NADSAR® H

(Telmisartan/Hydrochlorothiazide)

Tablets U.S.P. 40mg/12.5mg

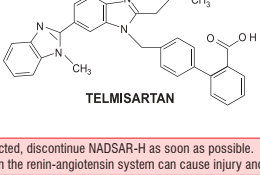
ٹیبلٹس یو۔ایس۔پی۔

۴۰ ملی گرام/۱۲.۵ ملی گرام

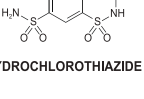
ناڈسار ایچ

(ٹیلمیسارٹن/ہائیڈروکلوروتھیازائیڈ)

DESCRIPTION: NADSAR H is a fixed dose combination of Telmisartan and Hydrochlorothiazide.



TELMISARTAN



HYDROCHLOROTHIAZIDE

QUALITATIVE AND QUANTITATIVE COMPOSITION:
NADSAR H Tablets 40mg/12.5mg U.S.P.
Each Bilayer Tablet Contains:
Telmisartan U.S.P 40mg
Hydrochlorothiazide U.S.P. 12.5mg

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

CLINICAL PHARMACOLOGY: Mechanism of Action: Telmisartan: Telmisartan blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin by selectively blocking the binding of angiotensin to the AT1, receptor in many tissues, such as vascular smooth muscle and the adrenal gland. Its action is therefore independent of the pathways for angiotensin synthesis. **Hydrochlorothiazide:** Hydrochlorothiazide is a thiazide diuretic. Thiazides affect the renal tubular mechanisms of electrolyte reabsorption, directly increasing excretion of sodium salt and chloride in approximately equivalent amounts. Indirectly, the diuretic action of hydrochlorothiazide reduces plasma volume. **Pharmacokinetics: Telmisartan:** Following oral administration, peak concentrations (Cmax) 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 and 160 mg the bioavailability was 42% and 58%, respectively. The pharmacokinetics of orally administered telmisartan are nonlinear over the dose range 20-160 mg, with greater than proportional increases of plasma concentrations (Cmax and AUC) with increasing doses. Telmisartan shows bi-exponential decay kinetics with a terminal elimination half-life of approximately 24 hours. Tough plasma concentrations of telmisartan with once daily dosing are about 10-25% of peak plasma concentrations. Hydrochlorothiazide: When plasma levels have been followed for at least 24 hours, the plasma half-life has been observed to vary between 5.6 and 14.8 hours. **Distribution: Telmisartan:** Telmisartan is highly bound to plasma proteins (> 99.5%), mainly albumin and α1 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. **Hydrochlorothiazide:** Hydrochlorothiazide crosses the placental but not the blood-brain barrier and is excreted in breast milk.

Metabolism And Elimination: Telmisartan: Most of the administered dose (> 97%) was eliminated unchanged in 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 acylglucuronide; the glucuronide of the parent compound is the only metabolite that has been identified in human plasma and urine. 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 appears to be independent of dose. **Hydrochlorothiazide:** Hydrochlorothiazide is not metabolized but is eliminated rapidly by the kidney. At least 61% of the oral dose is eliminated as unchanged drug within 24 hours.

Renal Insufficiency: Telmisartan: No dosage adjustment is necessary in patients with decreased renal function. Telmisartan is not removed from blood by hemofiltration. **Hydrochlorothiazide:** Thiazides should be used with caution in severe renal disease. In patients with renal disease, thiazides may precipitate azotemia. Cumulative effects of the drug may develop in patients with impaired renal function.

HEPATIC INSUFFICIENCY: Telmisartan: In patients with hepatic insufficiency, plasma concentrations of Telmisartan are increased, and absolute bioavailability approaches 100%. **Hydrochlorothiazide:** Thiazide diuretics should be used with caution in patients with hepatic impairment. **GERIATRIC PATIENTS: Telmisartan:** The pharmacokinetics of telmisartan do not differ between the elderly and those younger than 65 year. Use with caution in impaired hepatic function or progressive liver disease since minor alterations of fluid and electrolyte balance or of serum ammonia may precipitate hepatic coma.

INDICATION: NADSAR H (Telmisartan/Hydrochlorothiazide) tablets are indicated for the treatment of hypertension, alone or with other antihypertensive agents. NADSAR H tablets may also be used as initial therapy in patients who are likely to need multiple drugs to achieve their blood pressure goals. Patients with moderate or severe hypertension are at relatively high risk for cardiovascular events (such as strokes, heart attacks, and heart failure), kidney failure, and vision problems, so prompt treatment is clinically relevant.

DOSAGE ADMINISTRATION: The usual starting dose of telmisartan is 40mg once a day; blood pressure response is dose related over the range of 20-80mg. Patients with depletion of intravascular volume should have the condition corrected or telmisartan tablets should be initiated under close medical supervision. Patients with biliary obstructive disorders or hepatic insufficiency should have treatment started under close medical supervision. Hydrochlorothiazide is effective in doses of 12.5mg to 50mg once daily. To minimize dose-independent side effects, it is usually appropriate to begin combination therapy only after a patient has failed to achieve the desired effect with monotherapy. The side effects of telmisartan are generally rare and apparently independent of dose; those of hydrochlorothiazide are a mixture of dose-dependent phenomena (primarily hypokalemia) and dose-independent phenomena (e.g., pancreatitis), the former much more common than the latter. Therapy with any combination of telmisartan and hydrochlorothiazide will be associated with both sets of dose-independent side effects. NADSAR H tablets may be administered with other antihypertensive agents & NADSAR H tablets may be administered with or without food.

