Active ingredient: nifedipine

1. WHAT IS ADALAT 20 MG RETARD AND WHAT IS IT USED FOR?
Adalat 20 mg retard is a medicine for the treatment of heart diseases which are accompanied by an insufficient supply of oxygen to the cardiac muscle and for the treatment of high blood pressure.

Adalat 20 mg retard is used when the patient experiences:
- complaints (e.g. pain or feelings of feeling of constriction in the chest area) in conjunction with conditions involving an insufficient supply of oxygen to the cardiac muscle in exertion situations: chronic stable angina pectoris (exertion angina)
- non-organ-related high blood pressure

2. WHAT DO YOU NEED TO BE AWARE OF BEFORE ADMINISTRATION OF Adalat 20 mg retard?
Adalat 20 mg may not be taken:
- if you are hypersensitive (allergic) to nifedipine or to one of the other excipients of Adalat 20 mg retard
- if you have suffered a shock
- if you suffer from a cardiac valve constriction (aortic stenosis)
- if you suffer from complaints (e.g. pain or feelings of feeling of constriction in the chest area) while at rest in conjunction with conditions involving an insufficient supply of oxygen to the cardiac muscle (unstable angina pectoris):
- if you have suffered an acute heart attack within the last 4 weeks
- if you are currently being administered drugs containing the active ingredient rifampicin (drug against tuberculosis)
- if you are pregnant, up to the 20th week of pregnancy
- if you are breast-feeding

Special caution is required with the administration of Adalat 20 mg retard:
Treatment with Adalat 20 mg retard requires regular monitoring on the part of the physician

- if you have low blood pressure (systolic less than 90 mmHg)
- if your are suffering from an insufficiently treated cardiac muscle weakness (decompensated cardiac insufficiency)
- if you are a dialysis patient with extremely high blood pressure and diminished amounts of blood in circulation, because a pronounced drop in blood pressure could occur
- if you are pregnant (see Section 2 “Pregnancy and lactation”)

A particular enzyme system (cytochrome P450 3A4) participates in the breaking down of nifedipine, the active ingredient in Adalat 20 mg retard. This enzyme system could be inhibited or reinforced by other drugs. The actions and side effects of Adalat 20 mg retard could be modified as a result (see Section 2 “Using Adalat 20 mg retard with other drugs”)

If you take Adalat 20 mg retard simultaneously with other drugs which inhibit this enzyme system, this could lead not only to an increase in the effects of Adalat 20 mg retard, but also to an increase in its side effects. Included among such drugs are the following, for example:

- certain antibiotics (e.g. erythromycin)
- certain anti-HIV drugs (e.g. ritonavir)
- certain drugs against fungal infections (e.g. ketoconazole)
- nefazodone and fluoxetine (agents against abnormally melancholy moods, antidepressants)
- quinupristin/dalfopristin (antibiotics)
- valproic acid (agent against epilepsy)
- cimetidine (agent against stomach and intestinal ulcers)

If Adalat 20 mg retard is taken simultaneously with one of these drugs, then blood pressure should be monitored and, if necessary, the possibility of reducing the dosage of Adalat 20 mg retard should be taken into consideration.

The breakdown of nifedipine may be delayed among patients with limited liver function. The doctor will...
therefore carefully monitor the course of treatment and reduce the dosage if this appears to be required.

This drug contains lactose. Please no not begin taking Adalat 20 mg retard until after you have consulted your physician if you know that you suffer from an intolerance to certain sugars.

Children
Adalat 20 mg retard is not recommended for administration to children because of the absence of data concerning harmlessness and efficacy.

Taking Adalat 20 mg retard with other drugs:
Please inform your physician or your pharmacist if you are taking or applying other medicinal products and/or have taken or applied them recently, even if they were ones that did not require a prescription.

Which other drugs have an influence on the effect of Adalat 20 mg retard?
A particular enzyme system (cytochrome P450 3A4) participates in the breaking down of nifedipine, the active ingredient in Adalat 20 mg retard. It is therefore possible that the simultaneous administration of drugs which have an influence on this enzyme system could in principle lead to interactions between these drugs and Adalat 20 mg retard.

Both the extent and the duration of the interactions should be taken into account if Adalat 20 mg retard is to be administered together with the drugs listed below.

