# Telsarta-D®

(Telmisartan+Hydrochlorothiazide Tablets)

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**COMPOSITION**

**Telsarta-D 40/12.5 mg Tablet**
Each tablet contains:
Telmisartan USP…….. 40 mg
Hydrochlorothiazide USP…… 12.5 mg

**Telsarta D 80/12.5 mg Tablet**
Each tablet contains:
Telmisartan USP..... 80 mg
Hydrochlorothiazide USP..... 12.5 mg
(USP Specs.)

**WARNING: PREGNANCY AND FETAL TOXICITY**
Drugs that act directly on the renin-angiotensin system such as Telmisartan can cause injury and death to the developing fetus when taken during pregnancy. When pregnancy is detected, Telmisartan containing products such as Telsarta-D should be discontinued as soon as possible.

**DESCRIPTION**
TELSARTA-D tablet is a combination product containing Telmisartan, an angiotensin II receptor blocker and hydrochlorothiazide, a thiazide diuretic. The combination is used as an antihypertensive.

Telmisartan, a non-peptide molecule, is chemically described as 4'-[(1,4'-dimethyl-2'-propyl[2,6'-bi-1Hbenzimidaz-ol]-1'-yl)methyl]-[1,1'-biphenyl]-2-carboxylic acid. Its empirical formula is $C_{33}H_{30}N_4O_2$ Hydrochlorothiazide is chemically described as 6-chloro-3,4-dihydro-2H-1,2,4-benzothiadiazine-7-sulfonamide 1,1-dioxide.
Its empirical formula is $C_7H_8ClN_3O_4S_2$

**CLINICAL PHARMACOLOGY**

**Mechanism of Action**
The combination product has synergistic effects on the overall reduction of blood pressure via the following ways:
Telmisartan
Angiotensin II is formed from angiotensin I in a reaction catalyzed by angiotensin-converting enzyme (ACE, kininase II). Angiotensin II is the principal pressor agent of the renin-angiotensin system, 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.
Telmisartan displaces angiotensin II with very high affinity from its binding site at the AT1 receptor subtype, which is responsible for the known actions of angiotensin II. Telmisartan does not exhibit any partial agonist activity at the AT1 receptor. Telmisartan selectively binds the AT1 receptor. The binding is long-lasting. Telmisartan does not show affinity for other receptors, including AT2 and other less characterized AT receptors.
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 such as cough.
Hydrochlorothiazide
Hydrochlorothiazide is a thiazide diuretic. Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium and chloride in approximately equivalent amounts.
The site of action of thiazide diuretics is primarily in the renal distal convoluted tubule. It has been shown that there is a high-affinity receptor in the renal cortex as the primary binding site for the thiazide diuretic action and inhibition of NaCl transport in the distal convoluted tubule. The mode of action of thiazides is through inhibition of the Na+Cl- symporter perhaps by competing for the Cl-site, thereby affecting electrolyte reabsorption mechanisms: directly increasing sodium and chloride excretion to an approximately equal extent, and indirectly by this diuretic action reducing plasma volume, with consequent increases in plasma renin activity, aldosterone secretion and urinary potassium loss, and a decrease 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.
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**Pharmacokinetics**

Telmisartan

***Absorption***
Absorption of Telmisartan is rapid although the amount absorbed varies. The mean absolute bioavailability for telmisartan is about 50 %. When telmisartan is taken with food, the reduction in the area under the plasma concentration-time curve (AUC0-∞) of telmisartan varies from approximately 6 % (40 mg dose) to approximately 19 % (160 mg dose). By 3 hours after administration, plasma concentrations are similar whether telmisartan is taken fasting or with food.
The small reduction in AUC is not expected to cause a reduction in the therapeutic efficacy. There is no linear relationship between doses and plasma levels. Cmax and to a lesser extent AUC, increase disproportionately at doses above 40 mg.

***Distribution***
Telmisartan is largely bound to plasma protein (>99.5 %), mainly albumin and alpha-1 acid glycoprotein. The mean steady state apparent volume of distribution (Vdss) is approximately 500 L.

***Metabolism***
Telmisartan is metabolized by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown for the conjugate.

