

FRONT



1. NAME OF THE MEDICINAL PRODUCT

Novtel 40mg Tablets
Novtel 80mg Tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Novtel 40mg Tablets: Each tablet contains 40mg of Telmisartan.
Novtel 80mg Tablets: Each tablet contains 80mg of Telmisartan.

For the full list of excipients, see section List of excipients.

3. PHARMACEUTICAL FORM

Tablets.
Novtel 40mg Tablets: White to off white, capsule shaped tablets, debossed with 'C11' on one side and plain on other side.
Novtel 80mg Tablets: White to off white, capsule shaped tablets, debossed with 'C12' on one side and plain on other side.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Hypertension

Treatment of essential hypertension.

Cardiovascular risk reduction

Novtel 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 of developing major cardiovascular events who are unable to take ACE inhibitors.

High risk of cardiovascular events can be evidenced by history of coronary artery disease, peripheral arterial disease, stroke, transient ischemic attack, or high-risk diabetes (insulin-dependent or non-insulin dependent) with evidence of end-organ damage. Novtel can be used in additional to other needed treatment (such as antihypertensive, antiplatelet or lipid-lowering therapy).

Studies of Telmisartan in this setting do not exclude that it 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.

4.2 Posology and method of administration

Adults

Treatment of essential hypertension

The recommended dose is 40 mg once daily. In cases where the target blood pressure is not achieved, telmisartan dose can be increased to a maximum of 80 mg once daily. Alternatively, telmisartan may be used in combination with thiazide-type diuretics such as hydrochlorothiazide, which has been shown to have an additive blood pressure lowering effect with telmisartan. 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.
In patients with severe hypertension treatment with telmisartan at doses up to 160 mg alone and in combination with hydrochlorothiazide 12.5 - 25 mg daily was well tolerated and effective.

Cardiovascular risk reduction

The recommended dose of Novtel is 80mg once a day and can be administered with or without food. It is not known whether doses lower than 80mg of telmisartan are effective in reducing the risk of cardiovascular morbidity and mortality.

When initiating Novtel therapy for cardiovascular risk reduction, monitoring of blood pressure is recommended, and if appropriate adjustment of medications that lower blood pressure may be necessary.

Novtel may be taken with or without food.

Renal impairment

No posology adjustment is required for patients with renal impairment, including those on haemodialysis. Telmisartan is not removed from blood by hemofiltration.

Hepatic impairment

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

Elderly

No dosing adjustment is necessary.

Children and adolescents

The safety and efficacy of Novtel for use in children below 18 years have not been established.

4.3 Contraindications

- Hypersensitivity to the active ingredient or any of the excipients
- Second and third trimesters of pregnancy
- Lactation
- Biliary obstructive disorders
- Severe hepatic impairment
- The concomitant use of Novtel with aliskiren is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m²)

4.4 Special warnings and precautions for use

Pregnancy:

Angiotensin II receptor antagonists should not be initiated during pregnancy. Unless continued angiotensin II receptor antagonist therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy.

When pregnancy is diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately, and if appropriate, alternative therapy should be started.

Renovascular hypertension:

There is an increased risk of severe hypotension and renal insufficiency when patients with bilateral renal artery stenosis or stenosis of the artery to a single functioning kidney are treated with medicinal products that affect the renin-angiotensin-aldosterone system.

Renal impairment and kidney transplant:

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

Intravascular volume depletion:

Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by vigorous diuretic therapy, dietary salt restriction, diarrhoea or vomiting. Such conditions, especially volume and/or sodium depletion, should be corrected before the administration of Telmisartan.

Dual blockade of the renin-angiotensin-aldosterone system:

As a consequence of inhibiting the renin-angiotensin-aldosterone system changes in renal function (including acute renal failure) have been reported in susceptible individuals, especially if combining medicinal products that affect this system. Dual blockade of the renin-angiotensin-aldosterone system (e.g. by adding an ACE- inhibitor or the direct renin-inhibitor aliskiren to an angiotensin II receptor antagonist) should therefore be limited to individually defined cases with close monitoring of renal function.

Other conditions with stimulation of the renin-angiotensin-aldosterone system:

In patients whose vascular tone and renal function depend predominantly on the activity of the renin-angiotensin-aldosterone system (e.g. patients with severe congestive heart failure or underlying renal disease, including renal artery stenosis), treatment with medicinal products that affect this system has been associated with acute hypotension, hyperazotaemia, oliguria, or rarely acute renal failure.

Primary aldosteronism:

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

Hyperkalaemia:

During treatment with medicinal products that affect the renin-angiotensin-aldosterone system hyperkalaemia may occur, especially in the presence of renal impairment and/or heart failure. Monitoring of serum potassium in patients at risk is recommended.

Based on experience with the use of medicinal products that affect the renin-angiotensin system, concomitant use with potassium-sparing diuretics, potassium supplements, salt substitutes containing potassium or other medicinal products that may increase the potassium level (heparin, etc.) may lead to an increase in serum potassium and should therefore be co-administered cautiously with Telmisartan.