Weakening of the effect of Adalat 20 mg retard by other drugs:
- phenytoin (active ingredient for the treatment of arrhythmias and epilepsy): Weakening of the efficacy of Adalat 20 mg retard. In the event of simultaneous administration of the two drugs, the reaction to nifedipine (active ingredient in Adalat 20 mg retard) should be observed and the possibility of increasing the dosage of Adalat 20 mg retard should be taken into consideration. The dosage of Adalat 20 mg retard may then also need to be readjusted again after discontinuation of the administration of phenytoin.
- carbamazepine and phenobarbital (active ingredients for the treatment of epilepsy): Simultaneous administration with Adalat 20 mg retard could lead to a weakening of the action of Adalat 20 mg retard.
- rifampicin (agent against tuberculosis): leads to an accelerated breakdown of nifedipine (active ingredient in Adalat 20 mg retard) in the body. Rifampicin may not be administered simultaneously during treatment with Adalat 20 mg retard because no effective levels of nifedipine will be reached in the blood (see also Section 2 “Adalat 20 mg retard may not be taken”).

Intensification of the Adalat 20 mg retard effects and side effects by other drugs:
If you take Adalat 20 mg retard simultaneously with the following other drugs, then your blood pressure should be monitored and, if necessary, a reduction of the Adalat 20 mg retard dosage should be taken into consideration (see also “Special caution is required with the administration of Adalat 20 mg retard”):
- certain antibiotics (e.g. erythromycin)
- fluoxetine and nefazodone (agents against abnormally melancholy moods, antidepressants)
- ritonavir (anti-HIV drug)
- certain drugs against fungal infections (e.g. ketoconazole)
- quinupristin/dalfopristin (antibiotics)
- cimetidine (agent against stomach and intestinal ulcers)
- valproic acid (agent against epilepsy)
- tricyclic antidepressants (drugs against depression)
- vasodilators (drugs for increasing the size of blood vessels)

How does Adalat 20 mg retard affect the action of other drugs?
Hypotensive drugs:
The hypotensive action of other drugs of various active ingredient groups can be enhanced by Adalat 20 mg retard, e.g. by:
- diuretics (agents for increasing urination)
- beta-receptor blockers (drugs against high blood pressure)
- ACE inhibitors (drugs against high blood pressure)
- angiotensin-receptor antagonists (drugs against high blood pressure)
- other calcium antagonists (drugs against high blood pressure)
- alpha-receptor blockers (drugs against high blood pressure and cardiac output deficiency)
- PDE 5 inhibitors (drugs for the treatment of erectile dysfunction)
- alpha-methyldopa (drugs against high blood pressure)

Simultaneous treatment with beta-receptor blockers (active ingredient group of hypotensive agents) could occasionally lead to signs of cardiac output deficiency in isolated cases. Your physician will monitor the course of treatment carefully in such cases.

- digoxin (active ingredient for enhancing cardiac strength),
- theophylline (active ingredient for expanding the bronchi): the concentrations of these drugs in the blood may increase. One should watch for signs of a digoxin overdose and, if necessary, the digoxin dosage should be reduced by the physician (in accordance with the determination of the digoxin concentration in the blood).
- vincristine (active ingredient for the treatment of tumors): The excretion of vincristine will be reduced, leading to a situation where the side effects of vincristine could increase. Your physician may possibly prescribe a reduction of the vincristine dosage.
- cephalosporins (active ingredients for the treatment of infections): The cephalosporin concentration in the blood may be elevated.
- quinidine (active ingredient for the treatment of arrhythmias): In isolated cases, the administration of Adalat 20 mg retard may cause a drop in the quinidine content of the blood, while discontinuation of Adalat 20 mg retard may cause a noticeable increase in the quinidine content of the blood (monitoring checkups of the quinidine content in blood!). Other cases have also been reported of an increase in the nifedipine concentration in the blood caused by quinidine. It is therefore recommended that blood pressure be monitored closely in cases where both drugs are being administered simultaneously. Depending on the circumstances, the dosage of Adalat 20 mg retard may need to be reduced.
- tacrolimus (active ingredient for the prevention of transplant rejection, e.g. following liver or kidney transplantations): Elevated blood levels of tacrolimus could occur in the presence of simultaneous administration of Adalat 20 mg retard, which means that the tacrolimus dosage should be reduced in individual cases. Regular monitoring of the blood levels of tacrolimus is recommended.

Taking Adalat 20 mg retard together with food and beverages:
The hypotensive action of Adalat 20 mg retard may be enhanced by grapefruit juice. This effect continues for at least three days after the last time grapefruit juice enters the patient’s system. The eating of grapefruit and the drinking of grapefruit juice should therefore be avoided during the time constraints connected with the Adalat 20 mg retard treatment (see also Section No. 3 «Type of application»).

