Bosch

For Medical Professional only

Corace® TABLETS
(Lisinopril)

کوریس ٹیبلیٹس
(لزینوپرل)

DESCRIPTION:
CORACE contains lisinopril, a synthetic peptide derivative, and an oral, long-acting angiotensin converting enzyme inhibitor. Lisinopril is chemically described as (S)-1-[N²-(1-carboxy-3-phenyl propyl)-L-lysyl]-L-proline dihydrate. Its empirical formula is $C_{21}H_{31}N_3O_5 \cdot 2H_2O$, with a molecular weight of 441.52. Lisinopril is a white to off-white, crystalline powder.

COMPOSITION:
Corace 5mg Tablets:
Each tablet Contains:
Lisinopril U.S.P. .....5mg as Lisinopril dihydrate
(Product Specs.: U.S.P.)

Corace 10mg Tablets:
Each tablet Contains:
Lisinopril U.S.P. .....10mg as Lisinopril dihydrate
(Product Specs.: U.S.P.)

Corace 20mg Tablets:
Each tablet Contains:
Lisinopril U.S.P. .....20mg as Lisinopril dihydrate
(Product Specs.: U.S.P.)

CLINICAL PHARMACOLOGY:
Pharmacodynamic Properties:
Pharmacotherapeutic group: Angiotensin-converting enzyme inhibitors, ATC Code: C09A A03

Mechanism of Action:
Lisinopril is a peptidyl dipeptidase inhibitor. It inhibits the angiotensin-converting enzyme (ACE) that catalyses the conversion of angiotensin I to the vasoconstrictor peptide, angiotensin II. Angiotensin II also stimulates aldosterone secretion by the adrenal cortex. Inhibition of ACE results in decreased concentrations of angiotensin II which results in decreased vasopressor activity and reduced aldosterone secretion. The latter decrease may result in an increase in the serum potassium concentration.
While the mechanism through which Lisinopril lowers blood pressure is believed to be primarily suppression of the renin-angiotensin-aldosterone system, Lisinopril is antihypertensive even in patients with low renin hypertension. ACE is identical to Kinase II an enzyme that degrades bradykinin. Whether increased levels of bradykinin, a potent vasodilatory peptide, play a role in the therapeutic effect of Lisinopril remains to be elucidated.

Pharmacokinetic Properties
Absorption:
Lisinopril is an orally active non-sulfhydryl-containing ACE inhibitor. Following oral administration of lisinopril, peak serum concentrations occur within about 7 hours, although there was a trend to a small delay in time taken to reach peak serum concentrations in acute myocardial infarction patients. Based on urinary recovery, the mean extent of absorption of lisinopril is approximately 25% with interpatient variability of 6-60% over the dose range studied (5-80 mg). The absolute bioavailability is reduced approximately 16% in patients with heart failure. Lisinopril absorption is not affected by the presence of food.

Distribution:
Lisinopril does not appear to be bound to serum proteins other than to circulating angiotensin-converting enzyme (ACE). Lisinopril crosses the blood-brain barrier poorly.

Elimination:
Lisinopril does not undergo metabolism and is excreted entirely unchanged into the urine. On multiple dosing, Lisinopril has an effective half-life of accumulation of 12.6 hours. The clearance of lisinopril is approximately 50 ml/min. Declining serum concentrations exhibit a prolonged terminal phase, which does not contribute to drug accumulation. This terminal phase probably represents saturable binding to ACE and is not proportional to dose.

SPECIFIC POPULATIONS
Renal impairment:
Impaired renal function decreases elimination of lisinopril, which is excreted via the kidneys, but this decrease becomes clinically important only when the glomerular filtration rate is below 30 mL/min. In mild to moderate renal impairment (creatinine clearance 30-80 mL/min), mean AUC was increased by 13% only, while a 4.5- fold increase in mean AUC was observed in severe renal impairment (creatinine clearance 5-30 mL/min).
Lisinopril can be removed by dialysis. During 4 hours of haemodialysis, plasma lisinopril concentrations decreased on average by 60%, with a dialysis clearance between 40 and 55 mL/min.

Hepatic impairment:
Impairment of hepatic function in cirrhotic patients resulted in a decrease in lisinopril absorption (about 30% as determined by urinary recovery), but an increase in exposure (approximately 50%) compared to healthy individuals due to decreased clearance.

