Adalat® OROS

Active ingredient : Nifedipine GITS

Extended release tablet
Antihypertensive/coronary treatment

COMPOSITION
1 extended-release tablet Adalat® OROS 30 contains 30 mg nifedipine

PRODUCT DESCRIPTION
Pink Tablet round biconvex, laser hole on one side.
ATC code : CO8 CA05

INDICATIONS .
1. Treatment of hypertension
2. Treatment of coronary heart disease
   - Chronic stable angina pectoris (angina of effort)
   - Post infarction angina pectoris (except in the first 8 days after acute myocardial infarction)

DOSAGE AND METHOD OF ADMINISTRATION
Dosage Regimen
As far as possible the treatment must be tailored to the needs of the individual.
Depending on the clinical picture in each case, the basic dose must be introduced gradually.
Unless otherwise prescribed, the following dosage guidelines are recommended for adults :

1.	For hypertension	1 Adalat® OROS 30 tablet once daily (1x 30mg/day) 2 Adalat® OROS 30 tablet once daily (1x 60 mg/day)
2.	For coronary heart disease	
	- chronic stable angina pectoris (angina of effort)	1 Adalat® OROS 30 tablet once daily (1x 30mg/day) 2 Adalat® OROS 30 tablet once daily (1x 60 mg/day)
	- post infarction angina pectoris (except in the first 8 days after acute myocardial infarction)	1 Adalat® OROS 30 tablet once daily (1x 30mg/day) 2 Adalat® OROS 30 tablet once daily (1x 60 mg/day)

In general therapy should be initiated with 30 mg once daily. Depending on the severity of the disease and the patient's response the dose can be increased in stages up to 60 mg once daily.

If in angina pectoris an adequate therapeutic effects has not been achieved after 14 days of the treatment, the patient should consult the doctor.

Duration of Treatment
The attending doctor will determine the duration of use.

Administration
The tablets must not be chewed or broken up!
As a rule the tablets are swallowed whole with a little liquid, irrespective of meal times.

ADDITIONAL INFORMATION ON SPECIAL POPULATIONS

Pediatric patients

The safety and efficacy of Adalat OROS in children below 18 years has not been established.

Geriatric patients

Based on pharmacokinetic data for Adalat OROS no dose adaptation in elderly people above 65 years is necessary.

Patients with hepatic impairment

In patients with mild, moderate impaired liver function careful monitoring and a dose reduction may be necessary. The pharmacokinetics of nifedipine has not been investigated in patients with severe hepatic impairment (see "*Special warnings and precautions for use*" and "*Pharmacokinetic properties*").

CONTRAINDICATIONS

Adalat® OROS must not be used in cases of known hypersensitivity to nifedipine or to any of the excipients.
Nifedipine is contraindicated in pregnancy before week 20 and during breastfeeding .
Adalat® OROS must not be used in cases of cardiovascular shock.
Adalat® OROS must not be used within the first 8 days after an acute episode of myocardial infarction.
Nifedipine must not be used in combination with rifampicin because no efficient plasma levels of nifedipine may be obtained due to enzyme induction
Adalat OROS must not be used in patients with Kock pouch (ileostomy after proctocolectomy)

FERTILITY

In single cases of in-vitro fertilization calcium antagonists like nifedipine have been associated with reversible biochemical changes in the spermatozoa's head section that may result in impaired sperm function. In those men who are repeatedly unsuccessful in fathering a child by in-vitro fertilization, and where no other explanation can be found, calcium antagonists like nifedipine should be considered as possible causes.

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Care must be exercised in patients with very low blood pressure (severe hypotension with systolic pressure less then 90 mm Hg), in cases of manifest heart failure and in the case of severe aortic stenosis.

There are no safety and efficacy data from well-controlled studies in pregnant women.
Animal studies have shown a variety of embryotoxic, placentotoxic and fetotoxic effects (see "*Preclinical safety data")* when administered during and after the period of organogenesis.

From the clinical evidence available a specific prenatal risk has not been identified. Although an increase in perinatal asphyxia, caesarean delivery as well as prematurity and intra-uterine growth retardation have been reported. It is unclear whether these reports are due to the underlying hypertension, its treatment or to a specific drug effect.

The available information is inadequate to rule out adverse drug effects on the unborn and newborn child. Therefore any use in pregnancy after week 20 requires a very careful individual risk benefit assessment and should only be considered if all other treatment options are either not indicated or have failed to be efficacious.

