrochlorothiazide
Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. At least 61% of the oral dose is eliminated as unchanged drug within 24 hours.

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

Geriatrics
The pharmacokinetics of telmisartan do 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 bioavailability approaches 100% (see **Posology and Method of Administration** section).

Preclinical Safety Data
Telmisartan showed no evidence of mutagenicity and relevant clastogenic activity in *in vitro* studies and no evidence of carcinogenicity in rats and mice. Studies with hydrochlorothiazide have shown equivocal evidence for a genotoxic or carcinogenic effect in some experimental models. However, the extensive human experience with hydrochlorothiazide has failed to show an association between its use and an increase in neoplasms.

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.

CLINICAL PARTICULARS
Therapeutic Indications
Telmisartan and hydrochlorothiazide tablets are indicated for the treatment of hypertension as a second line therapy. This fixed combination is not indicated for initial therapy (see **Posology and Method of Administration** section).

Posology and Method of Administration
Posology
TELMISAT® H/TELMISAT® 80 H should be taken in adult patients whose blood pressure is not adequately controlled by telmisartan alone. Individual dose titration with each of the two components is recommended before changing to the fixed dose combination. When clinically appropriate, direct change from mono-therapy to the fixed combination may be considered.

TELMISAT® H may be administered once daily in adult patients whose blood pressure is not adequately controlled by telmisartan 40 mg.

TELMISAT® 80 H may be administered once daily in adult patients whose blood pressure is not adequately controlled by telmisartan 80 mg

TELMISAT® H/TELMISAT® 80 H is not indicated for use in children and adolescents <18 years (see **Pharmacokinetic Properties** section)

Special Populations
Patients with renal impairment
No dosage adjustment is necessary in patients with mild or moderate renal impairment. In patients with more severe renal impairment, loop diuretics are preferred, so telmisartan and hydrochlorothiazide 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 hydrochlorothiazide 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 40/12.5 mg combination (see **Pharmacokinetic Properties** and **Special Warnings and Precautions for Use** section).

Elderly patients
No dose adjustment is necessary (see **Pharmacokinetic Properties** section).

Method of Administration
TELMISAT® H/TELMISAT® 80 H is for once-daily oral administration and should be taken with water, with or without food.
Telmisartan and hydrochlorothiazide tablets should be kept in the sealed strip due to the hygroscopic property of the tablets. Tablets should be taken out of the strip shortly before administration (see **Special Precautions for Disposal and Other Handling** section).

Contraindications
Telmisartan and hydrochlorothiazide tablets are contraindicated in the patients with following conditions:
- Hypersensitivity to any of the active substances (telmisartan, hydrochlorothiazide) 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, hypercalcemia
- Patients with anuria
- Co-administration of telmisartan and hydrochlorothiazide 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 **Contraindications** 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 hydrochlorothiazide 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 hydrochlorothiazide tablets should therefore be used with caution in these patients.

Renal Impairment
Telmisartan and hydrochlorothiazide 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 hydrochlorothiazide 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 hydrochlorothiazide 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
Thiazide 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 thiazide therapy.
An increase in cholesterol and triglyceride levels has been associated with thiazide diuretic therapy; however, at the low dose (12.5 mg), minimal or no effects were reported.
Hyperuricemia may occur or frank gout may be precipitated in some patients receiving thiazide therapy.

Electrolyte Imbalance
As for any patient receiving diuretic therapy, periodic determination of serum electrolytes should be performed at appropriate intervals.
Thiazides, including hydrochlorothiazide, 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.

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 has not been documented with telmisartan and hydrochlorothiazide combination, risk factors for the development of hyperkalemia include renal insufficiency and/or heart failure, and diabetes mellitus. Potassium-sparing diuretics,

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potassium supplements or potassium-containing salt substitutes should be co-administered cautiously with telmisartan and hydrochlorothiazide tablets (see **Drug Interactions** section).

Hyponatremia and hypochloremic alkalosis
There is no evidence that telmisartan and hydrochlorothiazide 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 should be discontinued before carrying out tests for parathyroid function.

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

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).

Acute Myopia and Secondary Angle-Closure Glaucoma:
Hydrochlorothiazide, a sulfonamide, can cause an idiosyncratic reaction, resulting in acute transient myopia and acute angle-closure glaucoma. Symptoms include acute onset of decreased visual acuity or ocular pain and typically occur within hours to weeks of drug initiation. Untreated angle-closure glaucoma can lead to permanent vision loss. The primary treatment is to discontinue hydrochlorothiazide as rapidly as possible. Prompt medical or surgical treatments may need to be considered, if the intraocular pressure remains uncontrolled. Risk factors for developing acute angle-closure glaucoma may include a history of sulfonamide or penicillin allergy.