Pediatrics:
Steady state peak plasma concentrations of lisinopril occurred within 6 hours, and the extent of absorption based on urinary recovery was about 28%.

Elderly:
Elder patients have higher blood levels and higher values for the area under the plasma concentration-time curve (increased approximately 60%).

THERAPEUTIC INDICATIONS:
It is used in the treatment of following.
- Treatment of hypertension.
- Treatment of symptomatic heart failure
- Short-term (6 weeks) treatment of hemodynamically stable patients within 24 hours of an acute myocardial infarction.

- Treatment of renal disease in hypertensive patients with Type 2 diabetes mellitus and incipient nephropathy.

DOSAGE AND ADMINISTRATION:
Lisinopril Tablets should be administered orally in a single daily dose. As with all other medication taken once daily, Lisinopril should be taken at approximately the same time each day. The absorption of Lisinopril Tablets is not affected by food. The dose should be individualised according to patient profile and blood pressure response.

Adults:
Hypertension
The recommended initial dose is 10 mg once a day. Adjust dosage according to blood pressure response. The usual dosage range is 20 to 40 mg per day administered in a single daily dose. Doses up to 80 mg have been used but do not appear to give a greater effect. If blood pressure is not controlled with CORACE alone, a low dose of a diuretic may be added. The recommended starting dose in adult patients with hypertension taking diuretics is 5 mg once per day.

Heart Failure
The recommended starting dose for CORACE, when used with diuretics and (usually) digitalis as adjunctive therapy is 5 mg once daily. The recommended starting dose in these patients with hyponatremia (serum sodium < 130 mEq/L) is 2.5 mg once daily. Increase as tolerated to a maximum of 40 mg once daily. Diuretic dose may need to be adjusted to help minimize hypovolemia, which may contribute to hypotension. The appearance of hypotension after the initial dose of CORACE does not preclude subsequent careful dose titration with the drug, following effective management of the hypotension.

Acute Myocardial Infarction
In hemodynamically stable patients within 24 hours of the onset of symptoms of acute myocardial infarction, give CORACE 5 mg orally, followed by 5 mg after 24 hours, 10 mg after 48 hours and then 10 mg once daily. Dosing should continue for at least 6 weeks. Initiate therapy with 2.5 mg in patients with a low systolic blood pressure (100-120 mmHg) during the first 3 days after the infarct. If hypotension occurs (systolic blood pressure ≤ 100 mmHg) consider doses of 2.5 or 5 mg. If prolonged hypotension occurs (systolic blood pressure <90 mmHg for more than 1 hour) discontinue CORACE.

Pediatric Patients 6 Years of Age and Older with Hypertension:
For pediatric patients with glomerular filtration rate >30 mL/min/1.73 m^2, the recommended starting dose is 0.07 mg/kg once daily (up to 5 mg total). Dosage should be adjusted according to blood pressure response up to a maximum of 0.61 mg/kg (up to 40 mg) once daily. Doses above 0.61 mg/kg (or in excess of 40 mg) have not been studied in pediatric patients.
CORACE is not recommended in pediatric patients <6 years or in pediatric patients with glomerular filtration rate <30 mL/min/1. 73m^2.

Patients with Renal Impairment:
No dose adjustment of CORACE is required in patients with creatinine clearance >30 mL/min. In patients with creatinine clearance 10-30 mL/min, reduce the initial dose of CORACE to half of the usual recommended dose (i.e., hypertension, 5 mg; heart failure or acute MI, 2.5 mg). For patients on hemodialysis or creatinine clearance <10 mL/min, the recommended initial dose is 2.5 mg once daily.

Elderly:
There was no age-related change in the efficacy or safety profile of the drug. The dosage should be adjusted according to the blood pressure response.

CONTRAINDICATIONS:
- Hypersensitivity to Lisinopril, to any of the excipients or any other angiotensin converting enzyme (ACE) inhibitor.
- History of angioedema associated with previous ACE inhibitor therapy.
- Concomitant use of Lisinopril with sacubitril/valsartan therapy. Lisinopril must not be initiated earlier than 36 hours after the last dose of sacubitril/valsartan.
- Hereditary or idiopathic angioedema.
- Second and third trimesters of pregnancy.
- The concomitant use of Lisinopril with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR <60mL/min/1.73 m^2).