Hepatic impairment:

Telmisartan is mostly eliminated in the bile. Patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance. Telmisartan should be used with caution in these patients.

Diabetes mellitus:

In diabetic patients with an additional cardiovascular risk, i.e. patients with diabetes mellitus and coexistent coronary artery disease (CAD), the risk of fatal myocardial infarction and unexpected cardiovascular death may be increased when treated with blood pressure lowering agents such as ARBs or ACE-inhibitors. In patients with diabetes mellitus CAD may be asymptomatic and therefore undiagnosed. Patients with diabetes mellitus should undergo appropriate diagnostic evaluation, e.g. exercise stress testing, to detect and to treat CAD accordingly before initiating treatment with Telmisartan.

Other:

As observed for angiotensin converting enzyme inhibitors, angiotensin receptor blockers including Telmisartan are apparently less effective in lowering blood pressure in black people than in non-blacks, possibly because of higher prevalence of low-renin states in the black hypertensive population.

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

4.5 Interaction with other medicinal products and other forms of interaction

Telmisartan may increase the hypotensive effect of other antihypertensive agents. Other interactions of clinical significance have not been identified.

Co-administration of telmisartan did not result in a clinically significant interaction with digoxin, warfarin, hydrochlorothiazide, glibenclamide, ibuprofen, paracetamol, simvastatin and amlodipine. For digoxin a 20% increase in median plasma digoxin trough concentration has been observed (39% in a single case), monitoring of plasma digoxin levels should be considered.

In one study the co-administration of telmisartan and ramipril led to an increase of up to 2.5 fold in the AUC₀₋₂₄ and C_{max} of ramipril and ramiprilat. The clinical relevance of this observation is not known.

Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors. Cases have also been reported with angiotensin II receptor antagonists including Telmisartan. Therefore, serum lithium level monitoring is advisable during concomitant use.

Treatment with NSAIDs (i.e. ASA at anti-inflammatory dosage regimens, COX-2 inhibitors and non-selective NSAIDs) is associated with the potential for acute renal insufficiency in patients who are dehydrated. Compounds acting on the Renin-Angiotensin-System like telmisartan may have synergistic effects. Patients receiving NSAIDs and Telmisartan should be adequately hydrated and be monitored for renal function at the beginning of combined treatment.

A reduced effect of antihypertensive drugs like telmisartan by inhibition of vasodilating prostaglandins has been reported during combined treatment with NSAIDs.

4.6 Fertility, pregnancy and lactation

The use of angiotensin II receptor antagonists is not recommended during the first trimester of pregnancy and should not be initiated during pregnancy. When pregnancy is diagnosed, treatment with angiotensin II receptor antagonists should be stopped immediately, and, if appropriate, alternative therapy should be started.

The use of angiotensin II receptor antagonists is contraindicated during the second and third trimester of pregnancy.

Non-clinical studies with telmisartan do not indicate teratogenic effect, but have shown fetotoxicity.

Angiotensin II receptor antagonists exposure during the second and third trimesters is known to induce human fetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia).

Unless continued angiotensin II receptor antagonist therapy is considered essential, patients planning pregnancy should be changed to alternative anti-hypertensive treatments which have an established safety profile for use in pregnancy.

Should exposure to angiotensin II receptor antagonists have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended.

Infants whose mothers have taken angiotensin II receptor antagonists should be closely observed for hypotension.

Telmisartan is contraindicated during lactation since it is not known whether it is excreted in human milk. Animal studies have shown excretion of telmisartan in breast milk.

Fertility:

No studies on fertility in humans have been performed. In non-clinical studies, an effect of Telmisartan on male and female fertility was not observed.

4.7 Effects on ability to drive and use machines

No studies on the effect on the ability to drive and use machines have been performed. However, when driving vehicles or operating machinery it should be taken into account that dizziness or drowsiness may occasionally occur when taking antihypertensive therapy.

4.8 Undesirable effects

The overall incidence of adverse events reported with telmisartan (41.4%) was usually comparable to placebo (43.9%) in patients treated for hypertension. The incidence of adverse events was not dose related and showed no correlation with gender, age or race of the patients.

The safety profile of Telmisartan in patients treated for cardiovascular risk reduction was consistent with that obtained in hypertensive patients.

The adverse drug reactions listed below have been accumulated from study in patients treated for hypertension and from post-marketing reports.

Infections and infestations:

Urinary tract infections (including cystitis), upper respiratory tract infections, sepsis including fatal outcome.

