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# CRESAR Tablets (Telmisartan)

**Black Box Warning: Fetal Toxicity**

- When pregnancy is detected, discontinue telmisartan as soon as possible.
- Drugs that act directly on the renin-angiotensin system can cause injury and death to the developing fetus.

## Composition

CRESAR 20
Each tablet contains:
Telmisartan...20 mg
CRESAR 40
Each tablet contains:
Telmisartan...40 mg
CRESAR 80
Each tablet contains:
Telmisartan...80 mg

## Dosage Form

Tablet

## Pharmacology

▶ Pharmacodynamics

Telmisartan is a non-peptide angiotensin II receptor blocker (ARB). 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 (RAS), with effects that include vasoconstriction, stimulation of synthesis and release of aldosterone, cardiac stimulation, and renal reabsorption of sodium. Telmisartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively blocking the binding of angiotensin II to the $AT_1$ 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.
There is also an receptor found in many tissues, but $AT_2$ is not known to be associated with cardiovascular homeostasis. Telmisartan has much greater affinity (>3000-fold) for the $AT_1$ receptor than for the $AT_2$ receptor.
Blockade of the RAS with ACE inhibitors, which inhibit the biosynthesis of angiotensin II from angiotensin I, is widely used in the treatment of hypertension. ACE inhibitors also inhibit the degradation of bradykinin, a reaction also catalyzed by ACE. Telmisartan does not inhibit the ACE (kininase II); hence, it does not affect the response to bradykinin. Whether this difference has clinical relevance is not yet known. Telmisartan does not bind to or block other hormone receptors or ion

channels known to be important in cardiovascular regulation.
Blockade of the angiotensin II receptor inhibits the negative regulatory feedback of angiotensin II on renin secretion, but the resulting increased plasma renin activity (PRA) and angiotensin II circulating levels do not overcome the effect of telmisartan on blood pressure.
In normal volunteers, a dose of telmisartan 80 mg inhibited the pressor response to an intravenous infusion of angiotensin II by about 90% at peak plasma concentrations, with approximately 40% inhibition persisting for 24 hours.
Plasma concentration of angiotensin II and PRA increased in a dose-dependent manner after a single administration of telmisartan to healthy subjects and repeated administration to hypertensive patients. The once-daily administration of up to 80 mg telmisartan to healthy subjects did not influence plasma aldosterone concentrations. In multiple-dose studies with hypertensive patients, there were no clinically significant changes in electrolytes (serum potassium or sodium), or in metabolic function (including serum levels of cholesterol, triglycerides, high density lipoprotein , low density lipoprotein , glucose, or uric acid).
In 30 hypertensive patients with normal renal function treated for 8 weeks with telmisartan 80 mg or telmisartan 80 mg in combination with hydrochlorothiazide 12.5 mg, there were no clinically significant changes from baseline in renal blood flow, glomerular filtration rate (GFR), filtration fraction, renovascular resistance, or creatinine clearance.

▶ Pharmacokinetics

## Absorption

Following oral administration, peak concentrations ($C_{max}$) of telmisartan are reached in 0.5-1 hour after dosing. 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 40 mg tablet and about 20% after a 160 mg dose. The absolute bioavailability of telmisartan is dose-dependent. At 40 mg and 160 mg, the bioavailability was 42% and 58%, respectively. The pharmacokinetics of orally administered telmisartan are nonlinear over the dose range of 20-160 mg, with greater than proportional increases of plasma concentrations ($C_{max}$ and AUC) with increasing doses. Telmisartan shows bi-exponential decay kinetics with a terminal elimination half-life of approximately 24 hours. Trough plasma concentrations of telmisartan with once daily dosing are about 10-25% of peak plasma concentrations. Telmisartan has an accumulation index in plasma of 1.5-2.0 upon repeated once daily dosing.

## Distribution

Telmisartan is highly bound to plasma proteins (>99.5%), mainly albumin and $(alpha)_1$-acid glycoprotein. Plasma protein binding is constant over the concentration range achieved with recommended doses. The volume of distribution for telmisartan is approximately 500 liters, indicating additional tissue binding.

