Active ingredient: Nifedipine

1. WHAT IS ADALAT LA 60 MG AND WHAT IS IT USED FOR?
Adalat LA 60 mg is a drug for treatment of high blood pressure. (Calcium antagonist, antihypertensive)
Adalat LA 60 mg is used for:
- Treatment of high blood pressure with no discoverable organic cause (essential hypertension).

2. WHAT SHOULD YOU BE AWARE OF BEFORE USING ADALAT LA 60 MG?
Adalat LA 60 mg must not be used if you
- are hypersensitive (allergic) to the active ingredient nifedipine or any of the other ingredients
- are in cardiovascular shock
- have severe narrowing of the blood vessel leading from the heart to the main artery (high-grade aortic stenosis)
- have unstable angina pectoris
- have suffered an acute myocardial infarction (heart attack) (in the last 4 weeks)
- have severe narrowing of the gastrointestinal tract
- have an artificial anus
- are taking rifampicin (a tuberculosis drug, see section 2, “When taking Adalat LA 60 mg with other drugs”) at the same time
- are pregnant (up until the 20th week) or breastfeeding.

Particular caution is required when using Adalat LA 60 mg:
In patients who:
- have a very serious heart weakness (decompensated heart failure)
- require dialysis and who also have high blood pressure (malignant hypertension) and decreased blood volume (hypovolaemia): widening of the blood vessels can cause a substantial drop in blood pressure.
- are pregnant (see section 2, “Pregnancy and breastfeeding”).

There have been reports of gastric calculus requiring surgery in very rare cases.
Symptoms of intestinal occlusion without a history of gastrointestinal disorders have been reported in isolated cases.
Diarrhoea persisting for several days (e.g. associated with Crohn’s disease, inflammatory intestinal disorders) may result in incomplete absorption of the active ingredient due to the retention time of the drug in the gastrointestinal tract being too short.
Treatment with Adalat LA 60 mg can lead to falsely elevated values in a diagnostic test for determination of suprarenal gland function (photometric determination of vanilmandelic acid in urine).
In isolated cases, use of nifedipine or similar active substances has been associated with impairment of sperm function on transferring the fertilized ovocytes into the uterus during artificial fertilization.
The tablet shells of Adalat LA 60 mg sustained-release tablets may be visible in the gastrointestinal tract when an X-ray examination using contrast media is carried out.
Nifedipine (the active ingredient in Adalat LA 60 mg) may break down more slowly in your body if you have a liver function disorder. Treatment should therefore be monitored carefully. It may be necessary to reduce the dosage in severe cases (see also section 3, “Dosage”).

Decomposition of nifedipine, the active ingredient of Adalat LA 60 mg, involves a specific enzyme system (cytochrome P450 3A4). This enzyme system can be inhibited or intensified by other drug products. This can lead to changes in the effects and side effects of Adalat LA 60 mg (see section 2, “When using Adalat LA 60 mg with other drug products:”).
Taking Adalat LA 60 mg at the same time as other drug products that inhibit this enzyme system can cause the effects of Adalat LA 60 mg to increase but can also intensify any of its side effects that may
Phenytoin (a drug used to treat cardiac arrhythmias and epilepsy): weakening of the action of Adalat LA 60 mg. If both drugs are being used concomitantly, your reaction to nifedipine (the active ingredient in Adalat LA 60 mg) should be monitored and an increased dosage of Adalat LA 60 mg considered if necessary. It may be necessary to adjust the dosage of Adalat LA 60 mg again after treatment with phenytoin has been discontinued.

- Carbamazepine and phenobarbitone (drugs used to treat epilepsy): concomitant use of Adalat LA 60 mg may weaken the effect of Adalat LA 60 mg.

Intensification of the effects and side effects of Adalat LA 60 mg caused by other drug products:
If you are taking Adalat LA 60 mg at the same time as any of the following drug products, your blood pressure should be monitored and, if necessary, a reduction in the Adalat LA 60 mg dosage should be considered.