Pregnancy and lactation
You may not take Adalat 20 mg retard during the entire first 20 weeks of a pregnancy, because experimental studies have revealed indications of fetal damage in connection with the active ingredient nifedipine. Sufficient experience with humans is not available. If the presence of a pregnancy is determined during treatment with Adalat 20 mg retard, then the treatment must be revised in consultation with a physician. Adalat 20 mg retard may be taken after the 20th week of pregnancy, following careful weighing of benefits and risks, in the event that other treatment options either do not come into question or if they have proven themselves to be ineffective.

In isolated cases, a connection was made between the administration of nifedipine or similar active ingredients and the impairment of sperm function in cases of artificial fertilization involving the retransfer of the fertilized egg cell into the uterus.

If treatment Adalat 20 mg retard is necessary while breast-feeding, then the baby should be weaned
from the breast in view of the fact that nifedipine (the active ingredient in Adalat 20 mg retard) migrates into the mother’s milk and no experience is available concerning possible effects on the infant.

**Driving and using machines:**
Treatment with this drug requires regular monitoring on the part of the physician. Individual responses to the drug may vary widely, altering reaction capability to such an extent that the ability to participate actively in road traffic, to operate machinery or to work without secure support may be impaired. This effect is even more pronounced at the time treatment starts, when dosages are increased, when there is a change of preparation and in conjunction with alcohol.

**Important information concerning certain excipients of Adalat 20 mg retard**
This drug contains lactose. Please note the instruction contained in the Section «Special caution is required with the administration of Adalat 20 mg retard»

**3. HOW SHOULD Adalat 20 mg retard BE TAKEN?**
Always take Adalat 20 mg retard precisely in accordance with your doctor’s instructions. Please consult your physician or pharmacist if you are not completely sure.

Treatment should be carried out on an individualized basis as much as possible in accordance with the degree of severity of the disease and the response of the patient.

The suggested dosage should be built up to gradually, depending on the respective clinical picture. Patients with limited liver function should be monitored closely; a reduction in dosage may be necessary.

The Adalat 20 mg retard dosage may need to be adjusted in the event of simultaneous administration of other drugs which inhibit or enhance a certain enzyme system (cytochrome P450 3A4) (see also Section 2 “Taking Adalat 20 mg retard with other drugs”).

High-pressure patients with severely impaired perfusion of the brain (cerebrovascular disease) should be treated with a lower dosage strength (nifedipine time-release tablets with 10 mg active ingredient). Individual adjustments of nifedipine time-release tablets with 10 mg of the active ingredient should be also be made for patients whose side effects from the nifedipine treatment would make it appear that more precise dosage increments would be desirable.

It is recommended that a time interval of 12 hours (not less than 4 hours, however) be observed between individual dosages of Adalat 20 mg retard.

**Dosage**
Unless otherwise prescribed, the usual dosage for adults is:

**Coronary heart disease**
1 time-release tablet of Adalat 20 mg retard 2 times daily (corresponding to 40 mg of nifedipine per day).
If higher dosages are necessary, then an incremental increase of the dosage to 40 mg 2 times daily is possible.

**High blood pressure**
1 time-release tablet of Adalat 20 mg retard 2 times daily (corresponding to 40 mg of nifedipine per day).
If higher dosages are necessary, then an incremental increase of the dosage to 40 mg 2 times daily is possible.

**Type of application**
To be taken orally.
Adalat 20 mg retard is to be taken after meals, unchewed and with sufficient fluid (e.g. a glass of water) - always best taken at the same time of day. Adalat 20 mg retard may not be taken together with grapefruit juice (see also Section 2 “Taking Adalat 20 mg retard together with food and beverages”).
As a rule, the time-release tablets are taken after meals.
Because of the sensitivity to light of the active ingredient nifedipine, the time-release tablets should not be cut into pieces, because then the protection against light afforded by the color-coating is no longer ensured.

**Duration of administration:**
The duration of the administration is determined by the attending physician.
Possible side effects:

**Blood and lymphatic system**
Rare: Changes of the blood picture such as reduction of red or white blood corpuscles and/or blood platelets (anemia, leukopenia, thrombopenia), skin and mucous membrane bleeding with reduced numbers of blood platelets (thrombocytopenic purpura).
Very rare: High-grade reduction of certain white blood corpuscles (agranulocytosis).

**Metabolic and nutritional disorders**
Rare: Elevation of blood sugar levels (hyperglycemia).

**Nervous system**
Very common: Headache, particularly at the beginning of treatment.
Common: Vertigo, stupor, feeling of weakness.
Occasional: nervousness, sleep disturbances or somnolence, paresthesias (e.g. prickling of the skin, furry sensation), diminished perception of contact stimuli (hypoesthesias), muscle trembling (tremor).