## Metabolism and Elimination

Following either intravenous or oral administration of $^{14}C$-labeled telmisartan, most of the administered dose (>97%) was eliminated unchanged in the feces via biliary excretion; only minute amounts were found in the urine (0.91% and 0.49% of total radioactivity, respectively).
Telmisartan is metabolized by conjugation to form a pharmacologically inactive acyl glucuronide; the glucuronide of the parent compound is the only metabolite that has been identified in human plasma and urine. After a single dose, the glucuronide represents approximately 11% of the measured radioactivity in plasma. The cytochrome P450 isoenzymes are not involved in the metabolism of telmisartan.
Total plasma clearance of telmisartan is >800 mL/min. Terminal half-life and total clearance appear to be independent of dose.

▶ Special Populations

*Renal Impairment:* No dosage adjustment is necessary in patients with decreased renal function. Telmisartan is not removed from blood by hemofiltration.

*Hepatic Impairment:* In patients with hepatic impairment, plasma concentrations of telmisartan are increased, and absolute bioavailability approaches 100%.
*Gender:* Plasma concentrations of telmisartan are generally 2-3 times higher in females than in males. In clinical trials, however, no significant increases in blood pressure response or in the incidence of orthostatic hypotension were found in women. No dosage adjustment is necessary.
*Geriatric:* The pharmacokinetics of telmisartan do not differ between the elderly and those younger than 65 years.
*Pediatric:* Telmisartan pharmacokinetics have not been investigated in patients <18 years of age.

## Indications

▶ Hypertension

Telmisartan is indicated for the treatment of hypertension, to lower blood pressure. Lowering blood pressure reduces the risk of fatal and nonfatal cardiovascular events, primarily strokes and myocardial infarctions.
It may be used alone or in combination with other antihypertensive agents

▶ Cardiovascular Risk Reduction

Telmisartan is indicated for reduction of the risk of myocardial infarction, stroke, or death from cardiovascular causes in patients 55 years of age or older at high risk developing major cardiovascular events who are unable to take ACE inhibitors.
High risk for cardiovascular events can be evidenced by a history of coronary artery disease, peripheral arterial disease, stroke, transient ischemic attack, or high-risk diabetes (insulin-dependent or non-insulin dependent) with the evidence of end-organ damage. Telmisartan can be used in addition to other needed treatment (such as antihypertensive, antiplatelet or lipid-lowering therapy).
Studies of telmisartan in this setting do not exclude the possibility that telmisartan may not preserve a meaningful fraction of the effect of the ACE inhibitor to which it was compared. Consider using the ACE inhibitor first, and, if it is stopped for cough only, consider re-trying the ACE inhibitor after the cough resolves.
Use of telmisartan with an ACE inhibitor is not recommended.

## Dosage And Administration

▶ Hypertension

Dosage must be individualized. The usual starting dose is CRESAR 40 once a day. Blood pressure response is dose-related over the range of 20-80 mg.
Most of the antihypertensive effect is apparent within two weeks and maximal reduction is generally attained after four weeks. When additional blood pressure reduction beyond that achieved with 80 mg telmisartan is required, a diuretic may be added.
No initial dosing adjustment is necessary for elderly patients or patients with renal impairment, including those on hemodialysis. Patients on dialysis may develop orthostatic hypotension; their blood pressure should be closely monitored.
CRESAR tablets may be administered with other antihypertensive agents.
CRESAR tablets may be administered with or without food.

▶ Cardiovascular Risk Reduction

The recommended dose is CRESAR 80 once a day and can be administered with or without food. It is not known whether

doses lower than 80 mg of telmisartan are effective in reducing the risk of cardiovascular morbidity and mortality. When initiating CRESAR therapy for cardiovascular risk reduction, monitoring of blood pressure is recommended, and if appropriate, adjustment of medications that lower blood pressure may be necessary.

