Twincard®

Telmisartan / Amlodipine Besylate

FORMS AND PRESENTATION
Twincard® 80/5: Tablets. Box of 30.
Twincard® 80/10: Tablets. Box of 30.
COMPOSITION
Twincard® 80/5: Each tablet contains Telmisartan 80mg and Amlodipine Besylate equivalent to Amlodipine 5mg.
Twincard® 80/10: Each tablet contains Telmisartan 80mg and Amlodipine Besylate equivalent to Amlodipine 10mg.
Excipients: Mannitol, sodium hydroxide, meglumine, povidone, sodium stearyl fumarate, magnesium stearate, microcrystalline cellulose, corn starch, iron oxide black, FD&C Blue, crospovidone.
PHARMACOLOGICAL PROPERTIES
Pharmacodynamic properties
Pharmacotherapeutic group: Agents acting on the renin-angiotensin system, angiotensin II receptor blockers (ARBs), and calcium channel blockers, ATC code: C09DB04.
This medicine combines two antihypertensive compounds with complementary mechanisms to control blood pressure in patients with essential hypertension: an angiotensin II receptor antagonist, telmisartan, and a dihydropyridinic calcium channel blocker, amlodipine.
The combination of these substances has an additive antihypertensive effect, reducing blood pressure to a greater degree than either component alone.
Telmisartan
Telmisartan is an orally active and specific angiotensin II receptor (type AT1) antagonist. Telmisartan displaces angiotensin II with a very high affinity from its binding site at the AT1 receptor subtype, which is responsible for the known actions of angiotensin II. Telmisartan selectively binds the AT1 receptor and the binding is long-lasting.
Telmisartan does not show affinity for other receptors, including AT2 and other less characterized AT receptors. Plasma aldosterone levels are decreased by telmisartan. Telmisartan does not inhibit human plasma renin or block ion channels, and does not inhibit angiotensin converting enzyme (kininase II), the enzyme which also degrades bradykinin. Therefore, it is not expected to potentiate bradykinin-mediated adverse reactions.
In humans, 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. After the first dose of telmisartan, the antihypertensive activity gradually becomes evident within 3 hours. The maximum reduction in blood pressure is generally attained 4 to 8 weeks after the start of treatment and is sustained during long-term therapy.
In patients with hypertension, telmisartan reduces both systolic and diastolic blood pressure without affecting pulse rate. The contribution of the medicinal product's diuretic and natriuretic effect to its hypotensive activity has still to be defined. The antihypertensive efficacy of telmisartan is comparable to that of substances representative of other classes of antihypertensive medicinal products (demonstrated in clinical trials comparing telmisartan to amlodipine, atenolol, enalapril, hydrochlorothiazide, and lisinopril).
Upon abrupt cessation of treatment with telmisartan, blood pressure gradually returns to pre-treatment values over a period of several days without evidence of rebound hypertension.
Amlodipine
Amlodipine is a calcium ion influx inhibitor of the dihydropyridine group (slow channel blocker or calcium ion antagonist) and inhibits the transmembrane influx of calcium ions into cardiac and vascular smooth muscle. The mechanism of the antihypertensive action of amlodipine is due to a direct relaxant effect on vascular smooth muscle, leading to reductions in peripheral vascular resistance and in blood pressure. Amlodipine binds to both dihydropyridine and non- dihydropyridine binding sites. Amlodipine is relatively vessel-selective, with a greater effect on vascular smooth muscle cells than on cardiac muscle cells.
In patients with hypertension, once daily dosing provides clinically significant reductions of blood pressure in both the supine and standing positions throughout the 24 hour interval. Due to the slow onset of action, acute hypotension is not a feature of amlodipine administration.
In hypertensive patients with normal renal function, therapeutic doses of amlodipine resulted in a decrease in renal vascular resistance and an increase in glomerular filtration rate and effective renal plasma flow, without change in filtration fraction or proteinuria.
Amlodipine has not been associated with any adverse metabolic effects or changes in plasma lipids and is suitable for use in patients with asthma, diabetes, and gout.
Pharmacokinetic properties
The rate and extent of absorption of telmisartan / amlodipine are equivalent to the bioavailability of telmisartan and amlodipine when administered as individual tablets.
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.
After oral administration of therapeutic doses, amlodipine is well absorbed with peak blood levels between 6-12 hours post dose. Absolute bioavailability has been estimated to be between 64 and 80 %. Amlodipine bioavailability is not affected by food ingestion.
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.
The volume of distribution of amlodipine is approximately 21 l/kg. In vitro studies have shown that approximately 97.5 % of circulating amlodipine is bound to plasma proteins in hypertensive patients.
Biotransformation
Telmisartan is metabolized by conjugation to the glucuronide of the parent compound. No pharmacological activity has been shown for the conjugate.
Amlodipine is extensively (approximatively 90 %) metabolized by the liver to inactive metabolites.
Elimination
Telmisartan is characterized by biexponential 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 faeces, mainly as an unchanged compound. Cumulative urinary excretion is <1 % of the dose. Total plasma clearance (Cltot) is high (approximately 1,000 ml/min) compared with hepatic blood flow (about 1,500 ml/min).
Amlodipine elimination from plasma is biphasic, with a terminal elimination half-life of approximately 30 to 50 hours consistent with once daily dosing. Steady-state plasma levels are reached after continuous administration for 7-8 days. Ten per cent of original amlodipine and 60 % of amlodipine metabolites are excreted in the urine. Amlodipine exhibits linear pharmacokinetics.
Pediatric population (age below 18 years)
No pharmacokinetic data are available in the pediatric population.