Careful monitoring of blood pressure must be exercised, also when administered nifedipine with i.v. magnesium sulfate, owing to the possibility of an excessive fall in blood pressure which could harm both mother and fetus.

As with other non-deformable material care should be used when administering Adalat® OROS in patients with pre-existing severe gastrointestinal narrowing because obstructive symptoms may occur.

Bezoars can occur in very rare cases and may require surgical intervention.

In single cases obstructive symptoms have been described without known history of gastrointestinal disorders.

When doing barium contrast X-ray Adalat® OROS may cause false positive effects (e.g. filling defects interpreted as polyp).

In patients with mild, moderate impaired liver function careful monitoring and a dose reduction may be necessary. The pharmacokinetics of nifedipine has not been investigated in patients with severe hepatic impairment (see "*Dosage and method of administration"* and "*Pharmacokinetic properties*"). Therefore, nifedipine should be used with caution in patients with severe hepatic impairment.

Adalat® OROS should be used in with caution in patients whose cardiac reserve is poor.

REPORTING OF SUSPECTED ADVERSE DRUG REACTION

Reporting suspected adverse reaction after product authorization is crucial for ongoing benefit-risk monitoring. Healthcare professionals are requested to report any suspected adverse reactions to PT Bayer Indonesia through email at drugsafety.indonesia@bayer.com .

INTERACTIONS WITH OTHER MEDICAMENTS AND OTHER FORMS OF INTERACTION
Drugs that affect nifedipine :
Nifedipine is metabolized via the cytochrome P450 3A4 system, located both in the intestinal mucosa and in the liver. Drugs that are known to either inhibit or to induce this enzyme system may therefore alter the first pass (after oral administration) or the clearance of nifedipine.

The extent as well as the duration of interactions should be taken into account when administering nifedipine together with the following drugs:

Blood pressure lowering drugs
The blood pressure lowering effect of nifedipine may be potentiated upon co-administration of other hypertensive drugs.
When nifedipine is administered simultaneously with β-receptor blockers, the patient should be carefully monitored, since fairly severe hypotension can occur. Deterioration of heart failure is also known to develop in isolated cases.

Nifedipine is metabolized via the cytochrome P450 3A4 system, located both in the intestinal mucosa and in the liver. Drugs that are known to either inhibit or to induce this enzyme system may therefore alter the first pass (after oral administration) or the clearance of nifedipine.

Digoxin : the simultaneous administration of nifedipine and digoxin may lead to reduced digoxin clearance and hence an increase in plasma concentrations of digoxin. The patient should therefore be checked for symptoms of digoxin overdose as a precaution and, if necessary, the glycoside dose should be reduced taking account of the plasma concentration of digoxin.

Cytochrome P450 3A4 system-inducing anti-epileptic drugs, such as phenytoin, carbamazepine and phenobarbitone Upon co-administration with phenytoin, the bioavailability of nifedipine is reduced and thus its efficacy weakened. When both drugs are concomitantly administered, the clinical response to nifedipine should be monitored and, if necessary, an increase of the nifedipine dose considered. If the dose of nifedipine is increased during co-admnistration of both drugs, a reduction of the nifedipine dose should be considered when the treatment with phenytoin is discontinued.

Quinidine : When nifedipine and quinidine have been administered simultaneously, lowered quinidine or, after discontinuation of nifedipine, a distinct increase in plasma concentrations of quinidine have been observed in individual cases. For this reason, when nifedipine is either additionally administered or discontinued, monitoring of the quinidine dose are recommended. Some authors reported increased plasma concentrations of nifedipine upon co-administration of both drugs, while others did not observe an alteration in the pharmacokinetics of nifedipine.
Therefore, the blood pressure should be carefully monitored, if quinidine is added to an existing therapy with nifedipine. If necessary, the dose of nifedipine should be decreased.

Quinupristin/Dalfopristin : Simultaneous administration of quinupristin/dalfopristin and nifedipine may lead to increased plasma concentrations of nifedipine.

Cimetidine : due to its inhibition of cytochrome P450 3A4, cimetidine elevates the plasma concentrations of nifedipine and may potentiate the antihypertensive effect.

Rifampicin : strongly induces the cytochrome P450 3A4 system. Upon co-administration with rifampicin, the bioavailability of nifedipine is distinctly reduced and thus its efficacy weakened. The use of nifedipine in combination with rifampicin is therefore contra-indicated.

