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

This package insert is continually updated: Please read carefully before using a new pack

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

TELSITE® H

Each uncoated bilayered tablet contains:
Telmisartan IP. .....40 mg
Hydrochlorothiazide I.P. .....12.5 mg
Excipients……q.s
Colour: Ferric Oxide Red USP-NF

Each uncoated bilayered tablet contains:
Telmisartan IP. .....80 mg
Hydrochlorothiazide I.P. .....12.5 mg
Excipients……q.s
Colour: Ferric Oxide Yellow USP-NF

THERAPEUTIC INDICATIONS
Telsite H is indicated for the treatment of essential hypertension as second line therapy.

DOSAGE & ADMINISTRATION

GENERAL
Adults
Telmisartan/hydrochlorothiazide should be taken in 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 monotherapy to the fixed combination may be considered.

- Telmisartan/hydrochlorothiazide 40 mg/12.5 mg tablets: Telmisartan/hydrochlorothiazide 40 mg/12.5 mg may be administered once daily in patients whose blood pressure is not adequately controlled by telmisartan 40 mg alone. Telmisartan/hydrochlorothiazide is also available at the dose strength 80 mg/12.5 mg.

- Telmisartan/hydrochlorothiazide 80 mg/12.5 mg tablets: Telmisartan/hydrochlorothiazide 80 mg/12.5 mg may be administered once daily in patients whose blood pressure is not adequately controlled by telmisartan 80 mg alone. Telmisartan/hydrochlorothiazide is also available at the dose strengths 40 mg/12.5 mg.

SPECIAL POPULATIONS

Pediatric patients
The safety and efficacy of telmisartan/hydrochlorothiazide in children and adolescents aged below 18 have not been established. No data are available.

Elderly patients
No dose adjustment is necessary.

Hepatic impairment
In patients with mild to moderate hepatic impairment the posology should not exceed telmisartan/hydrochlorothiazide 40 mg/12.5 mg once daily. Telmisartan/hydrochlorothiazide is not indicated in patients with severe hepatic impairment. Thiazides should be used with caution in patients with impaired hepatic function.

Renal impairment
Periodic monitoring of renal function is advised.

ADMINISTRATION
Telmisartan/hydrochlorothiazide tablets are for once-daily oral administration and should be taken with liquid, with or without food.

CONTRAINDICATIONS
- Hypersensitivity to any of the active substances or to any of the excipients listed in relevant section of the appropriate labelling document.
- Hypersensitivity to other sulphonamide-derived substances (since hydrochlorothiazide is a sulphonamide-derived medicinal product).
- Second and third trimesters of pregnancy.
- Cholestasis and biliary obstructive disorders.
- Severe hepatic impairment.
- Severe renal impairment (creatinine clearance <30 ml/min).
- Refractory hypokalemia, hypercalcemia.
- The concomitant use of telmisartan/hydrochlorothiazide with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR <60 ml/min/1.73 m^2)

WARNINGS AND PRECAUTIONS
Pregnancy
Angiotensin II receptor antagonists (AIIRAs) should not be initiated during pregnancy. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with AIIRA should be stopped immediately, and, if appropriate, alternative therapy should be started.

Hepatic impairment
Telmisartan/hydrochlorothiazide should not be given to patients with cholestasis, biliary obstructive disorders or severe hepatic insufficiency since telmisartan is mostly eliminated with the bile. These patients can be expected to have reduced hepatic clearance for telmisartan.

In addition, telmisartan/hydrochlorothiazide 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. There is no clinical experience with telmisartan/hydrochlorothiazide in patients with hepatic impairment.

Renovascular 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 renin-angiotensin-aldosterone system.

Renal impairment and kidney transplantation

Telmisartan/hydrochlorothiazide must not be used in patients with severe renal impairment (creatinine clearance <30ml/min). There is no experience regarding the administration of telmisartan/hydrochlorothiazide in patients with recent kidney transplantation. Experience with telmisartan/hydrochlorothiazide is modest in the 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.

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, diarrhea or vomiting. Such conditions should be corrected before the administration of telmisartan/hydrochlorothiazide.

Dual blockade of the renin-angiotensin-aldosterone system (RAAS)
There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers, or aliskiren increases the risk of hypotension, hyperkalemia, and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers, or aliskiren is therefore not recommended.
If dual blockade therapy is considered absolutely necessary, this should only occur under specialist supervision and subject to frequent close monitoring of renal function, electrolytes, and blood pressure. ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.