***Elimination***
Telmisartan is characterized by bi-exponential decay pharmacokinetics with a terminal elimination half-life of >20 hours. The maximum plasma concentration (Cmax) and to a smaller extent the area under the plasma concentration-time curve (AUC), increase disproportionately with dose. There is no evidence of clinically relevant accumulation of telmisartan taken at the recommended dose. Plasma concentrations were higher in females than in males, without relevant influence on efficacy.
After oral (and intravenous) administration, Telmisartan is nearly exclusively excreted with the feces, mainly as unchanged compound. Cumulative urinary excretion is <1 % of dose. Total plasma clearance (Cltot) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).

Hydrochlorothiazide

***Absorption***
The absorption of hydrochlorothiazide, after an oral dose, is rapid (tmax about 2 h). The increase in mean AUC is linear and dose proportional in the therapeutic range.
The effect of food on hydrochlorothiazide absorption, if any, has little clinical significance. Absolute bioavailability of hydrochlorothiazide is 70% after oral administration.

***Distribution***
The apparent volume of distribution is 4–8 L/kg.
Circulating hydrochlorothiazide is bound to serum proteins (40–70%), mainly serum albumin. Hydrochlorothiazide also accumulates in erythrocytes at approximately 3 times the level in plasma.

***Metabolism***
Hydrochlorothiazide is not metabolized.

***Elimination***
Hydrochlorothiazide is eliminated predominantly as unchanged drug. Hydrochlorothiazide is eliminated from plasma with a half-life averaging 6 to 15 hours in the terminal elimination phase. There is no change in the kinetics of hydrochlorothiazide on repeated dosing, and accumulation is minimal when dosed once daily. There is more than 95% of the absorbed dose being excreted as unchanged compound in the urine. The renal clearance is composed of passive filtration and active secretion into the renal tubule.

**Pharmacokinetics in special populations**

**Telmisartan and Hydrochlorothiazide**

**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 - 60 ml/min, mean about 50 ml/min) no dosage adjustment is necessary in patients with decreased renal function.

Telmisartan is highly bound to plasma protein in renallly compromised patients and cannot be removed by dialysis. The elimination half-life is not changed in patients with renal impairment. In the presence of renal impairment, mean peak plasma levels and AUC values of hydrochlorothiazide are increased and the urinary excretion rate is reduced. In patients with mild to moderate renal impairment, a 3-fold increase in hydrochlorothiazide AUC has been observed. In patients with severe renal impairment an 8-fold increase in AUC has been observed. Hydrochlorothiazide is contraindicated in patients with severe renal impairment.

Clearance of hydrochlorothiazide can be achieved by dialysis.

**Hepatic Impairment**
Pharmacokinetic studies in patients with hepatic impairment showed an increase in absolute bioavailability of Telmisartan up to nearly 100 %. The elimination half-life is not changed in patients with hepatic impairment.

Hepatic disease does not significantly affect the pharmacokinetics of hydrochlorothiazide

**Elderly**
The pharmacokinetics of Telmisartan does not differ between the older people and those younger than 65 years.
Limited data suggest that the systemic clearance of hydrochlorothiazide is reduced in both healthy and hypertensive elderly subjects compared to young healthy volunteers.

**Gender**
Differences in plasma concentrations of Telmisartan were observed, with Cmax and AUC being approximately 3 and 2-fold higher, respectively, in females compared to males. No dosage adjustment is necessary.

There was a trend towards higher plasma concentrations of hydrochlorothiazide in female than in male subjects. This is not considered to be of clinical relevance.

**INDICATIONS**

• Telsarta- D is indicated to treat hypertension in adults whose blood pressure is not adequately controlled on telmisartan alone. Telsarta-D may be used alone or in combination with other antihypertensive agents.

**DOSAGE AND ADMINISTRATION**

Telsarta-D 40 mg/12.5 mg tablet may be administered once daily in patients whose blood pressure is not adequately controlled by Telmisartan 40 mg. Dose may be titrated up to 80 mg of temisartan and 25 mg of HCT after 2-4 weeks, if necessary. Telsarta-D 80/12.5 mg tablet may be administered once daily in patients whose blood pressure is not adequately controlled by Telmisartan 80 mg

**Dosing Considerations in Special Populations:**

**Renal impairment**
Periodic monitoring of renal function is advised in patients receiving Telsarta-D. In severe renal impairment and anuria Telsarta-D tablets must not be used due to the hydrochlorothiazide component.