**Eyes**
Occasional: Slight, temporary change in visual perception.
Rare: Weak-sightedness.

**Cardiovascular system**
Very common: Fluid retention, e.g. in the lower legs caused by an expansion of the blood vessels (peripheral edemas), particularly at the beginning of the treatment.
Common: Heart palpitations.
Occasional: Chest pain, elevation of pulse frequency (tachycardia), brief periods of fainting (syncope), drop in blood pressure (hypotonic circulatory system reaction). Attacks of angina pectoris can occur, particularly at the beginning of the treatment; attacks may increase in terms of frequency, duration and severity among patients with existing angina pectoris.
Very rare: Heart attack.

**Lung**
Occasional: Difficult breathing (dyspnea).

**Skin**
Common: reddening of the face (flush), erubescence with sensation of heat (erythema), painful swelling

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<thead>
<tr>
<th>Frequency</th>
<th>Description</th>
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<tbody>
<tr>
<td>Very common</td>
<td>Occurring in more than 1 in 10 treated patients</td>
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<tr>
<td>Common</td>
<td>Occurring in fewer than 1 in 10, but occurring in more than 1 in 100 treated patients,</td>
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<td>Occasional</td>
<td>Occurring in fewer than 1 in 100, but occurring in more than 1 in 1000 treated patients</td>
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<tr>
<td>Rare</td>
<td>Occurring in fewer than 1 in 1000, but occurring in more than 1 in 10,000 treated patients</td>
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<tr>
<td>Very rare</td>
<td>Occurring in fewer than 1 in 10,000 treated patients, including isolated cases</td>
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and reddening of arms and legs (erythromelalgia), particularly at the beginning of the treatment. Occasional: Skin oversensitivity reactions such as itching (pruritus), skin rash (exanthema), a swelling of the skin and the mucous membranes (angiœdema, facial edema), sweating. Rare: Hives (urticaria), small-area hemorrhaging in the skin and mucous membranes (purpura), skin inflammation following exposure to sunlight and UV radiation (photodermatitis). Prolonged treatment with Adalat 20 retard can lead to alterations of the gums (e.g. gingival hyperplasia) which will clear up completely following discontinuation of the therapy. Very rare: Scaly skin inflammation, grave detachment of skin (exfoliative dermatitis).

Kidneys and deferent urinary tract
Occasional: Temporary worsening of kidney function in cases of renal function disorders. Increased urgency and increased daily urinary excretion.

Liver
Occasional: Liver function disorders (intrahepatic cholestasis, transaminase elevations). Rare: Jaundice.

Gastrointestinal tract
Common: Queasiness.
Occasional: Gastrointestinal disorders such as upper abdominal complaints (dyspepsia), diarrhea, stomachache, constipation, flatulence, vomiting, dry mouth.
Rare: Sensation of fullness, ructus and loss of appetite.

Musculoskeletal system
Occasional: Muscular and joint pain (myalgias and arthralgias), muscle cramps.

Reproductive organs and breast
Rare: Enlargement of the male breast (gynacomastria), which disappears following discontinuation of Adalat 20 retard.

General disorders
Occasional: Fatigue, discomfort.
Rare: Allergic general reactions such as fever, swelling of the larynx (laryngeal edema), anaphylactic shock, bronchial muscle cramps ranging up to life-threatening breathing difficulties, which disappear after discontinuation of therapy with Adalat 20 retard. If one of the side effects listed is considerably inhibiting for you or if you notice other side effects that are not specified in these Instructions for Use, please inform your doctor or pharmacist.

5. HOW SHOULD ADALAT 20 MG RETARD BE STORED?
Keep drugs out of the reach and sight of children. Do not use the drug after the expiration date stated on the outer packaging and the blister strips. Store the blister strips in the outer packaging in order to shield the contents against light. Not to be stored above 30°C.

6. ADDITIONAL INFORMATION
What Adalat 20 mg retard contains: The active ingredient is: nifedipine. 1 Time-release tablet contains 20 mg of nifedipine. The other constituents are: Hypromellose, lactose monohydrate, Macrogol 4000, magnesium stearate, maize starch, microcrystalline cellulose, Polysorbate 80, iron (III) oxide (red iron oxide, E 172), titanium oxide (E 171).

Appearance of Adalat 20 mg and package contents:
Gray/pink, round time-release tablets, which are marked on one side with the “BAYER cross” and on the other side with “U 1”.

Adalat 20 mg retard time-release tablets are available in original packagings containing 30 tablets.

Manufacturer
Bayer Schering Pharma AG
Operations: 51368 Leverkusen
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