WARNINGS AND PRECAUTIONS:
Fetal Toxicity
CORACE can cause fetal harm when administered to a pregnant woman. Use of drugs that act on the renin-angiotensin system 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 CORACE as soon as possible.

Symptomatic hypotension
Symptomatic hypotension is seen rarely in uncomplicated hypertensive patients. In hypertensive patients receiving Lisinopril, hypotension is more likely to occur if the patient has been volume-depleted, e.g. by diuretic therapy, dietary salt restriction, dialysis, diarrhoea or vomiting, or has severe renin-dependent hypertension. In patients with heart failure, with or without associated renal insufficiency, symptomatic hypotension has been observed. This is most likely to occur in those patients with more severe degrees of heart failure, as reflected by the use of high doses of loop diuretics, hyponatraemia or functional renal impairment. In patients at increased risk of symptomatic hypotension, initiation of therapy and dose adjustment should be closely monitored. Similar considerations apply to patients with ischemic heart or cerebrovascular disease in whom an excessive fall in blood pressure could result in a myocardial infarction or cerebrovascular accident. If hypotension occurs, the patient should be placed in the supine position and, if necessary, should receive an intravenous infusion of normal saline. A transient hypotensive response is not a contraindication to further doses, which can be given usually without difficulty once the blood pressure has increased after volume expansion.

In some patients with heart failure who have normal or low blood pressure, additional lowering of systemic blood pressure may occur with Lisinopril. This effect is anticipated and is not usually a reason to discontinue treatment. If hypotension becomes symptomatic, a reduction of dose or discontinuation of Lisinopril may be necessary.

Hypotension in acute myocardial infarction
Treatment with Lisinopril must not be initiated in acute myocardial infarction patients who are at risk of further serious haemodynamic deterioration after treatment with a vasodilator. These are patients with systolic blood pressure of 100 mm Hg or lower, or those in cardiogenic shock. During the first 3 days following the infarction, the dose should be reduced if the systolic blood pressure is 120 mm Hg or lower. Maintenance doses should be reduced to 5 mg or temporarily to 2.5 mg if systolic blood pressure is 100 mm Hg or lower. If hypotension persists (systolic blood pressure less than 90 mm Hg for more than 1 hour) then Lisinopril should be withdrawn.

Aortic and mitral valve stenosis / hypertrophic cardiomyopathy
As with other ACE inhibitors, Lisinopril should be given with caution to patients with mitral valve stenosis and obstruction in the outflow of the left ventricle such as aortic stenosis or hypertrophic cardiomyopathy.

Renal function impairment
In cases of renal impairment (creatinine clearance <80 mL/min), the initial Lisinopril dosage should be adjusted according to the patient's creatinine clearance and then as a function of the patient's response to treatment. Routine monitoring of potassium and creatinine is part of normal medical practice for these patients.

In patients with heart failure, hypotension following the initiation of therapy with ACE inhibitors may lead to some further impairment in renal function. Acute renal failure, usually reversible, has been reported in this situation.

In some patients with bilateral renal artery stenosis or with a stenosis of the artery to a solitary kidney, who have been treated with angiotensin-converting enzyme inhibitors, increases in blood urea and serum creatinine, usually reversible upon discontinuation of therapy, have been seen. This is especially likely in patients with renal insufficiency. If renovascular hypertension is also present, there is an increased risk of severe hypotension and renal insufficiency.

Hypersensitivity/Angioedema
Angioedema of the face, extremities, lips, tongue, glottis and/or larynx has been reported rarely in patients treated with angiotensin-converting enzyme inhibitors, including Lisinopril. This may occur at any time during therapy. In such cases, Lisinopril should be discontinued promptly and appropriate treatment and monitoring should be instituted to ensure complete resolution of symptoms prior to dismissing the patients. Even in those instances where

swelling of only the tongue is involved, without respiratory distress, patients may require prolonged observation since treatment with antihistamines and corticosteroids may not be sufficient. Very rarely, fatalities have been reported due to angioedema associated with laryngeal oedema or tongue oedema. Patients with involvement of the tongue, glottis or larynx, are likely to experience airway obstruction, especially those with a history of airway surgery. In such cases emergency therapy should be administered promptly. This may include the administration of adrenaline and/or the maintenance of a patent airway. The patient should be under close medical supervision until complete and sustained resolution of symptoms has occurred.