Blood and lymphatic system disorders:

Anaemia, eosinophilia, thrombocytopenia

Immune system disorders:

Anaphylactic reaction, hypersensitivity

Metabolism and nutrition disorders:

Hyperkalaemia, hypoglycaemia (in diabetic patients)

Psychiatric disorders:

Insomnia, depression, anxiety

Nervous system disorders:

Syncope (faint)

Eye disorders:

Visual disturbance

Ear and labyrinth disorders:

Vertigo

Cardiac disorders:

Bradycardia, tachycardia

Vascular disorders:

Hypotension, orthostatic hypotension

Respiratory, thoracic and mediastinal disorders:

Dyspnoea

Gastro-intestinal disorders:

Abdominal pain, diarrhoea, dyspepsia, flatulence, vomiting, dry mouth, stomach discomfort

Hepatobiliary disorders:

Hepatic function abnormal / liver disorder*

*Most cases of hepatic function abnormal / liver disorder from post-marketing experience with telmisartan occurred in patients in Japan, who are more likely to experience these adverse reactions.

Skin and subcutaneous tissue disorders:

Pruritus, hyperhidrosis, rash, angioedema (with fatal outcome), eczema, erythema, urticaria, drug eruption, toxic skin eruption

Musculoskeletal, connective tissue and bone disorders:

Back pain, muscle spasms (cramps in legs), myalgia, arthralgia, pain in extremity (leg pain), tendon pain (tendinitis like symptoms)

Renal and urinary disorders:

Renal impairment including acute renal failure

General disorders and administration site conditions:

Chest pain, asthenia (weakness), influenza-like illness

Investigations:

Blood creatinine increased, haemoglobin decreased, blood uric acid increased, hepatic enzymes increased, blood creatine phosphokinase (CPK) increased.

4.9 Overdose

Limited information is available with regard to overdose in humans. The most prominent manifestations of telmisartan overdose were hypotension and tachycardia, bradycardia also occurred. If symptomatic hypotension should occur, supportive treatment should be instituted. Telmisartan is not removed by haemodialysis.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Angiotensin II Antagonists, plain, ATC Code: C09CA07

Telmisartan is an orally effective and specific angiotensin II receptor (type AT1) antagonist. 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 characterised AT receptors. The functional role of these receptors is not known, nor is the effect of their possible overstimulation by angiotensin II, whose levels are increased by telmisartan. Plasma aldosterone levels are decreased by telmisartan. Telmisartan does not inhibit human plasma renin or block ion channels. Telmisartan does not inhibit angiotensin converting enzyme (kininase II), the enzyme which also degrades bradykinin. Therefore it is not expected to potentiate bradykinin-mediated adverse effects.

In man, an 80 mg dose of telmisartan almost completely inhibits the angiotensin II evoked blood pressure increase. The inhibitory effect is maintained over 24 hours and still measurable up to 48 hours.

5.2 Pharmacokinetic properties

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 (AUC_{0-∞}) 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.

Linearity/non-linearity

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. C_{max} 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 (V_{ss}) is approximately 500 L.

Biotransformation

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

Elimination

Telmisartan is characterised by biexponential decay pharmacokinetics with a terminal elimination half-life of >20 hours. The maximum plasma concentration (C_{max}) and, to a smaller extent, 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 faeces, mainly as unchanged compound. Cumulative urinary excretion is < 1% of dose.

Total plasma clearance (CL_{tot}) is high (approximately 1000 ml/min compared with hepatic blood flow (about 1500 ml/min).

Special Populations

Paediatric population

The pharmacokinetics of two doses of telmisartan were assessed as a secondary objective in hypertensive patients (n = 57) aged 6 to < 18 years after taking telmisartan 1 mg/kg or 2 mg/kg over a four-week treatment period. Pharmacokinetic objectives included the determination of the steady-state of telmisartan in children and adolescents, and investigation of age-related differences. Although the study was too small for a meaningful assessment of the pharmacokinetics of children under 12 years of age, the results are generally consistent with the findings in adults and confirm the nonlinearity of telmisartan, particularly for C_{max}.

Gender

Differences in plasma concentrations were observed, with C_{max} and AUC being approximately 3- and 2-fold higher, respectively, in females compared to males.

Elderly

The pharmacokinetics of telmisartan do not differ between the elderly and those younger than 65 years.

Renal impairment

In patients with mild to moderate and severe renal impairment, 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 patients 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.

6. PHARMACOLOGICAL PROPERTIES

6.1 List of excipients

Tablet core:

Mannitol, Sodium Hydroxide, Meglumine, Povidone, Sodium Stearyl Fumarate, Magnesium Stearate.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

Please refer to the expiry date on the product labels.

6.4 Special precautions for storage

Store below 30°C. Store in the original package. Protect from moisture.

6.5 Nature and contents of container

Alu/Alu blisters pack in the outer carton of 1 x 10's, 3 x 10's, 6 x 10's, 10 x 10's, 50 x 10's, 100 x 10's. Not all packs sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MANUFACTURER

Manufactured by:

Novugen Pharma Sdn. Bhd.
No. 27, Jalan Lengkok Teknologi 2,
Taman Teknologi Enstek Fasa 1,
71760 Bandar Baru Enstek,
Negeri Sembilan, Malaysia.

Product Registration Holder:

Novugen Pharma Sdn. Bhd.
No. 3, Jalan Jururancang U1/21,
Hicom Glenmarie Industrial Park
40150 Shah Alam, Selangor, Malaysia.

8. DATE OF REVISION

02/09/2025