- Certain antibiotics (e.g. erythromycin)
- Fluoxetine and nefazodone (antidepressives)
- Ritonavir (anti-HIV drug)
- Certain antifungal drugs (e.g. ketoconazole)
- Quinupristin / dalfopristin (antibiotics)
- Valproic acid (a drug used to treat epilepsy)
- Cimetidine (a drug used to treat gastric and intestinal ulcers)
- Certain antifungal drugs (e.g. ketoconazole)
- Quinupristin / dalfopristin (antibiotics)
- Valproic acid (a drug used to treat epilepsy)
- Tricyclic antidepressives (drugs used to treat depression)
- Vasodilators (drugs that dilate the vessels)

What effect does Adalat LA 60 mg have on the action of other drugs?
Antihypertensive substances:
Adalat LA 60 mg can intensify the blood pressure-reducing effect of other drug products from various groups of active substances, such as:

- Diuretics
- Beta blockers (antihypertension drugs)
- ACE inhibitors (antihypertension drugs)
- Angiotensin receptor antagonists (antihypertension drugs)
- Other calcium antagonists (antihypertension drugs)

- Rifampicin (a drug used to treat tuberculosis) leads to accelerated decomposition of nifedipine (the active ingredient in Adalat LA 60 mg) in the body. Rifampicin should not be administered at the same time as Adalat LA 60 mg as it will not be possible to obtain effective blood concentrations of nifedipine (see also section 2, “Adalat LA 60 mg must not be used”).

What other drugs affect the way Adalat LA 60 mg works?
Decomposition of nifedipine, the active ingredient of Adalat LA 60 mg, involves a specific enzyme system (cytochrome P450 3A4). As a result, any concomitant use of drugs that influence this enzyme system can lead to interaction between the drug in question and Adalat LA 60 mg.

Both the extent and the duration of interactions should be taken into consideration if it is planned to administer Adalat LA 60 mg concomitantly with the following drugs.

Reduced efficacy of Adalat LA 60 mg caused by other drug products:
- Phenytoin (a drug used to treat cardiac arrhythmias and epilepsy): weakening of the action of Adalat LA 60 mg. If both drugs are being used concomitantly, your reaction to nifedipine (the active ingredient in Adalat LA 60 mg) should be monitored and an increased dosage of Adalat LA 60 mg considered if necessary. It may be necessary to adjust the dosage of Adalat LA 60 mg again after treatment with phenytoin has been discontinued.
- Alpha blockers (drug products to treat hypertension and cardiac failure)
- PDE5 inhibitors (drug products to treat erectile dysfunction)
- Alpha-methyldopa (antihypertension drug)

Signs of heart failure may be observed in individual cases in patients who are taking beta blockers (group of antihypertension active substances) at the same time. Your doctor will monitor your progress carefully in this case.

- Digoxin (used mainly to treat cardiac output deficiency) and theophylline (used to treat respiratory diseases): if Adalat LA 60 mg is taken at the same time, the blood concentrations of these substances can rise; monitoring of these blood concentrations is therefore recommended.

- Quinidine (used to treat cardiac arrhythmias): in isolated cases, Adalat LA 60 mg causes a decrease in quinidine blood concentrations, or a significant rise in quinidine blood concentrations can occur after discontinuing therapy with Adalat LA 60 mg; the quinidine concentration in the blood should therefore be monitored. In other cases a rise in the nifedipine concentration in blood as a result of therapy with quinidine has been reported. It is therefore recommended to carefully monitor the patient’s blood pressure if both drug products are being taken concomitantly. If necessary, the dosage of Adalat LA 60 mg should be reduced.

- Tacrolimus (active substance to prevent rejection of the transplanted organ after liver and kidney transplants): concomitant use of Adalat LA 60 mg can lead to elevated levels of tacrolimus in blood; it may be necessary to reduce the tacrolimus dose in isolated cases. Regular monitoring of the blood level of tacrolimus is recommended.

- Vincristine (a drug used to treat cancer): nifedipine (the active ingredient of Adalat LA 60 mg) decreases the excretion of vincristine, which means that the side effects of vincristine may increase. Consideration should therefore be given to reducing the dose of vincristine.

