DILTIAZEM HYDROCHLORIDE

NOVOPTIN

30mg TABLET

℞

CALCIUM CHANNEL BLOCKER

FORMULATION:
Each tablet contains:
Diltiazem Hydrochloride 30mg

DESCRIPTION:
Diltiazem Hydrochloride belongs to a group of medicines known as calcium channel blockers or calcium antagonists.
NOVOPTIN is white to off - white, round, convex, one side scored tablet. In blister pack of 20's (Box of 100's).

WHAT IS IN THE MEDICINE?
Diltiazem is a white, odorless, crystalline powder, or small crystals. Freely soluble in water, in chloroform, in formic acid, and in methyl alcohol; sparingly soluble in dehydrated alcohol; insoluble in ether.
Diltiazem (NOVOPTIN) hydrochloride belongs to a group of medicines called calcium channel blockers (which interfere with the movement of calcium in heart muscle cells). These medicines work to lower blood pressure and ease anginal chest pain by preventing the narrowing of blood vessels.

STRENGTH OF THE MEDICINE: See Formulation

WHAT IS NOVOPTIN TABLET USED FOR?
Oral:
Unstable Angina Pectoris including Angina Due to Coronary Artery Spasm or Following Myocardial Infarction:
Diltiazem is indicated for the treatment of angina pectoris due to coronary artery spasm.
Diltiazem has been shown to be effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
Chronic Stable Angina (Classic Effort-associated Angina): Diltiazem (NOVOPTIN) is indicated for the management of chronic stable angina in patients who cannot tolerate therapy with beta-blockers and/ or nitrates or who remain symptomatic despite adequate doses of these agents.
Hypertension: Diltiazem is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive medications, such as diuretics.
Kidney Transplantation : Diltiazem is indicated for the prevention of graft failure following kidney transplantation. Diltiazem is indicated for the reduction of ciclosporin A nephrotoxicity during immunosuppressive therapy after kidney transplantation.

HOW MUCH AND HOW OFTEN SHOULD YOU USE THIS MEDICINE?
Oral:
Ischemic Heart Disease (Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm):
The initial dose is 120 mg/day in equally divided doses, administered preferably before meals, and at bedtime; dosage should be increased gradually in equally divided doses (two to four times daily) at 1- to 2-day intervals until optimum response is obtained. The optimum dosage range appears to be 180 mg/day to 360 mg/day. Doses up to 480 mg/day may be administered in some cases.
Hypertension:
Dosages must be adjusted to each patient's needs. The initial dose is 120 mg/day to 240 mg/day in equally divided doses, administered preferably before meals, and at bedtime. Maximum antihypertensive effect is usually observed at 14 days of chronic therapy; therefore, dosage adjustments should be scheduled accordingly. The usual dosage range is 240 mg/day to 360 mg/day.
There is an additive antihypertensive effect when diltiazem is used with other antihypertensive agents. Therefore, the dosage of diltiazem or the concomitant antihypertensive(s) may need to be adjusted when adding one to the other.
Kidney Transplantation:
The initial dose is 120 mg/day in two equally divided doses. Depending on the patient's blood pressure, dosage may be increased up to a maximum of 360 mg/day given in three equally divided doses. The optimum dosage range appears to be 180 mg/day to 360 mg/day.
Concomitant Use With Other Cardiovascular Agents:
Nitroglycerin Therapy: Sublingual nitroglycerin (NTG) may be taken as required to abort acute anginal attacks during diltiazem therapy.
Prophylactic Nitrate Therapy: Although there have been no controlled studies to evaluate the anti-anginal effectiveness of this combination, diltiazem may be co-administered with short- and long-acting nitrates.
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Special Populations:
Use in Renal Impairment: There are no available data concerning dosage requirements in patients with impaired renal function. If the drug must be used in such patients, titration should be done cautiously.

WHEN SHOULD YOU NOT TAKE THIS MEDICINE?
Do not take **NOVOPTIN** tablets if you have an allergy to:
Diltiazem and other calcium channel blockers.
Symptoms of an allergic reaction to **NOVOPTIN** tablets may include:
Shortness of breath, wheezing or difficulty breathing in swelling, of the face, lips, tongue or other parts of the body . Rash, itching or hives of the skin.
Do not take **NOVOPTIN** tablets if you are pregnant
Do not take **NOVOPTIN** tablets if the packaging is torn or shows signs of tampering or if the tablets show visible signs of deterioration.
Do not take NOVOPTIN tablets after the expiry date printed on the pack .

