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

TELSITE® H
Telmisartan & Hydrochlorothiazide Tablets IP

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
Dosing Information
Initiate a patient whose blood pressure is not adequately controlled with telmisartan monotherapy 80 mg on Telsite H, 80 mg/12.5 mg once daily. Dose can be titrated up to 160 mg/25 mg after 2 to 4 weeks, if necessary.
Initiate a patient whose blood pressure is not adequately controlled by 25 mg once daily of hydrochlorothiazide, or is controlled but who experiences hypokalemia with this regimen on Telsite H 80 mg /12.5 mg once daily. Dose can be titrated up to 160 mg/25 mg after 2 to 4 weeks, if necessary.
Patients titrated to the individual components (telmisartan and hydrochlorothiazide) may instead receive the corresponding dose of Telsite H.

Telsite H may be administered with some other antihypertensive agents.

Dose Adjustment for Hepatic Impairment
Initiate patients with biliary obstructive disorders or hepatic insufficiency under close medical supervision using the 40 mg/12.5 mg combination. Telsite H tablets are not recommended for patients with severe hepatic impairment (*see Use in Specific Populations)*

CONTRAINDICATIONS
Telsite H tablets are contraindicated
- in patients with known hypersensitivity to any component of this product (see **Warnings and Precautions**).
- In patients with anuria
- For co-administration with aliskiren in patients with diabetes (*see Drug Interactions)*

WARNINGS AND PRECAUTIONS
Fetal Toxicity
Telmisartan
Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy

reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue Telsite H as soon as possible.

Hydrochlorothiazide
Thiazides cross the placental barrier and appear in cord blood. Adverse reactions include fetal or neonatal jaundice, thrombocytopenia (See Use in Specific Populations).

Hypotension in Volume-Depleted Patients
In patients with an activated renin-angiotensin system, such as volume- or salt-depleted patients (e.g., those being treated with high doses of diuretics), symptomatic hypotension may occur after initialization of treatment with Telsite H. Correct volume or salt depletion prior to administration of Telsite H.

Impaired Renal Function
Changes in renal function including acute renal failure can be caused by drugs that inhibit the renin-angiotensin system and by diuretics. Patients whose renal function may depend in part on the activity of the renin-angiotensin system (e.g., patients with renal artery stenosis, chronic kidney disease, severe congestive heart failure, or volume depletion) may be at particular risk of developing oliguria, progressive azotemia, or acute renal failure on Telsite H. Monitor renal function periodically in these patients. Consider withholding or discontinuing therapy in patients who develop a clinically significant decrease in renal function on Telsite H.

Electrolytes and Metabolic Disorders
Drugs, including telmisartan, that inhibit the renin-angiotensin system can cause hyperkalemia, particularly in patients with renal insufficiency, diabetes, or combination use with other angiotensin receptor blockers or ACE inhibitors and the concomitant use of other drugs that raise serum potassium levels [see Drug Interactions].

Hydrochlorothiazide can cause hypokalemia and hyponatremia. Thiazides have been shown to increase the urinary excretion of magnesium; this may result in hypomagnesemia. Hypomagnesemia can result in hypokalemia which may be difficult to treat despite potassium repletion. Monitor serum electrolytes periodically.

Hydrochlorothiazide decreases urinary calcium excretion and may cause elevations of serum calcium.

Hydrochlorothiazide may alter glucose tolerance and raise serum levels of cholesterol and triglycerides.

Hyperuricemia may occur or frank gout may be precipitated in certain patients receiving thiazide therapy. Because telmisartan decreases uric acid, telmisartan in combination with hydrochlorothiazide attenuates the diuretic-induced hyperuricemia.

Hypersensitivity Reaction
Hydrochlorothiazide
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 (See Contraindications).

Acute Myopia and Secondary Angle-Closure Glaucoma

Hydrochlorothiazide, a sulfonamide, can cause an idiosyncratic reaction, resulting in acute transient myopia, choroidal effusion 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.

Systemic Lupus Erythematosus
Thiazide diuretics have been reported to cause exacerbation or activation of systemic lupus erythematosus.

Postsympathectomy Patients
The antihypertensive effects of hydrochlorothiazide may be enhanced in the postsympathectomy patient.

DRUG INTERACTIONS
Agents Increasing Serum Potassium
Co-administration of telmisartan with other drugs that raise serum potassium levels may result in hyperkalemia. Monitor serum potassium in such patients.

Lithium
Increases in serum lithium concentrations and lithium toxicity have been reported with concomitant use of thiazide diuretics or angiotensin II receptor antagonists, including telmisartan. Monitor lithium levels in patients receiving Telsite H and lithium.

Non-Steroidal Anti-Inflammatory Agents including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors):
Telmisartan
Non-Steroidal Anti-Inflammatory Agents including Selective Cyclooxygenase-2 Inhibitors (COX-2 Inhibitors): In patients who are elderly, volume-depleted (including those on diuretic therapy), or with compromised renal function, co-administration of NSAIDs, including selective COX-2 inhibitors, with ARBs, including telmisartan, may result in deterioration of renal function, including possible acute renal failure. These effects are usually reversible. The antihypertensive effect of ARBs may be attenuated by NSAIDs. Therefore, monitor renal function periodically in patients receiving Telsite H and NSAIDs.