**Hepatic impairment**
In patients with mild to moderate hepatic impairment the dosage should not exceed Telsarta-D 40 mg/12.5 mg once daily. Telsarta-D tablets are not recommended for patients with severe hepatic impairment, cholestasis and biliary obstructive disorders

**Administration requirements**
TELSARTA-D tablets are for once-daily oral administration and should be taken with liquid, with or without food.

**CONTRAINDICATIONS**

• Patients with known hypersensitivity to Telmisartan or Hydrochlorothiazide or other sulphonamide-derived substances since hydrochlorothiazide is a sulphonamide-related drug.
• Concomitant use of Telmisartan containing products including Telsarta-D is contraindicated with Aliskiren in patients with diabetes and renal impairment (CrCl < 60 ml/min)
• Severe renal impairment (CrCl < 30 ml/min) and anuria (due to hydrochlorothiazide component).
• Severe hepatic impairment, cholestasis and biliary obstructive disorders
• Second and third trimesters of pregnancy
• Refractory hypokalaemia, hypercalcaemia.

**WARNINGS AND PRECAUTIONS**

**Pregnancy and Fetal toxicity**
Telmisartan containing products such as Telsarta-D should not be initiated during pregnancy. Its use in 2nd and 3rd trimesters of pregnancy is contraindicated and also not recommended during the 1st trimester. Unless continued 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 detected, treatment with Telsarta-D should be stopped immediately.

Hydrochlorothiazide containing products such as Telsarta-D should not be used for essential hypertension in pregnant women except in rare situations where no other treatment could be used.

Refer to USE IN SPECIAL POPULATIONS for details.

**Hypotension**
In patients with an activated renin-angiotensin system, such as volume- and/or salt-depleted patients receiving high doses of diuretics, intravascular hypovolemia and symptomatic hypotension may occur. This condition should be corrected prior to administration of Telmisartan/hydrochlorothiazide, or the treatment should start under close medical supervision.

If hypotension occurs, the patient 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.

**Impaired renal function**
Changes in renal function including acute renal failure can be caused by drugs that inhibit the renin-angiotensin system. 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 acute renal failure on Telmisartan containing products such as Telsarta-D. Renal function should be monitored periodically in these patients including creatinine, potassium and uric acid levels. Thiazide diuretic-associated azotaemia may occur in patients with impaired renal function.

Consider withholding or discontinuing therapy in patients who develop a clinically significant decrease in renal function on Telsarta-D.
Periodic monitoring of renal function is advised in patients receiving Telsarta-D with mild to moderate renal impairment. In severe renal impairment and anuria Telsarta-D tablets must not be used due to the hydrochlorothiazide component.

**Hyperkalemia**
Due to the antagonism of the angiotensin II (AT1) receptors by the telmisartan component of Telsarta-D, hyperkalaemia might occur. Although clinically significant hyperkalaemia has not been documented with Telmisartan and HCT, risk factors for the development of hyperkalaemia include renal insufficiency and/or heart failure, and diabetes mellitus.
Other risk facors include advanced age, dehydration, acute cardiac decompensation, metabolic acidosis, severe infectious diseases, cellular lysis (e.g. acute limb ischemia, rhabdomyolysis, extend trauma).
Hyperkalemia may also occur via concomitant use of Telsarta-D with potassium supplements, potassium-sparing diuretics, salt substitutes containing potassium, or other agents that may increase potassium levels (e.g. heparin, NSAIDs, selective COX-2 inhibitors, immunosuppressant drugs: cyclosporin or tacrolimus, trimethoprim etc.). Concomitant use should be avoided.

Monitoring of potassium should be undertaken as appropriate.

**Hepatic Impairment**
Use of Telmisartan containing products such as Telsarta-D is contraindicated in severe hepatic impairment, biliary cirrhosis and cholestasis. No dose adjustment is necessary for patients with mild-to-moderate liver disease however dose should not exceed 40 mg/12.5 mg once daily.
Due to its hydrochlorothiazide component, use of Telsarta-D can cause minor alterations of fluid and electrolyte balance which may precipitate hepatic coma in patients with impaired hepatic function or progressive liver disease.