CARE THAT SHOULD BE TAKEN WHEN TAKING THIS MEDICINE?
Cardiac Conduction: Diltiazem prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second - or third-degree AV block. Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction.
Congestive Heart Failure: Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in either cardiac index or in consistent negative effects on contractility (dp/dt). Experience with diltiazem used alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
Hypotension: Decreases in blood pressure associated with diltiazem therapy may occasionally result in symptomatic hypotension.
Acute Hepatic Injury : In rare instances, significant elevations in enzymes such as alkaline phosphatase, lactate dehydrogenase (LDH), serum glutamic oxaloacetic transaminase (SGOT), serum glutamic-pyruvic transaminase (SGPT), and other phenomena consistent with acute hepatic injury have been noted. These reactions have been reversible upon discontinuation of drug therapy.
Laboratory Monitoring:
Diltiazem hydrochloride is extensively metabolized by the liver and excreted by the kidneys and in the bile. As with any drug given over prolonged periods, laboratory parameters should be monitored at regular intervals.
General:
Dermatological events may be transient and may disappear despite continued use of diltiazem. However, skin eruptions progressing to erythema multiforme and/or exfoliative dermatitis (Epidermal necrolysis) have also been infrequently reported. Should a dermatological reaction persist, the drug should be discontinued.

UNDESIRABLE EFFECTS:
Tell your doctor immediately if you notice any of the following:
swelling of extremities such as ankles or fingers, headache and dizziness, stomach discomfort with nausea and vomiting, rash and tiredness, skin reactions, unusual heart rhythm,chest pain, shortness of breath, blurred vision, painful muscles

WHAT OTHER MEDICINE OR FOOD SHOULD BE AVOIDED WHILE TAKING THIS MEDICINE?
Tell your doctor if you are taking any other medicines, including medicines that you buy without a prescription from your pharmacy, supermarket or health food shop. Some medicines may interfere with **NOVOPTIN** tablets. These include:
beta-blockers - medicines used to treat disorders of the heart and blood vessels such as high blood pressure, angina and cardiac arrhythmia
digoxin - a medicine used to treat a certain type of cardiac arrhythmia
cimetidine - a medicine used to treat reflux and stomach ulcers
diazepam - a medicine used to treat anxiety
cyclosporin - a medicine used to suppress the immune system
amiodarone - a medicine used to treat a certain type of cardiac arrhythmia
carbamazepine - a medicine used to treat seizures
enflurane - an inhaled anaesthetic
nitroglycerin - a medicine used to treat angina, heart failure and heart attacks
theophylline - a medicine used to treat asthma
grapefruit - grapefruit should be avoided or not consumed less than 10 hours before or 2 hours after taking **NOVOPTIN** 30 mg.
Your doctor and pharmacist may have more information on medicines to be careful with or avoid while taking this medicine.

WHAT SHOULD YOU DO IF YOU MISS A DOSE?
If it is almost time for your next dose, skip the dose you missed and take your next dose when you are meant to. Otherwise, take it as soon as you remember and then go back to taking it as you would normally.
Do not take a double dose to make up for the dose that you missed. If you are not sure what to do, ask your doctor or pharmacist.

SIGNS AND SYMPTOMS OF OVERDOSE
An overdose may lead to severe low blood pressure leading to collapse, and a slow heart beat which may be accompanied by changes in heart rhythm and conduction.
Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive medical care should be employed in addition to gastric lavage.
The following measures may be considered.
Bradycardia: Administer atropine (0.60-1.0 mg); if there is no response to vagal blockade, cautiously administer isoproterenol
High-Degree AV Block: Treat as for bradycardia above; fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure: Administer inotropic agents (isoproterenol dopamine or dobutamine) and diuretics.
Hypotension: Administer vasopressors (e.g., dopamine or levarterenol bitartrate). Actual treatment and dosage should depend on the severity of the clinical situation.

WHAT TO DO WHEN YOU HAVE TAKEN MORE THAN THE RECOMMENDED DOSAGE?
Immediately telephone a doctor, or the Poisons Information Center or go to the accident and Emergency Department at your nearest hospital, if you think you or anyone else may have taken too many NOVOPTIN tablets. Do this even if there are no signs of discomfort or poisoning.