## Contraindications

In patients with known hypersensitivity (e.g., anaphylaxis or angioedema) to telmisartan or any other component of this product
Do not co-administer aliskiren with telmisartan in patients with diabetes mellitus or renal impairment (GFR <60 ml/min/1.73 $m^2$)
Second and third trimesters of pregnancy
Biliary obstructive disorders
Severe hepatic impairment

## Warnings And Precautions

▶ Drug Interactions

Aliskiren: Do not co-administer aliskiren with telmisartan in patients with diabetes. Avoid use of aliskiren with telmisartan in patients with renal impairment (GFR <60 mL/min).
Digoxin: When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. Therefore, monitor digoxin levels when initiating, adjusting, and discontinuing telmisartan for the purpose of keeping the digoxin level within the therapeutic range.
Lithium: Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ARBs including telmisartan. Therefore, monitor serum lithium levels during concomitant use.
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 non-steroidal anti-inflammatory drugs (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. Monitor renal function periodically receiving telmisartan and NSAID therapy. The antihypertensive effect of ARBs, including telmisartan may be attenuated by NSAIDs including selective COX-2 inhibitors.
Ramipril and Ramiprilat: Co-administration of telmisartan 80 mg once daily and ramipril 10 mg once daily to healthy subjects increases steady-state $C_{max}$ and AUC of ramipril 2.3- and 2.1-fold, respectively, and $C_{max}$ and AUC of ramiprilat 2.4- and 1.5-fold, respectively. In contrast, $C_{max}$ and AUC of telmisartan decrease by 31% and 16%, respectively. When co-administering telmisartan and ramipril, the response may be greater because of the possibility additive pharmacodynamic effects of the combined drugs, and also because of the increased exposure to ramipril and ramiprilat in the presence of telmisartan. Concomitant use of telmisartan and ramipril is not recommended.
Potassium Sparing Diuretics or Potassium Supplements: ARBs such as telmisartan, attenuate diuretic induced potassium loss. Potassium sparing diuretics e.g. spironolactone, eplerenone, triamterene, or amiloride, potassium supplements, or potassium-containing salt substitutes may lead to a significant increase in serum potassium. If concomitant use is indicated because of documented hypokalemia they should be used with caution and with frequent monitoring of serum potassium.
Diuretics (Thiazide or Loop Diuretics): Prior treatment with high dose diuretics such as furosemide (loop diuretic) and hydrochlorothiazide (thiazide diuretic) may result in volume depletion and in a risk of hypotension when initiating

therapy with telmisartan.
Other Antihypertensive Agents: The blood pressure lowering effect of telmisartan can be increased by concomitant use of other antihypertensive medicinal products.
Clinical trial data has shown that dual blockade of the RAS through the combined use of ACE-inhibitors, ARBs 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 RAS-acting agent.
Corticosteroids (Systemic Route): Co-administered with telmisartan, can lead to reduction in the antihypertensive effect.
Other Drugs: Co-administration of telmisartan did not result in a clinically significant interaction with acetaminophen, amlodipine, glyburide, simvastatin, warfarin or ibuprofen. Telmisartan is not metabolized by the cytochrome P450 system and had no effects in vitro on cytochrome P450 enzymes, except for some inhibition of CYP2C19. Telmisartan is not expected to interact with drugs that inhibit cytochrome P450 enzymes; it is also not expected to interact with drugs metabolized by cytochrome P450 enzymes, except for possible inhibition of the metabolism of drugs metabolized by CYP2C19.
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, amifostine. Furthermore, orthostatic hypotension may be aggravated by alcohol, barbiturates, narcotics or antidepressants.

▶ Hypotension

In patients with an activated RAS, such as volume- and/or salt-depleted patients (eg, those being treated with high doses of diuretics), symptomatic hypotension may occur after initiation of therapy with telmisartan. This condition should be corrected prior to administration of telmisartan, or treatment should start under close medical supervision with a reduced dose.
If hypotension does occur, 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.

▶ Hyperkalemia

Hyperkalemia may occur in patients on ARBs, particularly in patients with advanced renal impairment, heart failure, on renal replacement therapy, or on potassium supplements, potassium-sparing diuretics, potassium-containing salt substitutes or other drugs that increase potassium levels. Consider periodic determinations of serum electrolytes to detect possible electrolyte imbalances, particularly in patients at risk.
The main risk factors for hyperkalemia to be considered are:

- Diabetes mellitus, renal impairment, age (>70 years)
- Combination with one or more other medicinal products that affect the RAS and/or potassium supplements.
- Medicinal products or therapeutic classes of medicinal products that may provoke hyperkalemia are salt substitutes containing potassium, potassium-sparing diuretics, ACE inhibitors, ARBs, NSAIDs (including selective COX-2 inhibitors), heparin, immunosuppressives (cyclosporine or tacrolimus), and trimethoprim.
- Intercurrent events, in particular dehydration, acute cardiac decompensation, metabolic acidosis, worsening of renal function, sudden worsening of the renal condition (e.g. infectious diseases), cellular lysis (e.g. acute limb ischemia, rhabdomyolysis, extend trauma).