Diltiazem : decreases the clearance of nifedipine. The combination of both drugs should be administered with caution and a reduction of the nifedipine dose may be considered.

Cisapride : simultaneous administration of cisapride and nifedipine may lead to increased plasma concentrations of nifedipine. Upon co-administration of both drugs, the blood pressure should be monitored and, if necessary, a reduction of the nifedipine dose considered.

Drug-food interactions :
Grapefruit juice : Grapefruit juice inhibits the cytochrome P450 3A4 system. Administration of nifedipine together with grapefruit juice thus results in elevated plasma concentrations and prolonged action of nifedipine due to a decreased first pass metabolism or reduced clearance. As a consequence, the blood pressure lowering effect may be increased. After regular intake of grapefruit juice this effect may last for at least 3 days after the last ingestion of grapefruit juice.

Theoretical Potential Interactions
Macrolide antibiotics (e.g., erythromycin)
No interaction studies have been carried out between nifedipine and erythromycin. Erythromycin is known to inhibit the cytochrome P450 3A4 mediated metabolism of other drugs. Therefore the potential for an increase of nifedipine plasma concentrations upon co-administration of both drugs cannot be excluded.

Fluoxetine
A clinical study investigating the potential of a drug interaction between nifedipine and fluoxetine has not yet been performed. Fluoxetine has been shown to inhibit in-vitro the cytochrome P450 3A4 mediated metabolism of nifedipine. Therefore an increase of nifedipine plasma concentrations upon co-administration of both drugs cannot be excluded.

Anti-HIV protease inhibitors (e.g., ritonavir)
A clinical study investigating the potential of a drug interaction between nifedipine and certain anti-HIV protease inhibitors has not yet been performed. Drug of this class are known to inhibit the cytochrome P450 3A4 system. In addition drug of this class have been shown to inhibit in vitro the cytochrome P450 3A4 mediated metabolism of nifedipine. When administered together with nifedipine, a substantial increase in plasma concentrations of nifedipine due to a decreased first pass metabolism and a decreased elimination cannot be excluded.

Azole anti-mycotics (e.g., ketoconazole)
A formal interaction study investigating the potential of a drug interaction between nifedipine and ketoconazole, itraconazole or fluconazole has not yet been performed. Drugs of this class are known to inhibit the cytochrome P450 3A4 system. When administered orally together with nifedipine, a substantial increase in systemic bioavailability of nifedipine due to an increased absorption cannot be excluded. Upon co-administration, the blood pressure should be monitored and, if necessary, a reduction in the nifedipine dose considered.

Nefazodone
A clinical study investigating the potential of a drug interaction between nifedipine and nefazodone has not yet been performed. Nefazodone is known to inhibit the cytochrome P450 3A4 mediated metabolism of other drugs. Therefore an increase of nifedipine plasma concentrations upon co-administration of both drugs cannot be excluded.

Tacrolimus
Tacrolimus has been shown to be metabolized via cytochrome P450 3A4 system. Data recently published indicate that the dose of nifedipine administered simultaneously with tacrolimus may be reduced in individual cases. Upon co-administration of both drugs, the tacrolimus plasma concentrations should be monitored and, if necessary, a reduction in the tacrolimus dose considered.

Carbamazepine- Phenobarbitone
No formal studies have been performed to investigate the potential interaction between nifedipine and carbamazepine or phenobarbitone. As both drugs have been shown to reduce the plasma concentrations of the structurally similar calcium channel blocker nimodipine due to enzyme induction, a decrease in nifedipine plasma concentrations and hence a decrease in efficacy cannot be excluded.

Valproic acid : No formal studies have been performed to investigate the potential interaction between nifedipine and valproic acid. As valproic acid has been shown to reduce the plasma concentrations of the structurally similar calcium channel blocker nimodipine due to enzyme induction, an increase in nifedipine plasma concentrations and hence an increase in efficacy cannot be excluded.

Other forms of interaction
Nifedipine may cause falsely increased spectrophotometric values of urinary vanillyl-mandelic acid. However, measurement with HPLC is unaffected. Antagonists like nifedipine should be considered as possible causes.

