# Tasmi™

(Telmisartan)

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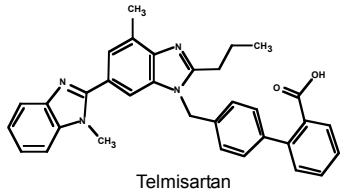
**20mg, 40mg & 80mg Tablets**

## DESCRIPTION

Tasmi (Telmisartan) is a non-peptide angiotensin II receptor (type $AT_1$) antagonist. It is chemically described as 4'-[(1, 4'-dimethyl-2'-propyl [2, 6'-bi-1H-benzimidazol]-1'-yl) methyl]-[1,1'-biphenyl]-2-carboxylic acid. Its molecular formula is $C_{33}H_{30}N_4O_2$ and the structural formula is:



Telmisartan

## QUANTITATIVE & QUALITATIVE COMPOSITION

TASMI (Telmisartan) Tablets are available for oral administration as:

1. TASMI Tablets 20mg
   Each tablet contains:
   Telmisartan USP… 20mg
2. TASMI Tablets 40mg
   Each tablet contains:
   Telmisartan USP… 40mg
3. TASMI Tablets 80mg
   Each tablet contains:
   Telmisartan USP… 80mg

## CLINICAL PHARMACOLOGY

**Mechanism of Action**

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 $AT_1$ 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 has much greater affinity (>3,000 fold) for the $AT_1$ receptor than for the $AT_2$ receptor. Blockade of renin-angiotensin system with ACE inhibitors, inhibits the biosynthesis of angiotensin II from angiotensin I and is widely used in the treatment of hypertension.

**Pharmacokinetics**

Telmisartan is rapidly absorbed from the gastrointestinal tract; the absolute oral bioavailability is dose-dependent and is about 42% following a 40mg dose and 58% following a 160mg dose. Peak plasma concentration of telmisartan is reached about 0.5 to 1 hour after an oral dose. Food slightly reduces the bioavailability of telmisartan, with a reduction in the area under the plasma concentration-time curve (AUC) of about 6% with the 40mg tablet and about 20% after a 160mg dose. Telmisartan is over 99% bound to plasma proteins, mainly albumin and $\alpha_1$-acid glycoprotein. The volume of distribution for telmisartan is approximately 500 liters indicating additional tissue binding. It is excreted almost entirely in the feces via bile, mainly as unchanged drug. The terminal elimination half-life of telmisartan is about 24 hours.

**Special Populations**

*Renal Impairment*

In mild to moderate and severe renally impaired patients doubling of plasma concentrations was observed. However, lower plasma concentrations were observed in patients with renal insufficiency undergoing dialysis. Telmisartan is highly bound to plasma protein in renal-insufficient subjects and cannot be removed by dialysis. The elimination half-life is not changed in patients with renal impairment.

*Hepatic Impairment*

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

## THERAPEUTIC INDICATIONS

TASMI (Telmisartan) Tablets are indicated for the treatment of essential hypertension. It may be used alone or in combination with other antihypertensive agents.

## DOSAGE AND ADMINISTRATION

Dosage of TASMI (Telmisartan) Tablets must be individualized; the usual starting dose of TASMI (Telmisartan) Tablets is 40mg once a day. Blood pressure response is dose related over the range of 20-80mg. TASMI (Telmisartan) Tablets may be taken with or without food.

***Adults***

The usual effective dose of TASMI (Telmisartan) Tablets is 40mg once daily. Some patients may already benefit at a daily dose of 20mg. In cases where the target blood pressure is not achieved, telmisartan dose can be increased to a maximum of 80mg once daily. When considering raising the dose, it must be borne in mind that the maximum antihypertensive effect is generally attained four-eight weeks after the start of treatment.

***Renal impaired patients***

No dose adjustment is required in patients with mild to moderate renal impairment. Limited experience is available in patients with severe renal impairment or hemodialysis. A lower starting dose of 20mg is recommended in these patients.

***Hepatic impaired patients***

In patients with mild to moderate hepatic impairment the dosage should not exceed 40mg once daily.

## ADVERSE REACTIONS

Adverse effects reported from telmisartan have generally been mild and transient in nature and have only infrequently required discontinuation of therapy. The incidence of adverse events were not dose related.