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.
Elderly
The pharmacokinetics of telmisartan do not differ in young and elderly patients.
The time to reach peak plasma concentrations of amlodipine is similar in elderly and younger subjects. In elderly patients, amlodipine clearance tends to decline with resulting increases in AUC and elimination half-life.
INDICATIONS
Treatment of essential hypertension in adults:
Add on therapy:
Twincard® is indicated in adults whose blood pressure is not adequately controlled on amlodipine 5 mg alone.
Replacement therapy:
Adult patients receiving telmisartan and amlodipine from separate tablets can instead receive tablets of telmisartan / amlodipine containing the same component doses.
CONTRAINDICATION
• Hypersensitivity to the active substances, to dihydropyridine derivatives, or to any of the excipients.
• Women in their second and third trimesters of pregnancy
• Biliary obstructive disorders and severe hepatic impairment
• Shock (including cardiogenic shock)
• Obstruction of the outflow tract of the left ventricle (e.g. high grade aortic stenosis)
• Hemodynamically unstable heart failure after acute myocardial infarction
The concomitant use of telmisartan/amlodipine with aliskiren-containing medicinal products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m^2).
PRECAUTIONS
Hepatic impairment
Telmisartan is mostly eliminated in the bile. Patients with biliary obstructive disorders or hepatic insufficiency can be expected to have reduced clearance.
The half-life of amlodipine is prolonged and AUC values are higher in patients with impaired liver function. Amlodipine should therefore be initiated at the lower end of the dosing range and caution should be used, both on initial treatment and when increasing the dose.
Telmisartan/amlodipine should therefore be used with caution in these patients.
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 (RAAS).
Renal impairment and kidney transplantation
In patients with mild to moderate and severe renal impairment, doubling of plasma concentrations of telmisartan 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. The pharmacokinetics of amlodipine are not significantly influenced by renal impairment.
When telmisartan/amlodipine 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/amlodipine in patients with a recent kidney transplant.
Intravascular hypovolemia
Symptomatic hypotension, especially after the first dose, may occur in patients who are volume and/or sodium depleted by e.g. vigorous diuretic therapy, dietary salt restriction, diarrhea or vomiting. Such conditions should be corrected before the administration of telmisartan. If hypotension occurs with telmisartan/amlodipine, the patient should be placed in the supine position and, if necessary, given an intravenous infusion of normal saline. Treatment can be continued once the blood pressure has been stabilized.
Dual blockade of the renin-angiotensin-aldosterone system (RAAS)
There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers, or aliskiren increases the risk of hypotension, hyperkalemia, and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers, or aliskiren is therefore not recommended.
If dual blockade therapy is considered absolutely necessary, this should only occur under specialist supervision and subject to frequent close monitoring of renal function, electrolytes, and blood pressure. ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy.
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, 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 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.
Unstable angina pectoris, acute myocardial infarction
There are no data to support the use of telmisartan/amlodipine in unstable angina pectoris and during or within one month of myocardial infarction.
Patients with cardiac failure
Calcium channel blockers, including amlodipine, should be used with caution in patients with congestive heart failure, as they may increase the risk of future cardiovascular events and mortality.
Diabetic patients treated with insulin or antidiabetics
In these patients, hypoglycemia may occur under telmisartan treatment. Therefore, in these patient's appropriate blood glucose monitoring should be considered; a dose adjustment of insulin or antidiabetics may be required when indicated.
Hyperkalemia
The use of medicinal products that affect the renin-angiotensin-aldosterone system may cause hyperkalemia. Hyperkalemia may be fatal in the elderly, in patients with renal insufficiency, in diabetic patients, in patients concomitantly treated with other medicinal products that may increase potassium levels, and/or in patients with intercurrent events.
Before considering the concomitant use of medicinal products that affect the renin-angiotensin-aldosterone system, the benefit-risk ratio should be evaluated. 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 renin-angiotensin-aldosterone system 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, angiotensin II receptor antagonists, non-steroidal anti-inflammatory medicinal products (NSAIDs, including selective COX-2 inhibitors), heparin, immunosuppressives (ciclosporin 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, extensive trauma).
Serum potassium should be monitored closely in these patients.
Effects on ability to drive and use machines
Telmisartan / amlodipine has a moderate influence on the ability to drive and use machines. Patients should be advised that they may experience adverse reactions such as syncope, somnolence, dizziness, or vertigo during treatment. Therefore, caution should be recommended when driving a car or using machines. If patients experience these adverse reactions, they should avoid potentially hazardous tasks.
PREGNANCY AND LACTATION
Pregnancy
The use of telmisartan (angiotensin II receptor antagonists) is not recommended during the first trimester of pregnancy. The use of angiotensin II receptor antagonists is contraindicated during the second and third trimesters of pregnancy.
Studies with telmisartan in animals have shown reproductive toxicity.
The safety of amlodipine in human pregnancy has not been established.
In animal studies, reproductive toxicity was observed at high doses.