Pharmacology: Pharmacodynamics:
The therapeutic benefits achieved with diltiazem are believed to be related to its ability to inhibit the influx of calcium ions during membrane depolarization of cardiac and vascular smooth muscle.
Mechanism of Action:
Although precise mechanisms of its antianginal actions are still being delineated, diltiazem is believed to act in the following ways:
Angina Due to Coronary Artery Spasm:
Diltiazem has been shown to be a potent dilator of both epicardial and subendocardial coronary arteries. Spontaneous and ergonovine-induced coronary artery spasm are inhibited.
Exertional Angina:
Diltiazem has been shown to produce increases in exercise tolerance, probably due to its ability to reduce myocardial oxygen demand. This is accomplished via reductions in heart rate and systemic blood pressure at submaximal and maximal exercise work loads.
Hypertension:
The antihypertensive effect of diltiazem is achieved primarily by relaxation of vascular smooth muscle and the resultant decrease in peripheral vascular resistance. The magnitude of blood pressure reduction is related to the degree of hypertension; thus, hypertensive individuals experience an antihypertensive effect, whereas there is only a modest fall in blood pressure in normotensive individuals.
In animal models, diltiazem interferes with the slow inward (depolarizing) current in excitable tissue. It causes excitation-contraction uncoupling in various myocardial tissues without changes in the configuration of the action potential. Diltiazem produces relaxation of coronary vascular smooth muscle and dilation of both large and small coronary arteries at drug levels that cause little or no negative inotropic effect. The resultant increases in coronary blood flow (epicardial and subendocardial) occur in ischemic and non-ischemic models and are accompanied by dose-dependent decreases in systemic blood pressure and decreases in peripheral resistance.
Hemodynamic and Electrophysiologic Effects:
Like other calcium antagonists, diltiazem decreases sinoatrial and AV conduction in isolated tissues and has a negative inotropic effect in isolated preparations. In the intact animal, prolongation of the AH interval can be seen at higher doses.
In man, diltiazem prevents spontaneous and ergonovine-provoked coronary artery spasm. It causes a decrease in peripheral vascular resistance and a modest fall in blood pressure and, in exercise tolerance studies in patients with ischemic heart disease, reduces the heart rate/blood pressure product for any given workload. Studies to date, primarily in patients with good ventricular function, have not revealed evidence of a negative inotropic effect; cardiac output, ejection fraction, and left ventricular end-diastolic pressure have not been affected. Resting heart rate is usually unchanged or slightly reduced by diltiazem. Intravenous diltiazem in doses of 20 mg prolongs AH conduction time and AV node functional and effective refractory periods by approximately 20%. Diltiazem-associated prolongation of the AH interval is not more pronounced in patients with first-degree heart block. In patients with sick sinus syndrome, diltiazem significantly prolongs sinus cycle length (up to 50% in some cases).
Chronic oral administration in doses of up to 360 mg/day has resulted in small increases in PR interval, but has not usually produced abnormal prolongation.
Diltiazem produces antihypertensive effects in both the supine and standing positions. Postural hypotension is infrequently noted upon suddenly assuming an upright position. No reflex tachycardia is associated with chronic antihypertensive effects. Diltiazem decreases vascular resistance, increases cardiac output (by increasing stroke volume), and produces a slight decrease or no change in heart rate. During dynamic exercise, increases in diastolic pressure are inhibited while maximum achievable systolic pressure is usually reduced. Heart rate at maximum exercise does not change or is slightly reduced. Chronic therapy produces no change or an increase in plasma catecholamines. No increased activity of the renin-angiotensin-aldosterone axis has been observed.

Pharmacokinetic Properties
Absorption:
Diltiazem is subject to an extensive first-pass effect, giving an absolute bioavailability (compared to IV dosing) of about 40%. Single oral doses of 30 mg to 120 mg result in detectable plasma levels within 30 to 60 minutes and peak plasma levels 2 to 3 hours after drug administration. There is a departure from dose linearity when single doses of diltiazem above 60 mg are given; a 120 mg dose gave plasma levels three times that of the 60 mg dose.
Distribution:
In vitro studies have shown that 70% to 80% of diltiazem is bound to plasma proteins. Competitive ligand-binding studies also have shown that binding is not altered by therapeutic concentrations of digoxin , hydrochlorothiazide, phenylbutazone, propranolol, salicylic acid, or warfarin. Therapeutic plasma levels of diltiazem appear to be in the range of 50 ng/mL to 200 ng/mL.
Metabolism:
Diltiazem undergoes extensive hepatic metabolism and undergoes biotransformation by cytochrome P-450 (CYP) 3A4; therefore, only 2% to 4% of the unchanged drug appears in the urine. In cases of serious liver damage, delayed biotransformation may be anticipated. Desacetyldiltiazem is also present in the plasma at levels of 10% to 20% of the parent drug and is 25% to 50% as potent a coronary vasodilatory as diltiazem.
Excretion:
The plasma elimination half-life following single- or multiple-drug administration is approximately 3.5 hours.

HOW SHOULD YOU KEEP THI MEDICINE?
Store at temperatures not exceeding 30°C
Keep the product out of sight and reach of children
Protect from heat, light and moisture

WHEN SHOULD YOU CONSULT YOUR DOCTOR?
* If any undesirable effects occurs.
* If you are pregnant or breastfeeding, consult a doctor before using the product.

STORE AT ROOM TEMPERATURES NOT EXCEEDING 30°C

AVAILABILITY:
Alu/PVC Clear Blister Pack of 20's (Box of 100's)

SHELF-LIFE 36 Months

Date of Revision : 07 February 2020

DR No. :

Manufactured by:
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