**Common:** Symptoms of infection (e.g., urinary tract infections including cystitis), upper respiratory tract infections including pharyngitis and sinusitis, abdominal pain, diarrhea, dyspepsia, eczema, arthralgia, back pain (e.g., sciatica), muscle spasms or pain in extremity, myalgia, chest pain and influenza-like illness.
**Uncommon:** Anxiety, visual disturbance, vertigo, dry mouth, flatulence, hyperhidrosis and tendonitis.
**Rare:** Stomach discomfort.

***Clinical Laboratory Findings:***

Infrequently, a hemoglobin decrease or a blood uric acid increase has been observed which occur more often during treatment with telmisartan than with placebo. Increase in creatinine or hepatic enzyme increase has been observed during treatment with telmisartan but these changes in laboratory findings occurred with a frequency similar to or lower than placebo.

In addition, cases with blood creatinine phosphokinase increase (CPK) have been reported.

*Liver Enzymes:* Occasional elevations of liver enzymes occurred in patients treated with telmisartan; all marked elevations occurred at a higher frequency with placebo. No telmisartan-treated patients discontinued therapy due to abnormal hepatic function.

**CONTRAINDICATIONS**

Telmisartan is contraindicated:

- In patients who are hypersensitive to telmisartan or any component of the product.
- During second and third trimesters of pregnancy and lactation.
- In patients with biliary obstructive disorders.
- In patients with severe hepatic impairment.
- In patients with severe renal impairment.
- In patients with hereditary fructose intolerance.

**WARNINGS**

**USE IN PREGNANCY**

When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, telmisartan should be discontinued as soon as possible.

**PRECAUTIONS**

- Symptomatic hypotension, especially after the first dose, may occur in patients who are volume or sodium depleted by vigorous diuretic therapy, dietary salt restriction and diarrhea or vomiting. Such conditions, especially volume or sodium depletion, should be corrected before administration of telmisartan.
- Patients on dialysis may develop orthostatic hypotension so their blood pressure should be closely monitored. The majority of telmisartan is eliminated in the bile. Patients with biliary obstructive disorders or severe hepatic insufficiency can be expected to have reduced clearance. Telmisartan should be used only with caution in these patients.
- 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.
- During treatment with medicinal products that affect the renin-angiotensin-aldosterone system hyperkalemia may occur, especially in the presence of renal impairment and/or heart failure. Monitoring of serum potassium in patients at risk is recommended.
- 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, hyperazotemia, oliguria or rarely acute renal failure.
- As with other vasodilators, special caution is indicated in patients suffering from aortic or mitral stenosis or obstructive hypertrophic cardiomyopathy.
- 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 is not recommended.
- When telmisartan is used in patients with impaired renal function, a periodic monitoring of potassium and creatinine serum levels is recommended.
- The safety and efficacy of telmisartan has not been established for the children under the age of 18 years.
- When driving vehicles or operating machinery it must be borne in mind that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy.

**Drug Interactions**

- *Digoxin:* It is recommended that digoxin levels be monitored when initiating, adjusting and discontinuing telmisartan to avoid possible over or under digitalization.
- Based on experience with the use of medicinal products that affect the renin-angiotensin system, concomitant use of potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicinal products, that may increase the potassium level (heparin, immunosuppresor (cyclosporine or tacrolimus), trimethoprim, ACE inhibitors, angiotensin II receptors antagonist, NSAIDS including selective COX II inhibitors etc) may lead to an increase in serum potassium and should therefore be co-administered cautiously with telmisartan.
- Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors and, rarely, with angiotensin II antagonists. If use of the combination proves necessary, careful monitoring of serum lithium levels is recommended.

**OVERDOSE**

The most likely manifestations of telmisartan overdosage are expected to be hypotension and tachycardia; bradycardia might also occur from parasympathetic (vagal) stimulation. Telmisartan is not removed by hemodialysis. The patient should be dosely 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 overdosage. Serum electrolytes and creatinine should be monitored frequently. If hypotension occurs, the patient should be placed in a supine position, with salt and volume replacement given quickly.

**HOW SUPPLIED**

TASMI (Telmisartan) Tablets 20mg are available in blister pack of 14's.
TASMI (Telmisartan) Tablets 40mg are available in blister pack of 14's.
TASMI (Telmisartan) Tablets 80mg are available in blister pack of 14's.

**STORAGE**

Store at 25°C (Excursions permitted between 15°C to 30°C).
Protect from sunlight and moisture.
The expiration date refers to the product correctly stored at the required conditions.

***Keep out of reach of children.***

***To be sold on prescription of a registered medical practitioner only.***

**Please read the contents carefully before use.**
**This package insert is continually updated from time to time.**

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