PREGNANCY AND LACTATION
Pregnancy
Nifedipine is contraindicated in pregnancy before week 20.
In animal studies nifedipine has been shown to produce embryotoxicity, fetotoxicity and teratogenicity.
Nifedipine has been shown to produce teratogenic findings in rats, mice and rabbits, including digital anomalies, malformation of the extremities, cleft palates, cleft sternum and malformation of the ribs.
Digital anomalies and malformation of the extremities are possibly result of compromised uterine blood flow, but have also been observed in animals treated with nifedipine solely after end of the organogenesis period.
Nifedipine administration was associated with a variety of embryotoxic, placentotoxic and fetotoxic effects, including stunted fetuses (rats, mice, rabbits), small placentas and underdeveloped chorionic villi (monkeys), embryonic and fetal deaths (rats, mice, rabbits) and prolonged pregnancy/decreased neonatal survival (rats; not evaluated in other species).

There are no adequate and well-controlled studies in pregnant women.

In-vitro fertilization
In single cases of in-vitro fertilization calcium antagonists like nifedipine have been associated with reversible biochemical changes in the spermatozoa`s head section that may result in impaired sperm function.
In those men who are repeatedly unsuccessful in fathering a child by *in vitro* fertilization, and where no other explanation can be found, calcium antagonists like nifedipine should be considered as possible causes.

Lactation
Nifedipine passes into the breast milk. As there is no experience of possible effects on infants, breastfeeding should first be stopped if nifedipine treatment becomes necessary during the breastfeeding period.

EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

Reactions to the drug, which vary in intensity from individual to individual, can impair the ability to drive or to operate machinery. This applies particularly at the start of the treatment, on changing the medication and in combination with alcohol.

UNDESIRABLE EFFECTS

Adverse drug reactions (ADRs) based on placebo-controlled studies with nifedipine sorted by CIOMS III categories of frequency (clinical trial data base: nifedipine n = 2,661; placebo n = 1,486; status: 22 Feb 2006 and the ACTION study: nifedipine n = 3,825; placebo n = 3,840) are listed below: 9495 ADRs listed under "common" were observed with a frequency below 3% with the exception of oedema (9.9%) and headache (3.9%).

The frequencies of ADRs reported with nifedipine containing products are summarised in the table below. Within each frequency grouping, undesirable effects are presented in order of decreasing seriousness. Frequencies are defined as common (≥1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100) and rare (≥ 1/10,000 to < 1/1,000). The ADRs identified only during the ongoing postmarketing surveillance, and for which a frequency could not be estimated, are listed under “Not known”.

System Organ Class (MedDRA)	Common	Uncommon	Rare	Not known
Blood and lymphatic system disorders				Agranulocytosis Leukopenia
Immune system disorders		Allergic reaction Allergic oedema / angioedema (incl. larynx oedema [1])	Pruritus Urticaria Rash	Anaphylactic/ anaphylactoid reaction
Psychiatric disorders		Anxiety reactions Sleep disorders		
Metabolism and nutrition disorders				Hyperglycaemia
Nervous system disorders	Headache	Vertigo Migraine Dizziness Tremor	Par-/ Dysaesthesia	Hypoaesthesia Somnolence
Eye disorders		Visual disturbances		Eye pain
Cardiac disorders		Tachycardia Palpitations		Chest pain (Angina Pectoris)
Vascular disorders	Oedema Vasodilatation	Hypotension Syncope		
Respiratory, thoracic, and mediastinal disorders		Nosebleed Nasal congestion		Dyspnea
Gastrointestinal disorders	Constipation	Gastrointestinal and abdominal pain Nausea Dyspepsia Flatulence Dry mouth	Gingival hyperplasia	Bezoar Dysphagia Intestinal obstruction Intestinal ulcer Vomiting Gastrooesophageal sphincter insufficiency
Hepatobiliary disorders		Transient increase in liver enzymes		
Skin and subcutaneous tissue disorders		Erythema		Toxic Epidermal Necrolysis Photosensitivity allergic reaction Palpable purpura

System Organ Class (MedDRA)	Common	Uncommon	Rare	Not known
Musculoskeletal and connective tissue disorders		Muscle cramps Joint swelling		Arthralgia Myalgia
Renal and urinary disorders		Polyuria Dysuria		
Reproductive system and breast disorders		Erectile dysfunction		
General disorders and administration site conditions	Feeling unwell	Unspecific pain Chills		

In dialysis patients with malignant hypertension and hypovolaemia, a distinct fall in blood pressure can occur as a result of vasodilatation.