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 renin-angiotensin-aldosterone system (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, hypercarotenemia, oliguria, or rarely acute renal failure.

Primary aldosteronism
Patients with primary aldosteronism generally will not respond to antihypertensive medicinal products acting through inhibition of the renin-angiotensin system. Therefore, the use of telmisartan/hydrochlorothiazide 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.

Metabolic and endocrine effects
Thiazide therapy may impair glucose tolerance, whereas hypoglycemia may occur in diabetic patients under insulin or antidiabetic therapy and telmisartan treatment. Therefore, in these patients blood glucose monitoring should be considered; a dose adjustment of insulin or antidiabetics 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 12.5 mg dose contained in telmisartan/hydrochlorothiazide 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 hypochloremia 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).

Hyperkaliemia

Conversely, due to the antagonism of the angiotensin II (AT_1) receptors by the telmisartan component of telmisartan/(hydrochlorothiazide), hyperkalemia might occur. Although clinically significant hyperkalemia has not been documented with telmisartan/hydrochlorothiazide, 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/hydrochlorothiazide.

Hyponatremia and hypochloremia alkalosis

There is no evidence that telmisartan/hydrochlorothiazide 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.

Hypomagnesaemia

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

Ethnic differences

As with all other AIIRAs, telmisartan is apparently less effective in lowering blood pressure in black patients than in non-blacks, possibly because of higher prevalence of low renin states in the black hypertensive population.

Other

As with any antihypertensive agent, excessive reduction of blood pressure in patients with ischemic cardiopathy or ischemic cardiovascular disease could result in a myocardial infarction or stroke.

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 a re-administration of the diuretic is deemed necessary, it is recommended to protect exposed areas to the sun or to artificial UVA.

Acute Respiratory Toxicity:
Severe cases of acute respiratory toxicity, including acute respiratory distress syndrome (ARDS) have been reported after taking hydrochlorothiazide. Pulmonary oedema typically develops within minutes to hours after hydrochlorothiazide intake. At the onset, symptoms include dyspnoea, fever, pulmonary deterioration and hypotension. If diagnosis of ARDS is suspected, Telsite H should be withdrawn and appropriate treatment should be given. Hydrochlorothiazide must not be administered to patients who previously experienced ARDS following intake of hydrochlorothiazide or another thiazide diuretic.

Nonmelanoma skin cancer
An increased risk of nonmelanoma skin cancer (NMSC) [basal cell carcinoma (BCC) and squamous cell carcinoma (SCC)] with increasing cumulative dose of hydrochlorothiazide (HCTZ) exposure has been observed in two epidemiological studies based on the Danish National Cancer Registry. Photosensitizing actions of HCTZ could act as a possible mechanism for NMSC.
Patients taking HCTZ should be informed of the risk of NMSC and advised to regularly check their skin for any new lesions and promptly report any suspicious skin lesions. Possible preventive measures such as limited exposure to sunlight and UV rays and, in case of exposure, adequate protection should be advised to the patients in order to minimize the risk of skin cancer. Suspicious skin lesions should be promptly examined potentially including histological examinations of biopsies. The use of HCTZ may also need to be reconsidered in patients who have experienced previous NMSC.

Choroidal effusion, acute myopia and angle-closure glaucoma
Hydrochlorothiazide, a sulfonamide, can cause an idiosyncratic reaction, resulting in choroidal effusion with visual field defect, 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 acute 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.

INTERACTIONS

Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin-converting enzyme inhibitors. Rare cases have also been reported with angiotensin II receptor antagonists (including telmisartan/hydrochlorothiazide). Coadministration of lithium and telmisartan/hydrochlorothiazide

is not recommended. If this combination proves essential, careful monitoring of serum lithium level is recommended during concomitant use.

Medicinal products associated with potassium loss and hypokalemia (e.g. other kaliuretic diuretics, laxatives, corticosteroids, ACTH, amphotericin, carbenoxolone, penicillin G sodium, salicylic acid and derivatives) If these substances are to be prescribed with the hydrochlorothiazide-telmisartan combination, monitoring of potassium plasma levels is advised. These medicinal products may potentiate the effect of hydrochlorothiazide on serum potassium.

