

AdalatCC advertisement.

[s.l.]: [s.n.], 1993

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We discovered it.

We tested it.

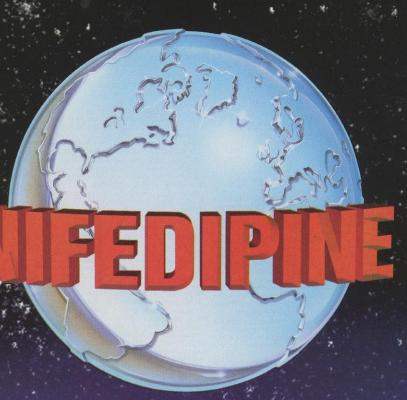
We introduced it.

We improved it.

We understand it.

We trust it.

We stand by it.



In 1975, Bayer AG introduced Adalat® (nifedipine) in Europe. We've since made the Adalat brand available in several formulations around the world, and nifedipine has been in clinical use for over twenty years. Backed by a worldwide clinical database of tens of thousands of patients and hundreds of clinical studies, the Adalat brand today provides therapy for millions of patients* around the globe.

In the United States. the one to prescribe is...

Once-A-Day



30mg, 60mg & 90mg

Providing a World of Confidence for Hypertension Control

Frequency and type of side effects, eg, peripheral edema, headache, flushing/heat sensation, dizziness and fatigue/asthenia, are typical of dihydropyridine calcium channel blockers.

Adalatic nifedipine

30mg, 60mg & 90mg

BRIEF SUMMARY CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION For Oral Use

INDICATION AND USAGE: ADALAT (C is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents.

CONTRAINDICATIONS: Known hypersensitivity to nifedipine.

WARNINGS: Excessive Hypotension: Alhough in most patients the hypotensive effect of nifedipine is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. Ever exponses have usually occurred during initial tritration or at the time of subsequent upward dosage adjustment, and may be more likely in patients using concomitant beta-flockers.

likely in patients using concomitant beta-flockers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients who received immediate release capules together with a beta-flocking agent and who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of infedipine and a beta-flocker, but the possibility that it may occur with nifedipine alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analyseisc sannot be ruled out. In nifedipine-treated patients where surgery using high dose tentanyl anesthesia is contemplated, the physician should be alware of these potential problems and, if the patient's condition permits, sufficient time (at least 36 hours) should be allowed for nifedipine to be washed out of the body prior to surgery.

Increased Angina and/or Myocardial Infarction: Rarely, patients, particularly those who have severe obstructive coronary artery disease, have developed well documented increased frequency, duration and/or severity of angina or acute myocardial infarction upon starting nifedipine or at the time of dosage increase. The mechanism of this effect is not established.

This effect is not established.

Beta-Blocker Withdrawal. When discontinuing a beta-blocker it is important to taper its dose, if possible, rather than stopping abruptly before beginning nifedipine. Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of nifedipine treatment will not prevent this occurrence and on occasion has been reported to increase it. Congestive Heart Failure: Rarely, patients (usually while receiving a beta-blocker) have developed heart failure after beginning infedigine. Patients with light partic stensis may be at greater risk for such an event, as the unloading effect of nifedigine would be expected to be of less benefit to these patients, owing to their fixed impedance to flow across the aortic valve

Flow across the acritic valve.

PRECAUTIONS: General - Hypotension: Because nifedipine decreases peripheral voscular resistance, careful monitoring of blood pressure during the initial administration and
titration of ADALAT Cc is suggested. Use observation is especially recommended for patients
already taking medications that are known to lower blood pressure (See WARNINGS).

Peripheral Edema: Mild to moderate peripheral edema occurs in a dose-dependent
manner with ADALAT Cc. The placebo subtracted rate is approximately 8% at 30 mg, 12%
at 60 mg and 19% at 90 mg daily. This edema is a localized phenomenon, thought be
associated with vasodilation of dependent arterioles and small blood vessels and not due
to left ventricular dystruction or generalized fluid retention. With patients whose hyper-tension is complicated by congestive heart failure, care should be taken to differentiate
this peripheral edema from the effects of increasing left ventricular dysfunction.