**Metabolic disorders**
Hydrochlorothiazide may alter glucose tolerance and raise serum levels of cholesterol and triglycerides. However, at the 12.5 mg dose contained in Telsarta-D, minimal or no effects were reported on cholesterol and triglycerides.
Telmisartan containing products such as Telsarta-D may cause hypoglycemia when used with insulin or other oral anti-diabetic agents. Blood monitoring of glucose may become essential in such patients and the dose adjustment of concomitant insulin or antidiabetic drug may be required

**Other electrolyte imbalances**
Hydrochlorothiazide in Telsarta-D can cause hypokalemia, hyponatremia and hypochloraemic alkalosis. Thiazides have been shown to increase the urinary excretion of magnesium; this may also result in hypomagnesemia. Hypomagnesemia can result in hypokalemia which may be difficult to treat despite potassium repletion. Monitor serum electrolytes periodically.
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.
*Hypokalaemia:* Although hypokalaemia may develop with the use of thiazide diuretics, concurrent therapy with telmisartan may reduce diuretic-induced hypokalaemia. The risk of hypokalaemia 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)
*Hyponatraemia and hypochloraemic alkalosis:* Hyponatremia may occur with Telsarta-D. Chloride deficit is generally mild and usually does not require treatment.
*Hypercalcaemia:* Thiazides including HCT in Telsarta-D 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 hypercalcaemia may be evidence of hidden hyperparathyroidism. Thiazides should be discontinued before carrying out tests for parathyroid function.
*Hypomagnesaemia:* Thiazides including HCT have been shown to increase the urinary excretion of magnesium, which may result in hypomagnesaemia.

**Hypersensitivity reactions**
Hypersensitivity reactions to hydrochlorothiazide in Telsarta-D may occur in patients with or without a history of allergy or bronchial asthma, but are more likely in patients with such a history. Such reactions are also anticipated in patients allergic to sulfonamide-type drugs.

**Acute Myopia and Secondary Angle-Closure Glaucoma**
Hydrochlorothiazide in Telsarta-D, 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 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.

**Systemic Lupus Erythematosus**
Thiazide diuretics such as HCT in Telsarta-D have been reported to cause exacerbation or activation of systemic lupus erythematosus.

**Post-sympathectomy Patients**
The antihypertensive effects of hydrochlorothiazide may be enhanced in the post-sympathectomy patients.

**Gout and hyperuricemia**
Hydrochlorothiazide may raise the serum uric acid level due to reduced clearance of uric acid and may cause or exacerbate hyper-uricemia and precipitate gout in susceptible patients. Dosage adjustment of uricosuric medications such as probenecid or sulfinpyrazone may be necessary. Because Telmisartan decreases uric acid, telmisartan in combination with hydrochlorothiazide attenuates the diuretic-induced hyperuricemia.

**Photosensitivity**
Cases of photosensitivity reactions have been reported with thiazides diuretics including HCT. If photosensitivity reaction occurs during treatment with Telsarta-D, it is recommended to stop the treatment. If a re-administration of the diuretic is deemed necessary, it is recommended to protect exposed areas of the body to the sun or to artificial UV light.

**Renal artery stenosis**
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 drugs that affect the renin-angiotensin-aldosterone system such as Telsarta-D. Blood urea and serum creatinine may increase in such patients. Use is not recommended.

**Kidney transplantation**
There is currently no experience on the safe use of Telmisartan/HCT in patients who have recently undergone kidney transplantation.

**Primary hyperaldosteronism**
Patients with primary hyperaldosteronism should not be treated with Telmisartan containing products such as Telsarta-D as their renin-angiotensin system is not activated. These patients will generally not respond to therapy with Telsarta-D.

**Aortic and mitral valve stenosis, obstructive hypertrophic cardiomyopathy**
As with all other vasodilators, special caution is indicated with use of Telmisartan containing products such as Telsarta-D in patients suffering from aortic or mitral stenosis, or hypertrophic obstructive cardiomyopathy (HOCM) due to the potential vaso-dilatory effect.

**Dual Blockade of the Renin-Angiotensin-Aldosterone System (RAAS)**
Dual blockade of the Renin-Angiotensin-Aldosterone System (RAAS) via concomitant use of ACE-inhibitors or Aliskiren in patients being treated with angiotensin II receptor blockers (such as Telmisartan), increases the risk of hypotension, hyperkalemia, syncope, stroke and decreased renal function (including acute renal failure). Use of Telmisartan containing products such as Telsarta-D is not recommended with Aliskiren or ACE inhibitors.