- Cephalosporins (drugs for treatment of bacterial infections): Increased plasma concentrations of cephalosporin have been observed following simultaneous administration of cephalosporins (e.g. cefixime) and nifedipine (the active ingredient of Adalat LA 60 mg).

**When taking Adalat LA 60 mg together with food and drinks**

Grapefruit juice can intensify the antihypertensive action of Adalat LA 60 mg. This effect persists for at least 3 days after the last consumption of grapefruit juice. You should therefore avoid eating grapefruit or drinking grapefruit juice if you are undergoing treatment with Adalat LA 60 mg (see also section 3, “Type of administration”).

**Pregnancy and lactation**

Adalat LA 60 mg should not be used during the first 20 weeks of pregnancy, as experimental studies with the active ingredient nifedipine have shown evidence of foetal damage. There is not sufficient evidence in humans. If you discover that you are pregnant while taking Adalat LA 60 mg, you must consult your doctor to arrange alternative treatment. As of the 20th week of pregnancy, Adalat LA 60 mg may only be taken after careful evaluation of the risk/benefit ratio and if other treatment options are not open to consideration or have proven to be ineffective.

If you need to take Adalat LA 60 mg while you are breast-feeding, you should wean your baby because nifedipine (the active ingredient in Adalat LA 60 mg) passes into breast milk and nothing is known about its possible effects on the baby.

**Children**

Adalat LA 60 mg is not intended for use in children, as insufficient information is available.

**Driving and operating machinery**

Treatment with this drug requires regular medical check-ups. Reactions to this drug may vary from one person to another, and the effect on reaction speed may be such that the patient’s ability to drive, to operate machinery and to work without a secure foothold may be impaired. This applies particularly at the start of treatment, when the dose is increased, when medication is changed and in conjunction with alcohol.
3. HOW SHOULD ADALAT LA 60 mg BE TAKEN?
Always take Adalat LA 60 mg exactly as directed by your doctor. Please ask your doctor or pharmacist if you are unsure how to use this medicine.

Dosage
Unless otherwise directed by your doctor, the standard dose for adults is one Adalat LA 60 mg sustained-release tablet daily (equivalent to 60 mg nifedipine daily).

The clinical picture may require the dose to be gradually increased to this level. 30 mg nifedipine sustained-release tablets are available for this purpose.

Dosage for patients with impaired liver function
The standard starting dose is one 30 mg nifedipine sustained-release tablet once daily. (30 mg nifedipine sustained release tablets are available for this purpose.) This is generally also the maintenance dose. Treatment should be monitored carefully.

Note: Adalat LA 60 mg contains a tablet coating that is excreted in the faeces after the active ingredient has been released.

In patients taking other drug products that inhibit or intensify a certain enzyme system (cytochrome P450 3A4), it may be necessary to adapt the dosage of Adalat LA 60 mg (see also section 2, “When taking Adalat LA 60 mg with other drug products.”).

Type of administration
Oral administration.

Adalat LA 60 mg sustained release tablets should be swallowed with plenty of liquid (e.g. a glass of water), preferably at the same time of day. The sustained-release tablets must not be chewed or divided. Adalat LA 60 mg must not be taken together with grapefruit juice (see also section 2, “When taking Adalat LA 60 mg with other drug products.”).

The sustained-release tablets can be taken independently of meals.

Duration of use
Your doctor will decide how long you should take the drug. Therapy of high blood pressure usually involves long-term treatment.

Please consult your doctor or pharmacist if you have the impression that the effects of Adalat LA 60 mg are too strong or too weak.

If you have taken a greater quantity of Adalat LA 60 mg than you were supposed to:
Depending on the degree of overdosage, there is a risk of a pronounced drop in blood pressure, clouding of consciousness and even coma, cardiac arrhythmia with deceleration or acceleration of the heart rate, elevated blood glucose levels (hyperglycaemia), insufficient blood supply to the major organs and shock caused by cardiac failure leading to accumulation of fluid in the lungs (pulmonary oedema).

If you think that you might have taken an overdose, you must inform your doctor immediately so that he can decide on what measures to take.

If you have forgotten to take Adalat LA 60 mg:
Do not take a double dose the next time if you have forgotten to take a dose. Simply continue treatment as prescribed.