Medicinal products that may increase potassium levels or induce hyperkalemia (e.g. ACE-inhibitors, potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium, cyclosporin, or other medicinal products such as heparin sodium)
If these medicinal products are to be prescribed with the hydrochlorothiazide-telmisartan combination, monitoring of potassium plasma levels is advised. Based on the experience with the use of other medicinal products that blunt the renin-angiotensin system, concomitant use of the above medicinal products may lead to increases in serum potassium and is, therefore, not recommended.

Medicinal products affected by serum potassium disturbances
Periodic monitoring of serum potassium and ECG is recommended when telmisartan/hydrochlorothiazide is administered with medicinal products affected by serum potassium disturbances (e.g. digitalis glycosides, antiarrhythmics) and the following torsades de pointes inducing medicinal products (which include some antiarrhythmics), hypokalemia being a predisposing factor to torsades de pointes.

- class Ia antiarrhythmics (e.g. quinidine, hydroquinidine, disopyramide)
- class III antiarrhythmics (e.g. amiodarone, sotalol, dofetilide, ibutilide)
- some antipsychotics (e.g. thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, sultopride, amisulpride, tiapride, pimozide, haloperidol, droperidol)
- others (e.g. bepridil, cisapride, diphemanil, erythromycin IV, halofantrin, mizolastin, pentamidine, sparfloxacine, terfenadine, vincamine IV.)

Digitalis glycosides
Thiazide-induced hypokalemia or hypomagnesemia favors the onset of digitalis-induced arrhythmia.

Digoxin:
When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. When initiating, adjusting, and discontinuing telmisartan, monitor digoxin levels in order to maintain levels within the therapeutic range.

Other antihypertensive agents
Telmisartan may increase the hypotensive effect of other antihypertensive agents.

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, hyperkalemia, and decreased renal function (including acute renal failure) compared to the use of a single RAAS-acting agent.

Antidiabetic medicinal products (oral agents and insulin)
Dosage adjustment of the antidiabetic medicinal products may be required.

Metformin
Metformin should be used with precaution: risk of lactic acidosis induced by a possible functional renal failure linked to hydrochlorothiazide.

Cholestyramine and Colestipol resins
Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins.

Nonsteroidal anti-inflammatory medicinal products
NSAIDs (i.e. acetylsalicylic acid at anti-inflammatory dosage regimens, COX-2 inhibitors and nonselective NSAIDs) may reduce the diuretic, natriuretic, and antihypertensive effects of thiazide diuretics and the antihypertensive effects of angiotensin II receptor antagonists.
In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function) the coadministration of angiotensin II receptor antagonists and agents that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter.

In one study the coadministration of telmisartan and ramipril led to an increase of up to 2.5 fold in the AUC_{0-24} and C_{max} of ramipril and ramiprilat. The clinical relevance of this observation is not known.

Pressor amines (e.g. noradrenaline)
The effect of pressor amines may be decreased.

Nondepolarizing skeletal muscle relaxants (e.g. tubocurarine)
The effect of nondepolarizing skeletal muscle relaxants may be potentiated by hydrochlorothiazide.

Medicinal products used in the treatment for gout (e.g. probenecid, sulfinpyrazone and allopurinol)
Dosage adjustment of uricosuric medications may be necessary as hydrochlorothiazide may raise the level of serum uric acid. Increase in dosage of probenecid or sulfinpyrazone may be necessary. Coadministration of thiazide may increase the incidence of hypersensitivity reactions of allopurinol.

Calcium salts
Thiazide diuretics may increase serum calcium levels due to the decreased excretion. If calcium supplements or calcium sparing medicinal products (e.g. vitamin D therapy) must be prescribed, serum calcium levels should be monitored and calcium dosage adjusted accordingly.

Beta-blockers and diazoxide
The hyperglycemic effect of beta-blockers and diazoxide may be enhanced by thiazides.

Anticholinergic agents (e.g. atropine, biperiden) may increase the bioavailability of thiazide-type diuretics by decreasing gastrointestinal motility and stomach emptying rate.

Amantadine
Thiazides may increase the risk of adverse effects caused by amantadine.

Cytotoxic agents (e.g. cyclophosphamide, methotrexate)
Thiazides may reduce the renal excretion of cytotoxic medicinal products and potentiate their myelosuppressive effects.