Concomitant use of Telmisartan containing products with Aliskiren is contraindicated in diabetes mellitus and in patients with renal impairment with creatinine clearance < 60 ml/min.
Concomitant use of Telmisartan containing products is generally not recommended with ACE inhibitors especially in patients with diabetic nephropathy.
If dual blockade therapy is considered absolutely necessary, this should only occur under specialist supervision with close monitoring of renal function, electrolytes and blood pressure.

**Effects on ability to drive and use machines**
No studies on the effects on the ability to drive have been performed. When driving vehicles or operating machines it should be taken into account that occasionally dizziness or drowsiness may occur when taking anti-hypertensive therapy such as Telsarta-D.

## ADVERSE REACTIONS

Adverse reactions reported with the combination of Telmisartan and hydrochlorothiazide are listed below:

**Infections and infestations**
*Rare*: Bronchitis, pharyngitis, sinusitis

**Immune system disorders**
*Rare*: Exacerbation or activation of systemic lupus erythematosus

**Metabolism and nutrition disorders**
*Uncommon*: Hypokalaemia
*Rare*: Hyperuricaemia, hyponatraemia

**Psychiatric disorders**
*Uncommon*: Anxiety
*Rare*: Depression

**Nervous system disorders**
*Common*: Dizziness
*Uncommon*: Syncope, paraesthesia
*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*: Dyspnoea
*Rare*: Respiratory distress (including pneumonitis and pulmonary edema)

**Gastrointestinal disorders**
*Uncommon*: Diarrhoea, dry mouth, flatulence
*Rare*: Abdominal pain, constipation, dyspepsia, vomiting, gastritis

**Hepatobiliary disorders**
*Rare*: Abnormal hepatic function/liver disorder

**Skin and subcutaneous tissue disorders**
*Rare*: Angioedema (also with fatal outcome), erythema, pruritus, rash, hyperhidrosis, urticaria

**Muscoloskeletal, connective tissue and bone 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

Adverse reactions known to occur with each component telmisartan or hydrochlorothiazide given singly may occur during treatment with Telsarta-D. The prescribing information for the respective drugs should be consulted for details.

## DRUG INTERACTIONS

*Aliskiren and ACE inhibitors*
Dual blockade of the Renin-Angiotensin-Aldosterone System (RAAS) via concomitant use of ACE-inhibitors or Aliskiren in patients being treated with angiotensin II receptor blockers (such as Telmisartan), increases the risk of hypotension, hyperkalemia, syncope, stroke and decreased renal function (including acute renal failure). Concomitant use of Telmisartan containing products such as Telsarta-D and Aliskiren is not recommended.
Concomitant use of Telmisartan containing products with Aliskiren is contraindicated in diabetes mellitus and in patients with renal impairment with creatinine clearance < 60 ml/min.

Concomitant use of Telmisartan products such as Telsarta-D is not recommended with ACE inhibitors due to additive effects on Renin-Angiotensin-Aldosterone System blockade.

In one study the co-administration of telmisartan and ramipril (an ACE inhibitor) led to an increase of up to 2.5 fold in the AUC 0-24 and Cmax of ramipril and ramiprilat.

*Lithium*
Increases in serum lithium concentrations and lithium toxicity have been reported during concomitant administration of Lithium with angiotensin II receptor antagonists. Monitor lithium levels in patients taking Telsarta-D.

*Drugs raising serum potassium*
Angiotensin II receptor antagonists such as Telmisartan in Telsarta-D reduce diuretic induced potassium loss. Potassium sparing diuretics e.g. spironolactone, eplerenone, triamterene, or amiloride, potassium supplements, potassium-containing salt substitutes may lead to a significant increase in serum potassium when used in conjunction with Telsarta-D. Other agents that may increase potassium levels include heparin, NSAIDs, selective COX-2 inhibitors, immunosuppressant drugs: cyclosporin or tacrolimus, trimethoprim etc. If concomitant use of these drugs with Telsarta-D is indicated because of documented hypokalemia, they should be used with caution and with frequent monitoring of serum potassium.