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Breast-feeding
Amlodipine is excreted in human milk. The proportion of the maternal dose received by the infant has been estimated with an interquartile range of 3 – 7%, with a maximum of 15%. The effect of amlodipine on infants is unknown.
Because no information is available regarding the use of telmisartan during breast-feeding, telmisartan/amlodipine is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while breast-feeding a newborn or preterm infant.

DRUG INTERACTIONS

Other antihypertensive medicinal products
The blood pressure lowering effect of telmisartan/amlodipine can be increased by concomitant use of other antihypertensive medicinal products.
Medicinal products with blood pressure lowering potential
Based on their pharmacological properties it can be expected that the following medicinal products may potentiate the hypotensive effects of all antihypertensives including this medicinal product, e.g. baclofen, amifostine, neuroleptics or antidepressants. Furthermore, orthostatic hypotension may be aggravated by alcohol.
Corticosteroids (systemic route)
Reduction of the antihypertensive effect.
Interactions linked to telmisartan
Concomitant use not recommended
Potassium sparing diuretics or potassium supplements
Angiotensin II receptor antagonists such as telmisartan, attenuate diuretic-induced potassium loss. Potassium sparing diuretics e.g. spirinolactone, 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.
Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with angiotensin converting enzyme inhibitors, and with angiotensin II receptor antagonists, including telmisartan. If the use of the combination proves necessary, careful monitoring of serum lithium levels is recommended.
Other antihypertensive agents acting on the renin-angiotensin-aldosterone system (RAAS)
Clinical trial data has shown that dual blockade of the RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers, 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 RAAS-acting agent.
Concomitant use requiring caution
Non-steroidal anti-inflammatory medicinal products
NSAIDs (i.e. acetylsalicylic acid at anti-inflammatory dose regimens, COX-2 inhibitors and non-selective NSAIDs) may reduce the antihypertensive effect of angiotensin II receptor antagonists.
In some patients with compromised renal function (e.g. dehydrated patients or elderly patients with compromised renal function), the co-administration of angiotensin II receptor antagonists and medicinal products that inhibit cyclo-oxygenase may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible. Therefore, the combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring of renal function after initiation of concomitant therapy and periodically thereafter.
Ramipril
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 Cmax of ramipril and ramiprilat. The clinical relevance of this observation is not known.
Concomitant use to be taken into account
Digoxin
When telmisartan was co-administered with digoxin, median increases in digoxin peak plasma concentration (49 %) and in trough concentration (20 %) were observed. When initiating, adjusting, and discontinuing telmisartan, monitor digoxin levels in order to maintain levels within the therapeutic range.
Interactions linked to amlodipine
Concomitant use requiring caution
CYP3A4 inhibitors
Concomitant use of amlodipine with strong or moderate CYP3A4 inhibitors (protease inhibitors, azole antifungals, macrolides like erythromycin or clarithromycin, verapamil or diltiazem) may give rise to significant increase in amlodipine exposure resulting in an increased risk of hypotension. The clinical translation of these PK variations may be more pronounced in the elderly. Clinical monitoring and dose adjustment may thus be required.
CYP3A4 inducers
Upon co-administration of known inducers of the CYP3A4, the plasma concentration of amlodipine may vary. Therefore, blood pressure should be monitored and dose regulation considered both during and after concomitant medication particularly with strong CYP3A4 inducers (e.g. rifampicin, hypericum perforatum).
Dantrolene (infusion)
In animals, lethal ventricular fibrillation and cardiovascular collapse are observed in association with hyperkalemia after administration of verapamil and intravenous dantrolene. Due to risk of hyperkalemia, it is recommended that the coadministration of calcium channel blockers such as amlodipine be avoided in patients susceptible to malignant hyperthermia and in the management of malignant hyperthermia.
Grapefruit and grapefruit juice