SIDE EFFECTS: Telmisartan: Adverse events that occurred in > 0.3% of 3500 patients treated with telmisartan monotherapy in controlled or open trials are, Autonomic Nervous System: impotence, increased sweating, flushing; Body as a Whole: allergy, fever, leg pain, malaise; Cardiovascular:

palpitation, dependent edema, angina pectoris, tachycardia, leg edema, abnormal ECG; CNS: 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; **Metabolic:** gout, hypercholesterolemia, diabetes mellitus; Musculoskeletal: arthritis, arthralgia, leg cramps; **Psychiatric:** anxiety, depression, nervousness; Resistance Mechanism: infection, fungal infection, abscess, otitis media; Respiratory: asthma, bronchitis, rhinitis, dyspnea, epistaxis; **Skin:** dermatitis, rash, eczema, pruritus; Urinary: micturition frequency, cystitis; **Vascular:** cerebrovascular disorder **Special Senses:** abnormal vision, conjunctivitis, tinnitus, earache. **Hydrochlorothiazide:** Other adverse experiences that have been reported with hydrochlorothiazide, without regard to causality, are listed as: Body as a whole: weakness, Digestive: pancreatitis, jaundice (intrahepatic cholestatic jaundice), sialadenitis, cramping, gastric irritation, **Hematologic:** aplastic anemia, agranulocytosis, leukopenia, hemolytic anemia, thrombocytopenia. Hypersensitivity: purpura, photosensitivity, urticaria, necrotizing angiitis (vasculitis and cutaneous vasculitis), fever, respiratory distress including pneumonitis and pulmonary edema, anaphylactic reactions, Metabolic: hyperglycemia, glycosuria, hyperuricemia Musculoskeletal: muscle spasm, **Nervous System/Psychiatric:** restlessness, Renal: renal failure, renal dysfunction, interstitial nephritis, **Skin:** erythema multiforme including Stevens-Johnson syndrome, exfoliative dermatitis including toxic epidermal necrolysis, Special Senses: transient blurred vision, xanthopsia.

DRUG INTERACTION: Telmisartan: Digoxin: When telmisartan was coadministered with digoxin, median increases in digoxin peak plasma concentration (49%) and in trough concentration (20%) were observed. It is, therefore, recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing telmisartan to avoid possible over- or under-digitalization. Warfarin: Telmisartan administered for 10 days slightly decreased the mean warfarin trough plasma concentration; this decrease did not result in a change in International Normalized Ratio (INR). Other Drugs: Coadministration of telmisartan did not result in a clinically significant interaction with acetaminophen, amlodipine, glibenclamide, simvastatin, hydrochlorothiazide 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. **Hydrochlorothiazide:** When administered concurrently, the following drugs may interact with thiazide diuretics: Alcohol, barbiturates, or narcotics: Potentiation of orthostatic hypotension may occur. Antidiabetic drugs (oral agents & insulin): Dosage adjustment of the antidiabetic drug may be required. Other antihypertensive drugs: Additive effect or potentiation. Cholestyramine & colestipol resins: Absorption of hydrochlorothiazide is impaired in the presence of anionic exchange resins. Single doses of either cholestyramine or colestipol resins bind the hydrochlorothiazide and reduce its absorption from the gastrointestinal tract by up to 85% and 43%, respectively. Corticosteroids, ACTH: Intensified electrolyte depletion, particularly hypokalemia. Pressor amines (e.g., norepinephrine): Possible decreased response to pressor amines but not sufficient to preclude their use. Skeletal muscle relaxants, nondepolarizing (e.g., tubocurarine): Possible increased responsiveness to the muscle relaxant. Lithium: Should not generally be given with diuretics. Diuretic agents reduce the renal clearance of lithium and add a high risk of lithium toxicity. Non-steroidal anti-inflammatory drugs: In some patients, the administration of a non-steroidal antiinflammatory agent can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing and thiazide diuretics. Therefore, when Telmisartan/ Hydrochlorothiazide and non-steroidal anti-inflammatory agents are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.

PRECAUTIONS: Pregnancy: Teratogenic Effects, Pregnancy Category D drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature in patients who were taking angiotensin converting enzyme inhibitors. When pregnancy is detected, discontinue telmisartan/hydrochlorothiazide combination as soon as possible. **NURSING MOTHERS: Telmisartan:** 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, decide whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother. **Hydrochlorothiazide:** Thiazides appear in human milk. 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:** Safety and effectiveness in pediatric patients have not been established.

OVER DOSAGE: Telmisartan: Limited data are available with regard to overdosage in humans. The most likely manifestations of overdosage with telmisartan tablets would be hypotension, dizziness, and tachycardia; bradycardia could occur from parasympathetic (vagal) stimulation. If symptomatic hypotension should occur, supportive treatment should be instituted. **Hydrochlorothiazide:** The most common signs and symptoms observed in patients are those caused by electrolyte depletion (hypokalemia, hypochloremia, hyponatremia) and dehydration resulting from excessive diuresis. If digitalis has also been administered, hypokalemia may accentuate cardiac arrhythmias. The degree to which hydrochlorothiazide is removed by hemodialysis has not been established.

CONTRAINDICATION: None

INSTRUCTIONS: Dosage as directed by the physician. Store at 20°C-25°C, Excursions permitted to 15°C to 30°C. Protect from heat, light and moisture. Keep all medicines out of the reach of children.

PRESENTATION: NADSAR H Tablets are available in Alu-Alu blister pack of 1x14's with leaflet.

ہدایات :

خوراک ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔
۲۰ سے ۲۵ ڈگری سینٹی گریڈ پر محفوظ رکھیں،
محفوظ رکھنے کی حد ۱۵ سے ۳۰ ڈگری سینٹی گریڈ ہے۔
گرمی، روشنی اور نمی سے محفوظ رکھیں۔
تمام دوائیں بچوں کی پہنچ سے دور رکھیں۔

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