OVERDOSE

Symptoms

The following symptoms are observed in cases of severe nifedipine intoxication.
Disturbances of consciousness to the point of coma, a drop in blood pressure, tachycardiac/bradycardiac heart rhythm disturbances, hyperglycaemia, metabolic acidosis, hypoxia, cardiogenic shock with pulmonary oedema.

Management of Overdose in Man

As far as treatment is concerned, elimination of the active substance and the restoration of stable cardiovascular conditions have priority.

After oral ingestion thorough gastric lavage is indicated, if necessary in combination with irrigation of the small intestine. Particularly in cases of intoxication with slow-released products like Adalat® OROS elimination must be as complete as possible, including the small intestine, to prevent the otherwise inevitable subsequent absorption of the active substance.

Haemodialysis serves no purpose, as nifedipine is not dialyzable, but plasmapheresis is advisable (high plasma protein binding, relatively low volume of distribution).

Bradycardiac heart rhythm disturbances may be treated symptomatically with 8-sympathomimetics, and in life-threatening bradycardiac disturbances of heart rhythm temporary pacemaker therapy can be advisable.

Hypotension as a result of cardiogenic shock and arterial vasodilatation can be treated with calcium (10-20ml of a 10% calcium gluconate solution administered slowly IV and repeated if necessary). As a result, the serum calcium can reach the upper normal range to slightly elevated levels. If an insufficient increase in blood pressure is achieved with calcium, vasoconstricting sympathomimetics such as dopamine or noradrenaline are additionally administered. The dosage of these drugs is determined solely by the effect obtained.

Additional liquid or volume must be administered with caution because of the danger of overloading the heart.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties

Nifedipine is a calcium antagonist of the 1,4-dihydropyridine type. Calcium antagonists reduce the transmembranal influx of calcium ions through the slow calcium channel into the cell. Nifedipine act particularly on the cells of the myocardium and the smooth muscle cells of the coronary arteries and the peripheral resistance vessels.

In the heart nifedipine dilates the coronary arteries, especially the large conductance vessels, even in the free wall segment of partially stenosed areas. Further, nifedipine reduces the vascular smooth muscle tone in coronary arteries and prevents vasospasm. The end-result is an increased poststenotic blood flow and an increased oxygen supply. Parallel to this, nifedipine reduces the oxygen requirement by lowering peripheral resistance (afterload). With long-term use, nifedipine can also prevent the development of new atherosclerotic lesions in the coronary arteries.

Nifedipine reduces the smooth muscle tone of the arterioles, thus lowering the increased peripheral resistance and consequently the blood pressure. At the beginning of the nifedipine treatment there may be a transient reflex increase in heart rate and thus in the cardiac output. However, this increase is not enough to compensate for the vasodilatation. In addition, nifedipine increases sodium and water excretion both in the short-term and long-term use. The blood-pressure-lowering effect of nifedipine is particularly pronounced in hypertensive patients.

PHARMACOKINETICS PROPERTIES

Adalat® OROS tablet are formulated to provide nifedipine at an approximately constant rate over 24 hours. Nifedipine is released from the tablet at a zero-order rate by membrane-controlled, osmotic push-pull process. The delivery rate is independent of gastrointestinal pH or motility. Upon swallowing, the biologically inert components of tablet remain intact during gastrointestinal transit and are eliminated in the faeces as an insoluble shell.

Absorption

After oral administration nifedipine is almost completely absorbed. The systemic availability of orally administered nifedipine immediate release formulations (Adalat capsules) is 45-68% owing to a first pass effect.

At steady-state the bioavailability of Adalat® OROS tablet ranges from 68-86% relative to Adalat® capsules. Administration in the presence of food slightly alters the early rate of absorption, but does not influence the extent of drug availability.

Plasma drug concentrations rise at a controlled rate after Adalat® OROS dose and reach a plateau at approximately 6 to 12 hours after the first dose. Following multiple days of dosing, relatively constant plasma concentrations at this niveau are maintained with minimum peak to trough fluctuations over 24 hours dosing interval ((C_{max}^{ss}-C_{min}^{ss})/C_{av}^{ss}=0.9-1.2)).

Distribution

Nifedipine is about 95% bound to plasma protein (albumin).

Biotransformation

After oral administration nifedipine is metabolized in the gut wall and in the liver, primarily by oxidative processes. These metabolites show no pharmacodynamic activity.