Close monitoring of serum potassium in at risk patients is recommended.

▶ Dual Blockade of the RAS

Dual blockade of the RAS with ARBs, ACE inhibitors, or aliskiren is associated with increased risks of hypotension, hyperkalemia, and changes in renal function (including acute renal failure) compared to monotherapy.

The ONTARGET trial enrolled 25,620 patients ≥55 years old with atherosclerotic disease or diabetes with end-organ damage, randomizing them to telmisartan only, ramipril only, or the combination, and followed them for a median of 56 months. Patients receiving the combination of telmisartan and ramipril did not obtain any additional benefit compared to monotherapy, but experienced an increased incidence of renal dysfunction (e.g., acute renal failure) compared with groups receiving telmisartan alone or ramipril alone.
In most patients no benefit has been associated with using two RAS inhibitors concomitantly. In general, avoid combined use of RAS inhibitors. Closely monitor blood pressure, renal function, and electrolytes in patients on telmisartan and other agents that affect the RAS.
Do not co-administer aliskiren with telmisartan in patients with diabetes. Avoid concomitant use of aliskiren with telmisartan in patients with renal impairment (GFR <60 mL/min/1.73 $m^2$).

▶ 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 RAS.

▶ Other Conditions with Stimulation of the RAS

In patients whose vascular tone and renal function depend predominantly on the activity of the RAS (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with medicinal products that affect this system such as telmisartan has been associated with acute hypotension, hyperazotemia, 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 RAS. Therefore, the use of telmisartan 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.

▶ Diabetic Patients Treated with Insulin or Antidiabetics

In these patients hypoglycemia may occur under telmisartan treatment. Therefore, in these patients an appropriate blood glucose monitoring should be considered; a dose adjustment of insulin or antidiabetics may be required, when indicated.

▶ 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.

▶ Renal Impairment

As a consequence of inhibiting the RAS, anticipate changes in renal function in susceptible individuals. In patients whose renal function may depend on the activity of the RAS (eg, patients with severe congestive heart failure or renal dysfunction), treatment with ACE inhibitors and ARBs has been associated with oliguria and/or progressive azotemia and (rarely) with acute renal failure and/or death. Similar results have been reported with telmisartan.
In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen (BUN) were observed. There has been no long-term use of telmisartan in patients with unilateral or bilateral renal artery stenosis but an effect similar to that seen with ACE inhibitors should be anticipated.

When telmisartan is used in patients with impaired renal function, periodic monitoring of potassium and creatinine serum levels is recommended. There is no experience regarding the administration of telmisartan in patients with recent kidney transplantation.

▶ Hepatic Impairment

As the majority of telmisartan is eliminated by biliary excretion, patients with biliary obstructive disorders or hepatic impairment can be expected to have reduced clearance. Initiate telmisartan at low doses and titrate slowly in these patients. Monitor the dose carefully in these patients.

▶ Pregnancy

*Category D*

Use of drugs that act on the RAS during the second and third trimesters of pregnancy reduces fetal renal function and increases fetal and neonatal morbidity and death. Resulting oligohydramnios can be associated with fetal lung hypoplasia and skeletal deformations. Potential neonatal adverse effects include skull hypoplasia, anuria, hypotension, renal failure, and death. When pregnancy is detected, discontinue telmisartan as soon as possible. These adverse outcomes are usually associated with use of these drugs in the second and third trimester of pregnancy. Most epidemiologic studies examining fetal abnormalities after exposure to antihypertensive use in the first trimester have not distinguished drugs affecting the RAS from other antihypertensive agents. Appropriate management of maternal hypertension during pregnancy is important to optimize outcomes for both mother and fetus.