Angiotensin-converting enzyme inhibitors cause a higher rate of angioedema in black patients than in non-black patients.

Patients with a history of angioedema unrelated to ACE inhibitor therapy may be at increased risk of angioedema while receiving an ACE inhibitor.

Anaphylactoid reactions
Anaphylactoid reactions have been reported in patients dialysed with high flux membranes (e.g. AN 69) and treated concomitantly with an ACE inhibitor. In these patients, consideration should be given to using a different type of dialysis membrane or different class of antihypertensive agent.

Rarely, patients receiving ACE inhibitors during low-density lipoproteins (LDL) apheresis with dextran sulphate have experienced life-threatening anaphylactoid reactions. These reactions were avoided by temporarily withholding ACE inhibitor therapy prior to each apheresis.

Desensitisation
Patients receiving ACE inhibitors during desensitisation treatment (e.g. hymenoptera venom) have sustained anaphylactoid reactions. In the same patients, these reactions have been avoided when ACE inhibitors were temporarily withheld but they have reappeared upon inadvertent re-administration of the medicinal product.

Hepatic failure
Very rarely, ACE inhibitors have been associated with a syndrome that starts with cholestatic jaundice and progresses to fulminant necrosis and (sometimes) death. The mechanism of this syndrome is not understood. Patients receiving Lisinopril who develop jaundice or marked elevations of hepatic enzymes should discontinue Lisinopril and receive appropriate medical follow-up.

Neutropenia/Agranulocytosis
Neutropenia/agranulocytosis, thrombocytopenia and anaemia have been reported in patients receiving ACE inhibitors. In patients with normal renal function and no other complicating factors, neutropenia occurs rarely. Neutropenia and agranulocytosis are reversible after discontinuation of the ACE inhibitor. Lisinopril should be used with extreme caution in patients with collagen vascular disease, immunosuppressant therapy, treatment with allopurinol or procainamide, or a combination of these complicating factors, especially if there is pre-existing impaired renal function. Some of these patients developed serious infections, which in a few instances did not respond to intensive antibiotic therapy. If Lisinopril is used in such patients, periodic monitoring of white blood cell counts is advised and patients should be instructed to report any sign of infection.

Cough
Cough has been reported with the use of ACE inhibitors. Characteristically, the cough is non-productive, persistent and resolves after discontinuation of therapy. ACE inhibitor-induced cough should be considered as part of the differential diagnosis of cough.

Surgery/anaesthesia
In patients undergoing major surgery or during anaesthesia with agents that produce hypotension, Lisinopril may block angiotensin II formation secondary to compensatory renin release. If hypotension occurs and is considered to be due to this mechanism, it can be corrected by volume expansion.

Hyperkalaemia
ACE inhibitors can cause hyperkalaemia because they inhibit the release of aldosterone. The effect is usually not significant in patients with normal renal function. However, in patients with impaired renal function, diabetes mellitus and/or in patients taking potassium supplements (including salt substitutes), potassium-sparing diuretics (e.g. spironolactone, triamterene or amiloride), other drugs associated with increase in serum potassium (e.g. heparin, trimethoprim or co-trimoxazole also known as trimethoprim/sulfamethoxazole) and especially aldosterone antagonists or angiotensin-receptor blockers, hyperkalaemia can occur. Potassium-sparing diuretics and angiotensin-receptor blockers should be used with caution in patients receiving ACE inhibitors, and serum potassium and renal function should be monitored.
Diabetic patients
In diabetic patients treated with oral antidiabetic agents or insulin, glycaemic control should be closely monitored during the first month of treatment with an ACE inhibitor.

DRUG INTERACTIONS:
Antihypertensive agents
When Lisinopril is combined with other antihypertensive agents (e.g. glyceryl trinitrate and other nitrates, or other vasodilators), additive falls in blood pressure may occur. The dual blockade of the renin-angiotensin-aldosterone system (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, hyperkalaemia and decreased renal function (including acute renal failure) compared to the use of a single RAAS-acting agent.

Medicines increasing the risk of angioedema
Concomitant use of ACE inhibitors with sacubitril/valsartan is contraindicated as this increases the risk of angioedema.