*Drugs decreasing serum potassium*
Drugs such as kaliuretic diuretics, laxatives, corticosteroids, ACTH, amphotericin, carbenoxolone, penicillin G sodium, salicylic acid and derivatives may be associated with potassium loss and induce hypokalemia on their own. If prescribed with Telmisartan-hydrochlorothiazide combination these drugs may potentiate the hypokalemic effect of hydrochlorothiazide. Monitoring of serum potassium is advised.

*Other drugs affecting serum potassium and inducing torsades de pointes*
Periodic monitoring of serum potassium and ECG is recommended when Telsarta-D is administered with drugs causing serum potassium disturbances (e.g. digitalis glycosides, antiarrhythmics) and may induce torsades de pointes, hypokalaemia being a predisposing factor to torsades de pointes. These drugs are listed below:
Class Ia antiarrythmics (e.g. quinidine, hydroquinidine, disopyramide)
Class III antiarrythmics (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, diphemanil, erythromycin IV, halofantrine, mizolastin, pentamidine, sparfloxacin, terfenadine, vincamine IV.)

*Drugs affecting serum sodium level*
The hyponatremic effect of diuretics such as hydrochlorothiazide may be intensified by concomitant administration of drugs such as antidepressants, antipsychotics, antiepileptics (mainly carbamazepine) etc. Caution is advised in long-term administration of these drugs with Telsarta-D.

*NSAIDs including selective COX-II inhibitors*
NSAIDs can attenuate the antihypertensive effect of angiotensin II antagonists including Telmisartan when administered simultaneously.

Furthermore, concomitant use of Telmisartan and NSAIDs may lead to worsening of renal function and an increase in serum potassium. Therefore, monitoring of renal function at the beginning of the treatment is recommended with Telsarta-D, as well as adequate hydration of the patient.

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

*Digoxin and digitalis glycosides*
When Telmisartan is co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) are expected. Monitor digoxin levels in patients taking Telsarta-D and digoxin concomitantly.

In addition, thiazide-induced hypokalaemia or hypomagnesaemia may also favour the onset of digoxin-induced arrhythmia. This may also occur with other digitalis glycosides.

*Antidiabetic agents*
Dosage adjustment of anti-diabetic drugs may be required when co-administered with hydrochlorothiazide products such as Telsarta-D

*Cholestyramine and colestipol resins*
Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Adjust 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.

*Metformin*
Metformin should be used with precaution with Telsarta-D: lactic acidosis may occur by a possible functional renal failure linked to hydrochlorothiazide.

*Pressor amines*
The effect of pressor amines such as noradrenaline be decreased with Telsarta-D

*Non-depolarizing skeletal muscle relaxants*
The effect of non-depolarizing skeletal muscle relaxants may be potentiated by hydrochlorothiazide in Telsarta-D.

*Allopurinol*
Co-administration of thiazide (hydrochlorothiazide) containing products such as Telsarta-D may increase the incidence of hypersensitivity reactions of allopurinol.

*Calcium supplements*
Thiazide diuretics may increase serum calcium levels due to the decreased excretion. If calcium supplements are prescribed concomitantly with Telsarta-D, serum calcium levels should be monitored and calcium dosage adjusted accordingly.

*B-blockers and Diazoxide*
The hyperglycaemic effect of beta-blockers and diazoxide may be enhanced by thiazides including hydrochlorothiazide in Telsarta-D

*Anticholinergic agents*
Anticholinergic agents (e.g. atropine, biperiden) may increase the bioavailability of hydrochlorothiazide by decreasing gastrointestinal motility and stomach emptying rate.

*Amantadine*
Hydrochlorthiazide containing products such as Telsarta-D may increase the risk of adverse effects caused by amantadine.

*Cytotoxic agents*
Thiazides (hydrochlorothiazide) containing products such as Telsarta-D may reduce the renal excretion of cytotoxic medicinal products such as cyclolophosphamide, methotrexate and potentiate their myelosuppressive effects

*CNS drugs*
Orthostatic hypotension may be aggravated via the concomitant use of Telsarta-D with alcohol, barbiturates, narcotics or antidepressants.

*Corticosteroids*
Reduction of anti-hypertensive effect of Telmisartan has been observed when used with corticosteroids.

*Methyldopa*
There have been isolated reports of hemolytic anemia in patients receiving concomitant treatment with methyldopa and hydrochlorothiazide.