Nifedipine is excreted in the form of its metabolites predominantly via kidneys, and about 5-15% are excreted via the bile in the faeces. The unchanges substance is recovered only in traces (below 1%) in the urine.

Elimination

The terminal elimination half-life is 1.7 to 3.4 hours in conventional formulations (Adalat® capsules). The terminal half-life after Adalat CR does not represent a meaningful parameter as a plateau- like plasma concentration is maintained during release from the tablets and absorption.

In cases of impaired kidney function no substantial changes have been detected in comparison with healthy volunteers.

In cases of impaired liver function, the total clearance is reduced. A dose reduction may be necessary in severe cases.

In a study comparing the pharmacokinetics of nifedipine in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment with those in patients with normal liver function, oral clearance of nifedipine was reduced by on average 48% (Child Pugh A) and 72% (Child Pugh B). As a result AUC and Cmax of nifedipine increased on average by 93% and 64% (Child Pugh A) and by 253% and 171% (Child Pugh B), respectively, compared to patients with normal hepatic function. The pharmacokinetics of nifedipine has not been investigated in patients with severe hepatic impairment (see "*Special warnings and precautions for use*")

PRECLINICAL SAFETY DATA

Toxicology

Acute toxicity : acute toxicity has been investigated in various animal species and the individual results are listed in the following table :

	LD_{50}(mg/kg)	
	Oral	**IV**
Mouse	454 (401-572)*	4.2 (3.8-4.6)*
Rat	1022 (950-1087)*	15.5 (13.7-17.5)*
Rabbit	250-500	2-3
Cat	~100	0.5-8
Dog	>250	2-3

* 95% confidence level

Subacute and subchronic toxicity : daily oral administration to rats (50mg/kg body weight) and to dogs (100mg/kg body weight) over period of 13 & 4 weeks respectively were tolerated without toxic effects.

After parenteral (IV) administration dogs tolerated up to 0.1mg/kg body weight/day for 6 days without damage. Daily IV administration of 2.5 mg/kg body weight in rats over a period of weeks was also tolerated without signs of damage.

Chronic toxicity : dogs tolerated up to 100 mg/kg body weight as a daily oral dose over a period of 1 year without toxic damage. In rats toxic effects occurred at concentration above 100 PPM in the feed (about 5-7 mg/kg body weight).

Carcinogenecity : A long-term study in rats (2 years) yielded no evidence of a carcinogenic effect of nifedipine.

Mutagenecity : To assess the mutagenic effects the Ames test, the Dominant-lethal-test, and the Micronucleous-test was performed in the mouse. No evidence of mutagenic effect of nifedipine could be found.

Reproduction toxicology
Nifedipine has been shown to produce teratogenic findings in rats and rabbits, including digital anomalies. Digital anomalies are possibly a result of compromised uterine blood flow.
Nifedipine administration was associated with a variety of embryotoxic, placentotoxic and fetotoxic effects, including stunted fetuses (rats, mice, rabbits), small placentas and underdeveloped chorionic villi (monkeys), embryonic and fetal deaths (rats, mice, rabbits) and prolonged pregnancy/decreased neonatal survival (rats; not evaluated in other species).
All of the doses associated with the teratogenic, embryotoxic or fetotoxic effects in animals were maternally toxic and several times the recommended maximum dose for humans.

PHARMACEUTICAL PARTICULARS
Incompatibilities
None

Excipients
Hypromellose 5 cp, Magnesium stearate, Polyethylene oxide, Sodium chloride, Ferric oxide red, Cellulose acetate, Macrogol 3350, Hydroxypropylcelluloce, Hypromellose 3 cp, Titanium dioxide, Propylene glycol, Opacode S-1-17823

Instruction for use / handling
The light sensitive active substance contained in Adalat® OROS is protected from light inside and outside its packaging. The tablet must be protected from humidity and must therefore only be removed from the foil immediately before use.

Storage :
Store below 30ºC

Note
Do not use after the expiry date.
Keep drugs out of reach children

PRESENTATION

Adalat® Oros 30
Reg No. XXXXXXXXX : Box, 3 blisters @ 10 tablets

Made by Bayer AG, Leverkusen – Germany
Imported by PT Bayer Indonesia, Depok – Indonesia
Packed by PT Actavis Indonesia, Jakarta – Indonesia

Harus dengan resep dokter