Concomitant treatment of ACE inhibitors with mammalian target of rapamycin (mTOR) inhibitors (e.g. temsirolimus, sirolimus, everolimus) or neutral endopeptidase (NEP) inhibitors (e.g. racecadotril), vildagliptin or tissue plasminogen activator may increase the risk of angioedema.

Diuretics
When a diuretic is added to the therapy of a patient receiving Lisinopril the antihypertensive effect is usually additive.

Patients already on diuretics and especially those in whom diuretic therapy was recently instituted, may occasionally experience an excessive reduction of blood pressure when Lisinopril is added. The possibility of symptomatic hypotension with Lisinopril can be minimised by discontinuing the diuretic prior to initiation of treatment with Lisinopril.

Hyperkalaemia
Although serum potassium usually remains within normal limits, hyperkalaemia may occur in some patients treated with Lisinopril. Use of potassium sparing diuretics (e.g. spironolactone, triamterene or amiloride), potassium supplements or potassium-containing salt substitutes, particularly in patients with impaired renal function, may lead to a significant increase in serum potassium. Care should also be taken when Lisinopril is coadministered with other agents that increase serum potassium, such as trimethoprim and co-trimoxazole (trimethoprim/sulfamethoxazole) as trimethoprim is known to act as a potassium-sparing diuretic like amiloride. Therefore, the combination of Lisinopril with the above-mentioned drugs is not recommended. If concomitant use is indicated, they should be used with caution and with frequent monitoring of serum potassium. If Lisinopril is given with a potassium-losing diuretic, diuretic-induced hypokalaemia may be ameliorated.

Ciclosporin
Hyperkalaemia may occur during concomitant use of ACE inhibitors with ciclosporin. Monitoring of serum potassium is recommended.

Heparin
Hyperkalaemia may occur during concomitant use of ACE inhibitors with heparin. Monitoring of serum potassium is recommended.

Lithium
Reversible increases in serum lithium concentrations and toxicity have been reported during concomitant administration of lithium with ACE inhibitors. Concomitant use of thiazide diuretics may increase the risk of lithium toxicity and enhance the already increased lithium toxicity with ACE inhibitors. Use of Lisinopril with lithium is not recommended, but if the combination proves necessary, careful monitoring of serum lithium levels should be performed.

Medicinal products (NSAIDs) including acetylsalicylic acid ≥ 3 g/day
When ACE-inhibitors are administered simultaneously with non-steroidal anti-inflammatory

drugs (i.e. acetylsalicylic acid at anti-inflammatory dosage regimens, COX-2 inhibitors and non-selective NSAIDs), attenuation of the antihypertensive effect may occur. Concomitant use of ACE-inhibitors and NSAIDs may lead to an increased risk of worsening of renal function, including possible acute renal failure, and an increase in serum potassium, especially in patients with poor pre-existing renal function. These effects are usually reversible. The combination should be administered with caution, especially in the elderly. Patients should be adequately hydrated and consideration should be given to monitoring renal function after initiation of concomitant therapy, and periodically thereafter.

Gold
Nitritoid reactions (symptoms of vasodilatation including flushing, nausea, dizziness and hypotension, which can be very severe) following injectable gold (for example, sodium aurothiomalate) have been reported more frequently in patients receiving ACE inhibitor therapy.

Tricyclic antidepressants / Antipsychotics / Anaesthetics
Concomitant use of certain anaesthetic medicinal products, tricyclic antidepressants and antipsychotics with ACE inhibitors may result in further reduction of blood pressure.

Sympathomimetics
Sympathomimetics may reduce the antihypertensive effects of ACE inhibitors.

Antidiabetics
Concomitant administration of ACE inhibitors and antidiabetic medicines (insulins, oral hypoglycaemic agents) may cause an increased blood glucose-lowering effect with risk of hypoglycaemia. This phenomenon appeared to be more likely to occur during the first weeks of combined treatment and in patients with renal impairment.

Acetylsalicylic acid, thrombolytics, beta-blockers, nitrates
Lisinopril may be used concomitantly with acetylsalicylic acid (at cardiologic doses), thrombolytics, Beta-blockers and/or nitrates.