In the unusual case that there is no appropriate alternative to therapy with drugs affecting the RAS for a particular patient, apprise the mother of the potential risk to the fetus. Perform serial ultrasound examinations to assess the intra-amniotic environment. If oligohydramnios is observed, discontinue telmisartan, unless it is considered lifesaving for the mother. Fetal testing may be appropriate, based on the week of pregnancy. Patients and physicians should be aware, however, that oligohydramnios may not appear until after the fetus has sustained irreversible injury. Closely observe infants with histories of in utero exposure to telmisartan for hypotension, oliguria, and hyperkalemia.

▶ Lactation

It is not known whether telmisartan is excreted in human milk, but telmisartan was shown to be present in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

▶ Pediatric Use

*Neonates with a History of In Utero Exposure to Telmisartan*

If oliguria or hypotension occurs, direct attention toward support of blood pressure and renal perfusion. Exchange transfusions or dialysis may be required as a means of reversing hypotension and/or substituting for disordered renal function.

Safety and effectiveness in pediatric patients have not been established.

▶ Geriatric Use

Of the total number of patients receiving telmisartan in hypertension clinical studies, 551 (19%) were 65 to 74 years of age and 130 (4%) were 75 years or older. No overall differences in effectiveness and safety were observed in these patients compared to younger patients and 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.

Of the total number of patients receiving telmisartan in the cardiovascular risk reduction study (ONTARGET), the percentage of patients ≥65 to <75 years of age was 42%; 15% of patients were ≥75 years old. No overall differences in

effectiveness and safety were observed in these patients compared to younger patients and 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.

## Undesirable Effects

The following adverse reaction is described elsewhere in labeling:
Renal dysfunction upon use with ramipril.
Serious adverse drug reactions include anaphylactic reactions and angioedema which may occur rarely (≥1/10,000 to <1/1,000), and acute renal failure.

▶ Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reactions rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

### Hypertension

Telmisartan has been evaluated for safety in more than 3700 patients, including 1900 treated for over 6 months and more than 1300 for over one year. Adverse experiences have generally been mild and transient in nature and have infrequently required discontinuation of therapy.
In placebo-controlled trials involving 1041 patients treated with various doses of telmisartan (20 to 160 mg) monotherapy for up to 12 weeks, the overall incidence of adverse events was similar to that in patients treated with placebo.
Adverse events occurring at an incidence of ≥1% in patients treated with telmisartan and at a greater rate than in patients treated with placebo, irrespective of their causal association, are presented in Table 1.

Table1. Adverse events occurring at an incidence of ≥1% in patients treated with telmisartan and at a greater rate than patients treated with placebo

| Adverse events | Telmisartan n = 1455% | Placebo n = 380% |
|---|---|---|
| Upper Respiratory Tract Infection | 7 | 6 |
| Back Pain | 3 | 1 |
| Sinusitis | 3 | 2 |
| Diarrhea | 3 | 2 |
| Pharyngitis | 1 | 0 |

In addition to the adverse events in the table, the following events occurred at a rate of ≥1% but were at least as frequent in the placebo group: influenza-like symptoms, dyspepsia, myalgia, urinary tract infection, abdominal pain, headache, dizziness, pain, fatigue, coughing, hypertension, chest pain, nausea, and peripheral edema. Discontinuation of therapy because of adverse events was required in 2.8% of 1455 patients treated with telmisartan and 6.1% of 380 placebo patients in placebo-controlled clinical trials.
The incidence of adverse events was not dose-related and did not correlate with gender, age, or race of patients.
The incidence of cough occurring with telmisartan in six placebo-controlled trials was identical to that noted for placebo-

treated patients (1.6%).

In addition to those listed above, adverse events that occurred in more than 0.3% of 3500 patients treated with telmisartan monotherapy in controlled or open trials are listed below. It cannot be determined whether these events were causally related to telmisartan:

Autonomic Nervous System: impotence, increased sweating, flushing

Body as a Whole: allergy, fever, leg pain, malaise

Blood Disorders: anemia, blood uric acid increased

Cardiovascular: palpitation, dependent edema, angina pectoris, tachycardia, leg edema, abnormal electrocardiography (ECG)

Central Nervous System: insomnia, somnolence, migraine, vertigo, paresthesia, involuntary muscle contractions, hypoesthesia