Hydrochlorothiazide
Administration of a non-steroidal anti-inflammatory agent, including a selective COX-2 inhibitor, can reduce the diuretic, natriuretic, and antihypertensive effects of diuretics. Therefore, when Telsite H and nonsteroidal anti-inflammatory agents including selective COX-2 inhibitors are used concomitantly, observe closely to determine if the desired effect of the diuretic is obtained.

Dual Blockade of the Renin-Angiotensin-Aldosterone System and Changes in Renal Function
Dual blockade of the renin-angiotensin-aldosterone system (RAS) with angiotensin blockers, ACE inhibitors, or aliskiren is associated with increased risks of hypotension, hyperkalemia, and renal impairment.

In general, avoid combined use of RAS inhibitors. Closely monitor blood pressure, renal function and electrolytes in patients on Telsite H and other agents that affect the RAS.
Do not co-administer aliskiren with Telsite H in patients with diabetes. Avoid concomitant use of aliskiren with Telsite H in patients with renal impairment (GFR <60 mL/min/1.73 m^2).

Digoxin:

When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. Monitor digoxin levels in patients taking concomitant Telsite H and digoxin.

Antidiabetic drugs (oral agents and insulin)
Dosage adjustment of the antidiabetic drug may be required when co-administered with hydrochlorothiazide.

Cholestyramine and Colestipol resins
Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Stagger the dosage of hydrochlorothiazide and the resin such that hydrochlorothiazide is administered at least 4 hours before or 4 to 6 hours after the administration of the resin.

USE IN SPECIFIC POPULATIONS

Pregnancy
Telsite H can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. When pregnancy is detected, discontinue Telsite H as soon as possible.

Telmisartan
Use of drugs that act on the RAS in the second and third trimesters of pregnancy can result in the following: oligohydramnios, reduced fetal renal function leading to anuria and renal failure, fetal lung hypoplasia, skeletal deformations, including skull hypoplasia, hypotension, and death. In the unusual case that there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system for a particular patient, apprise the mother of the potential risk to the fetus.

In patients taking Telsite H during pregnancy, perform serial ultrasound examinations to assess the intra-amniotic environment. Fetal testing may be appropriate, based on the week of gestation. If oligohydramnios is observed, discontinue Telsite H, unless it is considered lifesaving for the mother. 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 Telsite H for hypotension, oliguria, and hyperkalemia. If oliguria or hypotension occurs, support blood pressure and renal perfusion. Exchange transfusions or dialysis may be required as a means of reversing hypotension and replacing renal function.

Hydrochlorothiazide
Thiazides cross the placenta, and use of thiazides during pregnancy is associated with a risk of fetal or neonatal jaundice, thrombocytopenia, and possible other adverse reactions that have occurred in adults.

Lactation
Risk Summary
There is no information regarding the presence of Telsite H or telmisartan in human milk, the effects on the breastfed infant or the effects on milk production. Limited published studies report that hydrochlorothiazide is present in human milk. However, there is insufficient information to determine the effects of hydrochlorothiazide on the breastfed infant or the effects of hydrochlorothiazide on milk production. Telmisartan is present in the milk of lactating rats.

Because of the potential for serious adverse reactions in the breastfed infant including hypotension, hyperkalemia and renal impairment, advise a nursing woman not to breastfeed during treatment with Telsite H.

Pediatric Use
Safety and effectiveness of Telsite H in pediatric patients have not been established.

Neonates with a history of in utero exposure to Telsite H:
If oliguria or hypotension occurs, support blood pressure and renal perfusion. Exchange transfusions or dialysis may be required as means of reversing hypotension and/or substituting for disordered renal function.

Geriatric Use
In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal or cardiac function and of concomitant diseases or other drug therapy

Use in Patients with Hepatic Impairment
Patients with biliary obstructive disorders or hepatic insufficiency should initiate treatment under close medical supervision using the 40 mg/12.5 mg combination.

Telmisartan
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 and higher blood levels.

Hydrochlorothiazide
Minor alterations of fluid and electrolyte balance may precipitate hepatic coma in patients with impaired hepatic function or progressive liver disease.

Use in Patients with Renal Impairment
Safety and effectiveness of Telsite H in patients with severe renal impairment (CrCl ≤30 mL/min) have not been established. In patients with severe renal impairment, Telsite H tablets are not recommended. No dose adjustment is required in patients with mild (CrCl 60 to 90 mL/min) or moderate (CrCl 30 to 60 mL/min) renal impairment.

OVERDOSAGE
Telmisartan
Limited data are available with regard to overdosage in humans. The most likely manifestations 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. Telmisartan is not removed by hemodialysis.

Hydrochlorothiazide
The most common signs and symptoms observed in patients are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established. The oral LD50 of hydrochlorothiazide is greater than 10 g/kg in both mice and rats.

ADVERSE REACTIONS:

The most common adverse effects (≥2% of patients) were upper respiratory tract infection, dizziness, sinusitis, diarrhea, fatigue, influenza like symptoms and nausea

The following adverse reactions are discussed elsewhere in labeling:

- Hypotension *(see Warnings and Precautions)*
- Renal Impairment *(see Warnings and Precautions)*
- Electrolytes and Metabolic Disorders(*see Warnings and Precautions)*

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Updated: December 2021

Source:

- Micardis HCT leaflet (Boehringer Ingelheim Pharmaceuticals) dated August 2020 (accessed on 20th December 2020)
- For Hydrochlorothiazide : Source: CCDS Version18 dated 24 September 2020