General
Hypersensitivity reactions to hydrochlorothiazide may occur in patients with or without a history of allergy or bronchial asthma, but are more likely in patients with such a history.

Exacerbation or activation of systemic lupus erythematosus has been reported with the use of thiazide diuretics, including hydrochlorothiazide.

Cases of photosensitivity reactions have been reported with thiazide diuretics. If a photosensitivity reaction occurs during treatment, it is recommended to stop the treatment. If re-administration of the diuretic is deemed necessary, it is recommended to protect exposed areas from sun or to artificial UVA.

Drug Interactions
Telmisartan
Aliskiren
Do not co-administer aliskiren with telmisartan and hydrochlorothiazide 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 hydrochlorothiazide 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, hydrochlorothiazide or ibuprofen. Telmisartan is not metabolized by the cytochrome P450 system and had no effects *in vitro* on cytochrome P450 enzymes, except for some inhibition of CYP2C19.

Hydrochlorothiazide
When administered concurrently, the following drugs may interact with thiazide 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 hydrochlorothiazide is impaired in the presence of anionic exchange resins.

Corticosteroids, ACTH: intensified electrolyte depletion, particularly hypokalemia is observed.

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

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 hydrochlorothiazide tablets and NSAIDs are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

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 hydrochlorothiazide 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 hydrochlorothiazide 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 hydrochlorothiazide 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 hydrochlorothiazide tablets during breast-feeding, this combination is not recommended, and alternative treatments with better established safety profiles are preferable. Hydrochlorothiazide is excreted in human milk in small amounts. Thiazides in high doses cause intense diuresis and can inhibit the milk production. Therefore, telmisartan and hydrochlorothiazide 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
The common adverse effects observed in patients treated with telmisartan and hydrochlorothiazide in clinical trials were fatigue, dizziness, diarrhea, nausea, sinusitis pain, headache, cough, urinary tract infection and upper respiratory tract infection.

Telmisartan
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, hypoaesthesia
Gastrointestinal	flatulence, constipation, gastritis, dry mouth, 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, uric acid increased, 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.

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

System	Adverse Effects
Body as a whole	weakness
Digestive	pancreatitis, jaundice (intrahepatic cholestatic jaundice), sialadenitis, cramping, gastric irritation
Hematologic	aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia
Hypersensitivity	purpura, photosensitivity, urticaria, necrotizing angiitis (vasculitis and cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary edema, anaphylactic reactions
Metabolic	hyperglycemia, glycosuria, hyperuricemia
Musculoskeletal	muscle spasm
Nervous system/psychiatric	restlessness
Renal	renal failure, renal dysfunction, interstitial nephritis
Skin	erythema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidermal necrolysis
Special senses	transient blurred vision, xanthopsia

Others
Decrease in hemoglobin and hematocrit, Increase in serum creatinine and BUN, occasional elevation of liver enzymes and/or serum bilirubin have been reported with telmisartan and hydrochlorothiazide combination therapy in controlled clinical trials for change in serum electrolytes (see **Special Warnings and Precautions for Use** section).

Overdose
Symptoms
The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia, dizziness, vomiting, increase in serum creatinine, and acute renal failure. Overdose with hydrochlorothiazide is associated with electrolyte depletion (hypokalemia, hypochloremia) and hypovolemia resulting from excessive diuresis. The most common signs and symptoms of overdose are nausea and somnolence. Hypokalemia may result in muscle spasms and/or accentuate arrhythmia associated with the concomitant use of digitalis glycosides or certain anti-arrhythmic medicinal products.

Treatment
Since telmisartan is not cleared by hemodialysis, patients should be closely monitored, and the treatment should be symptomatic and supportive. Management depends on the time since ingestion and the severity of the symptoms. Suggested measures include induction of emesis and/or gastric lavage. Activated charcoal may be useful in the treatment of overdose. Serum electrolytes and creatinine should be monitored frequently. If hypotension occurs, the patient should be placed in a supine position, with salt and volume replacements given quickly.

PHARMACEUTICAL PARTICULARS
Incompatibilities
Not applicable.

Shelf Life: Please refer to strip/carton.

Storage and Precautions
Store protected from moisture, at temperature not exceeding 30°C.
Keep out of reach of children.

Special Precautions for Disposal and Other Handling
Tablets should be taken out of the strip shortly before administration because of the hygroscopic nature of the tablets.
Any unused medicinal product should be disposed in accordance with the local requirements.

Nature and Contents of Container
TELMISAT® H/TELMISAT® 80 H is supplied as 10 tablets in a strip and 10 such strips in a carton.
Pack size: 10 x10 Tablets

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

® - Registered trade mark

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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.**

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