Gastrointestinal: flatulence, constipation, gastritis, vomiting, dry mouth, hemorrhoids, gastroenteritis, enteritis, gastroesophageal reflux, toothache, nonspecific gastrointestinal disorders, stomach discomfort, hepatic enzyme increased, dysgeusia

Metabolic: gout, hypercholesterolemia, diabetes mellitus

Musculoskeletal: arthritis, arthralgia, leg cramps, muscle spasms, pain in extremity

Psychiatric: anxiety, depression, nervousness

Resistance Mechanism: infection, fungal infection, abscess, otitis media

Respiratory: asthma, bronchitis, rhinitis, dyspnea, epistaxis

Skin: dermatitis, rash, eczema, pruritus, hyperhidrosis

Urinary*:* micturition frequency, cystitis

Vascular*:* cerebrovascular disorder

Special Senses: abnormal vision, conjunctivitis, tinnitus, earache, visual disturbances

During initial clinical studies, a single case of angioedema was reported (among a total of 3781 patients treated).

*Clinical Laboratory Findings*

In placebo-controlled clinical trials, clinically relevant changes in standard laboratory test parameters were rarely associated with administration of telmisartan tablets.

Hemoglobin: A greater than 2 g/dL decrease in hemoglobin was observed in 0.8% telmisartan patients compared with 0.3% placebo patients. No patients discontinued therapy because of anemia.

Creatinine: A 0.5 mg/dL rise or greater in creatinine was observed in 0.4% telmisartan patients compared with 0.3% placebo patients. One telmisartan-treated patient discontinued therapy because of increases in creatinine and blood urea nitrogen.

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

### Cardiovascular Risk Reduction

Because common adverse reactions were well characterized in studies of telmisartan in hypertension, only adverse events leading to discontinuation and serious adverse events were recorded in subsequent studies of telmisartan for cardiovascular risk reduction. In TRANSCEND (N=5926, 4 years and 8 months of follow-up), discontinuations for adverse events were 8.4% on telmisartan and 7.6% on placebo. The only serious adverse events at least 1% more common on telmisartan than placebo were intermittent claudication (7% vs 6%) and skin ulcer (3% vs 2%).

▶ Post-marketing Experience

The following adverse reactions have been identified during post-approval use of telmisartan. Because these reactions

are reported voluntarily from a population of uncertain size, it is not always possible to estimate reliably their frequency or establish a causal relationship to drug exposure. Decisions to include these reactions in labeling are typically based on one or more of the following factors: (1) seriousness of the reaction, (2) frequency of reporting, or (3) strength of causal connection to telmisartan.
The most frequent spontaneously reported events include: headache, dizziness, asthenia, coughing, nausea, fatigue, weakness, edema, face edema, lower limb edema, angioneurotic edema, urticaria, hypersensitivity, sweating increased, erythema, chest pain, atrial fibrillation, congestive heart failure, myocardial infarction, blood pressure increased, hypertension aggravated, hypotension (including postural hypotension), hyperkalemia, syncope, dyspepsia, diarrhea, pain, urinary tract infection, erectile dysfunction, back pain, abdominal pain, muscle cramps (including leg cramps), myalgia, bradycardia, eosinophilia, thrombocytopenia, uric acid increased, abnormal hepatic function/liver disorder, renal impairment including acute renal failure, anemia, increased creatine phosphokinase (CPK), anaphylactic reaction, tendon pain (including tendonitis, tenosynovitis), drug eruption (toxic skin eruption mostly reported as toxicoderma, rash, and urticaria), hypoglycemia (in diabetic patients), and angioedema (with fatal outcome).
Rare cases of rhabdomyolysis, interstitial lung disease and sepsis including fatal outcome have been reported in patients receiving ARBs, including telmisartan.

## Overdosage

Limited data are available related to overdosage in humans. The most likely manifestations of overdosage 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.

## Shelf-Life

Two years

## Storage & Handling Instruction

Store in a cool dry place

## Packaging Information

CRESAR 20: Aluminium strip of 10 tablets
CRESAR 40: Aluminium strip of 10 tablets
CRESAR 80: Aluminium strip of 10 tablets
*Last Updated: June 2016*
*Last Reviewed: June 2016*

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