Administration of telmisartan / amlodipine with grapefruit or grapefruit juice is not recommended since bioavailability may be increased in certain patients resulting in increased blood pressure lowering effects.
Concomitant use to be taken into account
Tacrolimus
There is a risk of increased tacrolimus blood levels when co-administered with amlodipine but the pharmacokinetic mechanism of this interaction is not fully understood. In order to avoid the toxicity of tacrolimus, administration of amlodipine in a patient treated with tacrolimus requires monitoring of tacrolimus blood levels and dose adjustment of tacrolimus when appropriate.
Cyclosporine
No drug interaction studies have been conducted with cyclosporine and amlodipine in healthy volunteers or other populations with the exception of renal transplant patients, where variable trough concentration increases (average 0% - 40%) of cyclosporine were observed. Consideration should be given for monitoring cyclosporine levels in renal transplant patients on amlodipine, and cyclosporine dose reductions should be made as necessary.
Mechanistic Target of Rapamycin (mTOR) Inhibitors
mTOR inhibitors such as sirolimus, temsirolimus, and everolimus are CYP3A substrates. Amlodipine is a weak CYP3A inhibitor. With concomitant use of mTOR inhibitors, amlodipine may increase exposure of mTOR inhibitors.
Simvastatin
Co-administration of multiple doses of 10 mg of amlodipine with simvastatin 80 mg resulted in an increase in exposure to simvastatin up to 77 % compared to simvastatin alone. Therefore, the dose of simvastatin in patients on amlodipine should be limited to 20 mg daily.

ADVERSE EFFECTS

Adverse reactions have been ranked under headings of frequency using the following convention: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).
Infections and infestations: upper respiratory tract infection including pharyngitis and sinusitis, urinary tract infection including cystitis (uncommon); sepsis including fatal outcome, cystitis (rare).
Blood and lymphatic system disorders: anemia (uncommon); thrombocytopenia, eosinophilia (rare); leukocytopenia, thrombocytopenia (very rare).
Immune system disorders: hypersensitivity, anaphylactic reaction (rare); hypersensitivity (very rare).
Metabolism and nutrition disorders: hyperkalemia (uncommon); hypoglycemia in diabetic patients (rare); hyperglycemia (very rare).
Psychiatric disorders: mood change (uncommon); depression, anxiety, insomnia, confusion (rare).
Nervous system disorders: dizziness (common); somnolence, migraine, headache, paraesthesia (uncommon); syncope, peripheral neuropathy, hypoaesthesia, dysgueusia, tremor (rare); extrapyramidal syndrome, hypertonia (very rare).
Eye disorders: visual disturbance (common); visual impairment (uncommon);
Ear and labyrinth disorders: vertigo, tinnitus, bradycardia, palpitations (uncommon); tachycardia (rare); myocardial infarction, arrhythmia, ventricular tachycardia, atrial fibrillation (very rare).
Vascular disorders: hypotension, orthostatic hypotension, flushing (uncommon); vasculitis (very rare).
Respiratory, thoracic, and mediastinal disorders: cough, dyspnea, rhinitis (uncommon); interstitial lung disease (very rare).
Gastrointestinal disorders: altered bowel habits including diarrhea and constipation (common); abdominal pain, nausea, flatulence (uncommon); vomiting, gingival hypertrophy, dyspepsia, dry mouth, stomach discomfort (rare); pancreatitis, gastritis (very rare).
Hepato-biliary disorders: hepatic function abnormal, liver disorder (rare); hepatitis, jaundice, hepatic enzyme elevations mostly consistent with cholestasis (very rare).
Skin and subcutaneous tissue disorders: pruritus, hyperhidrosis, alopecia, purpura, skin discoloration (uncommon); eczema, erythema, rash, angioedema, drug eruption, toxic skin eruption, urticaria (rare); angioedema, erythema multiforme, urticaria, exfoliative dermatitis, Stevens-Johnson syndrome, photosensitivity (very rare); toxic epidermal necrolysis (not known).
Musculoskeletal and connective tissue disorders: ankle swelling (common); arthralgia, muscle spasms (cramps in legs), myalgia (uncommon); back pain, pain in extremity, tendon pain (rare).
Renal and urinary disorders: renal impairment including acute renal failure, micturition disorder, pollakiuria (uncommon); nocturia (rare).
Reproductive system and breast disorders: peripheral oedema (common); asthenia, chest pain, fatigue, oedema, pain (uncommon); malaise, influenza-like illness (rare).
Investigations: hepatic enzymes increased, blood creatinine increased, weight increased, weight decreased (uncommon); blood uric acid increased, blood creatine phosphokinase increased, hemoglobin decreased (rare).