If you want to interrupt treatment with Adalat LA 60 mg:
You should always consult your doctor before deciding to interrupt the course of treatment or stop taking Adalat LA 60 mg altogether.

If you have any more questions about using this medicinal product, consult your doctor or pharmacist.

4. WHAT SIDE EFFECTS ARE POSSIBLE?
Like all drug products, Adalat LA 60 mg may cause side effects, but which do not necessarily occur in all treated patients. Side-effects are categorised below according to how often they occur:

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very frequent</td>
<td>more than 1 in 10 treated patients</td>
</tr>
<tr>
<td>Frequent</td>
<td>fewer than 1 in 10, but more than 1 in 100 treated patients</td>
</tr>
<tr>
<td>Uncommon</td>
<td>fewer than 1 in 100, but more than 1 in 1,000 treated patients</td>
</tr>
<tr>
<td>Rare</td>
<td>fewer than 1 in 1,000, but more than 1 in 10,000 treated patients</td>
</tr>
<tr>
<td>Very rare</td>
<td>fewer than 1 in 10,000 treated patients, including isolated cases</td>
</tr>
</tbody>
</table>

Possible side effects

**Very frequent**
At the start of treatment especially, headaches and peripheral oedema (accumulation of fluid, e.g. in the lower leg) may occur due to widening of the blood vessels; these side effects are usually transient.
In rare cases, especially in older male patients receiving long-term therapy, enlargement of the mammary glands (gynaecomastia) has been observed; however, so far this has been reversible in all cases after discontinuing medication.

In rare cases, long-term treatment can result in gum changes (gingival hyperplasia) which are completely reversible after discontinuation of therapy with Adalat LA 60 mg.

In equally rare cases, acute general allergic reactions (anaphylactic reactions) can occur such as fever, swelling of the larynx (oedema of the glottis), and spasms in the bronchial muscles which can cause shortness of breath to a potentially fatal degree; these reactions are reversible after withdrawal of the drug.

In rare cases, a rise in the blood glucose level has been observed. This is an especially important consideration in patients with diabetes mellitus.

Very rare

In very rare cases, treatment with Adalat LA 60 mg caused disorders of intestinal transit with symptoms of intestinal occlusion (e.g. flatulence, colic-like pain) and oesophagitis, bezoars, and intestinal ulcers. In addition, a marked reduction in certain blood cells (agranulocytosis) and scaly inflammation of the skin (exfoliative dermatitis) were reported.

In isolated cases involving in vitro fertilisation, treatment with calcium antagonists such as nifedipine (the active ingredient in Adalat LA 60 mg) has been associated with transient changes to sperm and impaired sperm function.

Inform your doctor or pharmacist if you are significantly impaired by any of the listed side effects, or if you notice side effects that are not listed in this leaflet.

5. HOW SHOULD ADALAT LA 60 MG BE STORED?
Keep medicines out of the reach of children.
Do not use this medicinal product after the expiry date printed on the blister and the cardboard box.

Storage conditions:
No special storage conditions are required for this product.
Not to be stored above 30°C = 86°F
6. FURTHER INFORMATION

What Adalat LA 60 mg sustained-release tablets contain:
The active ingredient is nifedipine.
1 Adalat LA 60 mg sustained-release tablet contains 60 mg nifedipine.
The other ingredients are: Cellulose acetate, ferric(III) oxide (E 172), hydroxypropyl cellulose, hydroxypropyl methylcellulose, macrogol 3350, macrogol 200 000, macrogol 5 million, magnesium stearate, sodium chloride, propylene glycol, titanium(IV) oxide (E 171).

Appearance of Adalat LA 60 mg sustained-release tablets and pack contents:
Round, pink, convex sustained-released tablets marked with “ADALAT 60” on one side.
Adalat LA 60 mg sustained-release tablets are available in original packs containing 30 (N1), 50 (N2) and 100 (N3) sustained-release tablets.

Manufacturer
Bayer Schering Pharma AG
Site: 51368 Leverkusen
These instructions for use were last revised in January 2009.