Based on their pharmacological properties it can be expected that the following medicinal products may potentiate the hypotensive effects of all antihypertensives including telmisartan: Baclofen, manifesting. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics, or antidepressants

USE IN SPECIFIC POPULATIONS

Pregnancy

The use of AIIRAs is not recommended during the first trimester of pregnancy. The use of AIIRAs is contraindicated during the second and third trimesters of pregnancy.

There are no adequate data from the use of telmisartan/hydrochlorothiazide in pregnant women. Studies in animals have shown reproductive toxicity.

Epidemiological evidence regarding the risk of teratogenicity following exposure to ACE-inhibitors during the first trimester of pregnancy has not been conclusive; however, a small increase in risk cannot be excluded. Whilst there is no controlled epidemiological data on the risk with AIIRAs, similar risks may exist for this class of drugs. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately, and, if appropriate, alternative therapy should be started.

Exposure to AIIRA therapy during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalemia). Should exposure to AIIRAs have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended. Infants whose mothers have taken AIIRAs should be closely observed for hypotension.

There is limited experience with hydrochlorothiazide during pregnancy, especially during the first trimester. Animal studies are insufficient. Hydrochlorothiazide crosses the placenta. Based on the pharmacological mechanism of action of hydrochlorothiazide its use during the second and third trimester may compromise foe to-placental perfusion and may cause fetal and neonatal effects like icterus, disturbance of electrolyte balance, and thrombocytopenia. Hydrochlorothiazide should not be used for gestational edema, gestational hypertension, or preeclampsia due to the risk of decreased plasma volume and placental hypoperfusion, without a beneficial effect on the course of the disease.

Hydrochlorothiazide should not be used for essential hypertension in pregnant women except in rare situations where no other treatment could be used.

Lactation

Because no information is available regarding the use of telmisartan/hydrochlorothiazide during breastfeeding, telmisartan/hydrochlorothiazide is not recommended and alternative treatments with better established safety profiles during breastfeeding are preferable, especially while nursing a newborn or preterm infant.

Hydrochlorothiazide is excreted in human milk in small amounts. Thiazides in high doses causing intense diuresis can inhibit the milk production. The use of telmisartan/hydrochlorothiazide during breastfeeding is not recommended. If telmisartan/hydrochlorothiazide is used during breastfeeding, doses should be kept as low as possible.

Fertility

In preclinical studies, no effects of telmisartan and hydrochlorothiazide on male and female fertility were observed.

OVERDOSAGE

There is limited information available for telmisartan with regard to overdose in humans. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

Signs and symptoms

The most prominent manifestations of telmisartan overdose were hypotension and tachycardia; bradycardia, dizziness, vomiting, increase in serum creatinine, and acute renal failure have also been reported. 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.

Management

Telmisartan is not removed by hemodialysis. The patient 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.

PHARMACOLOGICAL PROPERTIES

Mechanism of Action

Telmisartan is an orally effective and specific angiotensin II receptor subtype 1 (AT_1) antagonist. Telmisartan displaces angiotensin II with very high affinity from its binding site at the AT_1 receptor subtype, which is responsible for the known actions of angiotensin II. Telmisartan does not exhibit any partial agonist activity at the AT_1 receptor. Telmisartan selectively binds the AT_1 receptor. The binding is long-lasting. Telmisartan does not show affinity for other receptors, including AT_2 and other less characterized AT receptors. The functional role of these receptors is not known, nor is the effect of their possible overstimulation by angiotensin II, whose levels are increased by telmisartan.

Plasma aldosterone levels are decreased by telmisartan. Telmisartan does not inhibit human plasma renin or block ion channels. Telmisartan does not inhibit angiotensin-converting enzyme (kininase II), the enzyme which also degrades bradykinin. Therefore, it is not expected to potentiate bradykinin-mediated adverse effects.
An 80 mg dose of telmisartan administered to healthy volunteers almost completely inhibits the angiotensin II evoked blood pressure increase. The inhibitory effect is maintained over 24 hours and still measurable up to 48 hours.

Hydrochlorothiazide is a thiazide diuretic. The mechanism of the antihypertensive effect of thiazide diuretics is not fully known. Thiazides have an effect on the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium and chloride in approximately equivalent amounts. The diuretic action of hydrochlorothiazide reduces plasma volume, increases plasma renin activity, increases aldosterone secretion, with consequent increases in urinary potassium and bicarbonate loss, and decreases in serum potassium. Presumably through blockade of the renin-angiotensin-aldosterone system, coadministration of telmisartan tends to reverse the potassium loss associated with these diuretics. With hydrochlorothiazide, onset of diuresis occurs in 2 hours, and peak effect occurs at about 4 hours, while the action persists for approximately 6-12 hours.