ADVERSE EFFECTS:
Common:
Dizziness, headache, orthostatic effects (including hypotension), cough, renal dysfunction

Uncommon:
Mood alterations, paraesthesia, vertigo, taste disturbance, sleep disturbances, hallucinations, myocardial infarction or cerebrovascular accident, possibly secondary to excessive hypotension in high risk patients, palpitations, tachycardia, Raynaud's phenomenon, nausea, abdominal pain and indigestion, rash, pruritus, impotence, fatigue, asthenia,

Rare:
Decreases in haemoglobin, decreases in haematocrit, mental confusion, olfactory disturbance, dry mouth, urticaria, alopecia, psoriasis, hypersensitivity/angioneurotic edema: angioneurotic edema of the face, extremities, lips, tongue, glottis, and/or larynx, uraemia, acute renal failure, syndrome of inappropriate antidiuretic hormone secretion (SIADH), gynaecomastia.

Very Rare:
Bone marrow depression, anaemia, thrombocytopenia, leucopenia, neutropenia, agranulocytosis, haemolytic anaemia, lymphadenopathy, autoimmune disease, pancreatitis, intestinal angioedema, hepatitis - either hepatocellular or cholestatic, jaundice and hepatic failure, sweating, pemphigus, toxic epidermal necrolysis, Stevens-Johnson Syndrome, erythema multiforme, cutaneous pseudolymphoma, fever, vasculitis, myalgia, arthralgia/arthritis, positive antinuclear antibodies (ANA), elevated red blood cell sedimentation rate (ESR), eosinophilia and leucocytosis, rash, photosensitivity or other dermatological manifestations, oliguria/anuria.

Not Known:
Anaphylactic/anaphylactoid reaction, depressive symptoms, syncope.
USE IN PREGNANCY AND LACTATION:
Pregnancy:
The use of ACE inhibitors is not recommended during the first trimester of pregnancy. The use of ACE inhibitors is contraindicated during the second and third trimester of pregnancy. When pregnancy is diagnosed, treatment with ACE inhibitors should be stopped immediately, and, if appropriate, alternative therapy should be started.
Exposure to ACE inhibitor therapy during the second and third trimesters is known to induce human fetotoxicity. Infants whose mothers have taken ACE inhibitors should be closely observed for hypotension.

Lactation:
Lisinopril is not recommended and alternative treatments with better established safety profiles during breast-feeding are preferable, especially while nursing a newborn or preterm infant.

OVERDOSE:
Symptoms associated with overdosage of ACE inhibitors may include hypotension, circulatory shock, electrolyte disturbances, renal failure, hyperventilation, tachycardia, palpitations, bradycardia, dizziness, anxiety, and cough.
The recommended treatment of overdose is intravenous infusion of normal saline solution. If hypotension occurs, the patient should be placed in the shock position. If available, treatment with angiotensin II infusion and/or intravenous catecholamines may also be considered. If ingestion is recent, take measures aimed at eliminating Lisinopril (e.g. emesis, gastric lavage, administration of absorbents and sodium sulphate). Lisinopril may be removed from the general circulation by haemodialysis.
Pacemaker therapy is indicated for therapy-resistant bradycardia. Vital signs, serum electrolytes and creatinine concentrations should be monitored frequently.

SHELF LIFE:
3 Years

STORAGE:
Protect from heat, sunlight & moisture.
Store at controlled room temperature (20°C-25°C).
The expiration date refer to the product correctly stored at the required condition.
Keep out of the reach of children.
Patients and healthcare professionals can also report suspected adverse drug reaction at ade@bosch-pharma.com.
To be sold on prescription of a registered medical practitioner only.

PRESENTATION:
Corace 5mg Tablets: Cold Form & Cold Seal (Alu Alu) blister pack of 2x10's.
Corace 10mg Tablets: Cold Form & Cold Seal (Alu Alu) blister pack of 2x10's.
Corace 20mg Tablets: Cold Form & Cold Seal (Alu Alu) blister pack of 2x10's.

ہدایات :
دھوپ، گرمی اور نمی سے محفوظ کمرے کے درجہ حرارت (۲۰۔۲۵ ڈگری سینٹی گریڈ) پر رکھیں۔
بچوں کی پہنچ سے دُور رکھیں۔
صرف مستند ڈاکٹر کے نسخے پر فروخت کے لئے۔

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