DOSAGE AND ADMINISTRATION

The recommended dose of this medicinal product is one tablet per day or as prescribed by the physician.
The maximum recommended dose is one tablet 80 mg telmisartan/10 mg amlodipine per day. This medicinal product is indicated for long term treatment.
Individual dose titration with the components (i.e. amlodipine and telmisartan) is recommended before changing to the fixed dose combination. When clinically appropriate, direct change from monotherapy to the fixed combination may be considered.
Patients treated with 10 mg amlodipine who experience any dose limiting adverse reactions such as oedema, may be switched to Twincard® 80 mg/10 mg half a tablet once daily, reducing the dose of amlodipine without reducing the overall expected antihypertensive response.
Replacement therapy
Patients receiving telmisartan and amlodipine from separate tablets can instead receive tablets of Twincard® containing the same component doses in one tablet once daily.
Elderly (> 65 years)
No dose adjustment is necessary for elderly patients. Little information is available in very elderly patients.
Renal impairment
Limited experience is available in patients with severe renal impairment or hemodialysis. Caution is advised when using telmisartan/amlodipine in such patients as amlodipine and telmisartan are not dialysable.
No posology adjustment is required for patients with mild to moderate renal impairment.
Hepatic impairment
Twincard® is contraindicated in patients with severe hepatic impairment.
In patients with mild to moderate hepatic impairment, telmisartan/amlodipine should be administered with caution. For telmisartan the posology should not exceed 40 mg once daily.
Pediatric population
The safety and efficacy of telmisartan/amlodipine in children aged below 18 years have not been established.
Method of administration
Oral use.
Twincard® can be taken with or without food. It is recommended to take Twincard® with some liquid.

OVERDOSAGE

Symptoms
Signs and symptoms of overdose are expected to be in line with exaggerated pharmacological effects. The most prominent manifestations of telmisartan overdose are expected to be hypotension and tachycardia; bradycardia, dizziness, increase in serum creatinine, and acute renal failure have also been reported. Overdose with amlodipine may result in excessive peripheral vasodilatation and possibly a reflex tachycardia. Marked and probably prolonged systemic hypotension up to and including shock with fatal outcomes have been reported.
Treatment
The patient should be closely 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 overdose of both telmisartan and amlodipine.
Serum electrolytes and creatinine should be monitored frequently. If hypotension occurs, the patient should be placed in a supine position with an elevation of extremities, with salt and volume replacement given quickly. Supportive treatment should be instituted.
Intravenous calcium gluconate may be beneficial in reversing the effects of calcium channel blockade. Gastric lavage may be worthwhile in some cases. In healthy volunteers, the use of charcoal up to 2 hours after administration of amlodipine 10 mg has been shown to reduce the absorption rate of amlodipine. Telmisartan and Amlodipine are not removed by hemodialysis.

STORAGE CONDITIONS

Store below 30°C
Keep in original pack in intact conditions

Marketing Authorization Holder and Manufacturer:
Benta S.A.L. - Lebanon

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