DRIVING A VEHICLE OR PERFORMING OTHER HAZARDOUS TASKS

Telmisartan/hydrochlorothiazide can have influence on the ability to drive and use machines. Dizziness or drowsiness may occasionally occur when taking telmisartan/hydrochlorothiazide.

ADVERSE REACTIONS:

Summary of the safety profile

The most common reported adverse reaction is dizziness. Serious angioedema may occur rarely (≥1/10,000 to <1/1,000).

Telmisartan/hydrochlorothiazide 40 mg/12.5 mg and 80 mg/12.5 mg: The overall incidence of adverse reactions reported with telmisartan/hydrochlorothiazide was comparable to those reported with telmisartan alone in randomized controlled trials involving 1471 patients randomized to receive telmisartan plus hydrochlorothiazide (835) or telmisartan alone (636). Dose-relationship of adverse reactions was not established and they showed no correlation with gender, age, or race of the patients.

Tabulated list of adverse reactions

Adverse reactions reported in all clinical trials and occurring more frequently ($p \leq 0.05$) with telmisartan plus hydrochlorothiazide than with placebo are shown below according to system organ class. Adverse reactions known to occur with each component given singly but which have not been seen in clinical trials may occur during treatment with telmisartan/hydrochlorothiazide.

The following CIOMS frequency rating is used, when applicable:
Very common ≥ 10%; Common ≥ 1 and < 10%; Uncommon ≥ 0.1 and < 1%;
Rare ≥ 0.01 and < 0.1%; Very rare < 0.01%; Not known (cannot be estimated from available data).

Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness.

System organ class	Frequency	Adverse reactions
Infections and infestations	Rare	Bronchitis, pharyngitis, sinusitis
Immune system disorders	Rare	Exacerbation or activation of systemic lupus erythematosus[1]
Metabolism and nutrition disorders	Uncommon	Hypokalemia
	Rare	Hyponatremia
Psychiatric disorders	Uncommon	Anxiety
	Rare	Depression
Nervous system disorders	Common	Dizziness
	Uncommon	Syncope, paresthesia
	Rare	Insomnia, sleep disorders
Eye disorders	Rare	Visual disturbance, vision blurred
Ear and labyrinth disorders	Uncommon	Vertigo
Cardiac disorders	Uncommon	Tachycardia, arrhythmias
Vascular disorders	Uncommon	Hypotension, orthostatic hypotension
Respiratory, thoracic, and mediastinal disorders	Uncommon	Dyspnea
	Rare	Respiratory distress (including pneumonitis and pulmonary edema)
Gastrointestinal disorders	Uncommon	Diarrhea, dry mouth, flatulence
	Rare	Abdominal pain, constipation, dyspepsia, vomiting, gastritis
Hepatobiliary disorders	Rare	Abnormal hepatic function/liver disorder[2]
Skin and subcutaneous tissue disorders	Rare	Angioedema (also with fatal outcome), erythema, pruritus, rash, hyperhidrosis, urticaria
Musculoskeletal and connective tissue disorders	Uncommon	Back pain, muscle spasms, myalgia
	Rare	Arthralgia, muscle cramps, pain in limb
Reproductive system and breast disorders	Uncommon	Erectile dysfunction
General disorders and administration site conditions	Uncommon	Chest pain
	Rare	Influenza-like illness, pain
Investigations	Uncommon	Blood uric acid increased
	Rare	Blood creatinine increased, blood creatine phosphokinase increased, hepatic enzyme increased

[1]: Based on postmarketing experience.
[2]: For further description, please see subsection *Description of selected adverse reactions.*

Additional information on individual components

Adverse reactions previously reported with one of the individual components may be potential adverse reactions with telmisartan/hydrochlorothiazide, even if not observed in clinical trials with telmisartan/hydrochlorothiazide.

Telmisartan
Adverse reactions occurred with similar frequency in placebo and telmisartan-treated patients.

The overall incidence of adverse reactions reported with telmisartan (41.4%) was usually comparable to placebo (43.9%) in placebo-controlled trials. The following adverse reactions listed below have been accumulated from all clinical trials in patients treated with telmisartan for hypertension or in patients 50 years or older at high risk of cardiovascular events.