*Iodine contrast media*
In case of diuretic-induced dehydration with hydrochlorothiazide, there may be an increased risk of acute renal failure, especially with high doses of the iodine contrast agents used in radiographic procedures. Patients on Telsarta-D therapy should be rehydrated before the administration of these agents.

## USE IN SPECIAL POPULATIONS

**Pregnancy**
Telmisartan/hydrochlorothiazide is declared as US FDA Pregnancy Category D drug. Use of drugs that act on the renin-angiotensin system including Angiotensin II receptor antagonists (AIIRAs) during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death.

Exposure to the fetus during pregnancy can be associated with oligohydramnios with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death.
Telmisartan containing products such as Telsarta-D should not be initiated during pregnancy. Its use in 2nd and 3rd trimesters of pregnancy is contraindicated and also not recommended during the 1st trimester. Unless continued 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 detected, treatment with Telsarta-D should be stopped immediately.
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 feto-placental perfusion and may cause fetal and neonatal effects like icterus, disturbance of electrolyte balance and thrombocytopenia.
Hydrochlorothiazide containing products such as Telsarta-D should not be used for essential hypertension in pregnant women except in rare situations where no other treatment could be used.
In the unusual case that there is no appropriate alternative to therapy with drugs affecting the renin-angiotensin system for a particular patient, the mother should be apprised of the potential risk to the fetus.

Perform serial ultrasound examinations to assess the intra-amniotic environment. If oligohydramnios is observed, discontinue Telmisartan containing products unless it is considered life saving for the mother.
Exposed infants whose mothers have taken AIIRAs should be closely observed.
Fetal testing may be appropriate. Ultrasound check of renal function and skull is recommended. If oliguria or hypotension occurs in neonates with a history of in utero exposure to Telmisartan, support of blood pressure and renal perfusion should be provided. Exchange transfusions or dialysis may be required as a means of reversing hypotension and/or substituting for disordered renal function.

**Nursing mothers**
It is not known whether telmisartan is excreted in human milk, but telmisartan was shown to be present in the milk of lactating rats. Thiazides appear in human milk. Because of the potential for adverse effects on the nursing infant, decide whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

**Elderly**
No overall differences in effectiveness and safety of Telmisartan/hydrochlorothiazide were observed in elderly patients compared to younger patients. Other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out. 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.

**Renal impairment**
Safety and effectiveness of Telmisartan/hydrochlorothiazide in patients with severe renal impairment (CrCl ≤30 mL/min) have not been established. 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.

Telsarta-D is contraindicated in patients with severe renal impairment due to its HCT component.

**Hepatic impairment**
In patients with mild to moderate hepatic impairment the dosage should not exceed Telsarta-D 40 mg/12.5 mg once daily. Telsarta-D tablets are not recommended for patients with severe hepatic impairment, cholestasis and biliary obstructive disorders

Minor alterations of fluid and electrolyte balance may precipitate hepatic coma in patients with impaired hepatic function or progressive liver disease receiving Telsarta-D therapy, due to its HCT component.

## OVER DOSAGE

*Telmisartan*
Limited data are available with regard to overdosage of telmisartan in humans. The most likely manifestations of overdosage with telmisartan are hypotension, dizziness, and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. Increase in serum creatinine, and acute renal failure have also been reported. If symptomatic hypotension should occur, supportive treatment should be instituted; the patient should be placed in a supine position, with salt and volume replacements given quickly. Telmisartan is not removed by hemodialysis. Suggested measures also include induction of emesis and/or gastric lavage. Activated charcoal may be useful in the treatment of overdose.

*Hydrochlorothiazide*
The most common signs and symptoms observed in patients with a hydrochlorothiazide overdose are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. The most common signs and symptoms of overdose are nausea and somnolence. Hypokalemia may result in muscle spasms. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

## PRESENTATION
Telsarta-D 40/12.5 mg Tablet : Pack of 14 Tablets.
Telsarta-D 80/12.5 mg Tablet : Pack of 14 Tablets.

## INSTRUCTIONS
Use as advised by the physician.
Keep all medicines out of the reach of children.
To be sold on the prescription of a registered medical practitioner only.
Protect from light, heat and moisture.
Store below 30°C.
For suspected adverse drug reaction, email us at reports@pharmevo.biz

For more information on our products
call PharmAssist helpline 0800-82222
Monday to Friday 9:00 am to 6:00 pm
or email us at : pharmassist@pharmevo.biz

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