System organ class	**Frequency**	**Adverse reactions**
Infections and infestations	Uncommon	Upper respiratory tract infection, urinary tract infection including cystitis
	Rare	Sepsis including fatal outcome[3]
Blood and lymphatic system disorders	Uncommon	Anemia
	Rare	Eosinophilia, thrombocytopenia
Immune system disorders	Rare	Hypersensitivity, anaphylactic reactions
Metabolism and nutrition disorders	Uncommon	Hyperkalemia
	Rare	Hypoglycemia (in diabetic patients)
Cardiac disorders	Uncommon	Bradycardia
Nervous system disorders	Rare	Somnolence
Respiratory, thoracic, and mediastinal disorders	Uncommon	Cough
	Very rare	Interstitial lung disease[3]
Gastrointestinal disorders	Rare	Stomach discomfort
Skin and subcutaneous tissue disorders	Rare	Eczema, drug eruption, toxic skin eruption
Musculoskeletal and connective tissue, and bone disorders	Rare	Arthrosis, tendon pain
Renal and urinary disorders	Uncommon	Renal impairment (including acute renal failure)
General disorders and administration site conditions	Uncommon	Asthenia
Investigations	Rare	Hemoglobin decreased

[3]For further description, please see subsection *Description of selected adverse reactions.*

Hydrochlorothiazide
Hydrochlorothiazide may cause or exacerbate hypovolemia which could lead to electrolyte imbalance

Adverse reactions of unknown frequency reported with the use of hydrochlorothiazide alone include:

System organ class	**Frequency**	**Adverse reactions**

Infections and infestations	Not known	Sialadenitis
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	Not known	Nonmelanoma skin cancer (basal cell carcinoma and squamous cell carcinoma)
Blood and lymphatic system disorders	Rare	Thrombocytopenia (sometimes with purpura)
	Not known	Aplastic anemia, hemolytic anemia, bone marrow failure, leukopenia, neutropenia, agranulocytosis
Immune system disorders	Not known	Anaphylactic reactions, hypersensitivity
Endocrine disorders	Not known	Diabetes mellitus inadequate control
Metabolism and nutrition disorders	Common	Hypomagnesaemia
	Rare	Hypercalcaemia
	Very rare	Hypochloraemic alkalosis
	Not known	Anorexia, appetite decreased, electrolyte imbalance, hypercholesterolemia, hyperglycemia, hypovolemia
Psychiatric disorders	Not known	Restlessness
Nervous system disorders	Rare	Headache
	Not known	Light-headedness
Respiratory, thoracic, and mediastinal disorders	Not known	**Acute respiratory distress syndrome (ARDS)**
Eye disorders	Not known	Xanthopsia, **acute myopia, acute angle-closure glaucoma, choroidal effusion**
Vascular disorders	Not known	Vasculitis necrotizing
Gastrointestinal disorders	Common	Nausea
	Not known	Pancreatitis, stomach discomfort
Hepatobiliary disorders	Not known	Jaundice hepatocellular, jaundice cholestatic
Skin and subcutaneous tissue disorders	Not known	Lupus-like syndrome, photosensitivity reactions, skin vasculitis, toxic epidermal necrolysis, erythema multiforme
Musculoskeletal, connective tissue, and bone disorders	Not known	Weakness
Renal and urinary disorders	Not known	Nephritis interstitial, renal dysfunction, glycosuria
General disorders and administration site conditions	Not known	Pyrexia
Investigations	Not known	Triglycerides increase

Description of selected adverse reactions

Hepatic function abnormal / liver disorder

Most cases of hepatic function abnormal / liver disorder from postmarketing experience with telmisartan occurred in Japanese patients. Japanese patients are more likely to experience these adverse reactions.

Sepsis
In the PRoFESS trial, an increased incidence of sepsis was observed with telmisartan compared with placebo. The event may be a chance finding or related to a mechanism currently not known.

Interstitial lung disease
Cases of interstitial lung disease have been reported from postmarketing experience in temporal association with the intake of telmisartan. However, a causal relationship has not been established.

Nonmelanoma skin cancer
Based on available data from epidemiological studies, cumulative dose-dependent association between HCTZ and NMSC has been observed.

Post Marketing

Adverse reactions with Telmisartan

Skin and subcutaneous tissue disorders	
Not known	Psoriasis and Psoriasis exacerbation

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