Information for Patients: ADALAT CC is an extended release tablet and should be swallowed whole and taken on an empty stomach. It should not be administered with food. Do not chew, divide or crush tablets.

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Laboratory Tests: Rore, usually transient, but occasionally significant elevations of enzymes such as alkaline phosphatase, CPK, LDH, SGOT, and SGPT have been noted. The relationship to nifedipine therapy is uncertain in most cases, but probable in some. These laboratory obnormalities have rarely been associated with clinical symptomes; hover, cholestasis, with or without joundice has been reported. A small increase (<5%) in mean alkaline phosphatase was noted in patients treated with ADALAT CC. This was an isolated finding and it rarely resulted in values which fell outside the normal range. Rore instances of allergic hepatitis have been reported with mideligine treatment. In controlled studies, ADALAT CC did not adversely affect serum unic acid, glucose, cholesterol or potassium.

ADALAI CL did not adversely affect serum unic acid, glucose, cholesteral or potassum. Nifedipine, like other calcium channel blockers, decreases platelet aggregation in vitro. Limited clinical studies have demonstrated a moderate but statistically significant decrease in platelet aggregation and increase in bleeding time in some nitedipine patients. This is thought to be a function of inhibition of calcium transport across the platelet membrane. No clinical significance for these findings has been demonstrated. Positive direct (combs' test with or without hemolytic anemia has been reported but a causal relationship between rifedipine administration and positivity of this laboratory test, including hemolysis, could not be determined.

test, including hemolysis, could not be determined. Although rifiedipine has been used safely in patients with renal dysfunction and has been reported to exert a beneficial effect in certain cases, rare reversible elevations in BUN and serum creatinine have been reported in patients with pre-existing chronic renal insufficiency. The relationship to intelligine therapy is uncertain in most cases but probable in some.

Drug Interactions: Beta-adrenergic blocking agents: (See WARNINGS).

ADALAT CC was well tolerated when administered in combination with a beta blocker in 187 hypertensive patients in a placebo-controlled clinical trial. However, there have been accasional literature reports suggesting that the combination of intelliptine and beta-adrenergic blocking drugs may increase the likelihood of congestive heart failure, severe hypotension, or exacerbation of angina in patients with cardiovascular disease.

Severe importance, or exceleration to ranginar in patients with elevated digaxin levels, and there is a possible interaction between digaxin and ADALAT CC, it is recommended that digaxin levels be monitored when initiating, adjusting, and discontinuing ADALAT CC to avoid possible over- or under-digitalization.

to avoin possible over-or under-algularization.

Coumarin Anticoagulants: There have been rare reports of increased prothrombin time in patients taking coumarin anticoagulants to whom nifedipine was administered. However, the relationship to nifedipine therapy is uncertain.

Quinidine: There have been rare reports of an interaction between quinidine and nifedipine (with a decreased plasma level of quinidine).

Inteldipine (with a decreased plasma level of quinidine).

Gmetidine: Both the peak plasma level of rifedipine and the AUC may increase in the presence of cimeditine. Rantidine produces smaller non-significant increases. This effect of cimedidine may be mediated by its known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of infedipine. If infedipine therapy is initiated in a patient currently receiving cimetidine, courlous intration is advised.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Nifedipine was administered orally to rats for two years and was not shown to be carcinogenic. When given torst prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose. In vivo mutagenicity studies were negative. Pregnancy: Pregnancy Category C. In rodents, rabbits and monkeys, nifedipine has been shown to have a variety of embryotoxic, placentotoxic and tetotoxic effects, including stunted fetuses (rats, mice and rabbits), digital anomalies (rats and rabbits), the derimities (mice), cleft platel (mice), somal plate (mice), somal

The digital anomalies seen in infedipine-exposed rabbit puss are strikingly similar to those seen in puss exposed to phenytoin, and these are in turn similar to the planageal deformities that are the most common malformation seen in human children with in utero exposure to phenytoin.

There are no adequate and well-controlled studies in pregnant women. ADALAT CC should be used during pregnancy only if the potential benefit usines the potential risk to the letus. **Nursing Mothers:** Midelpine is excreted in human milk. Therefore, a decision should be made to discontinue nursing or to discontinue the drug tables. nade to discontinue nursing or to discontinue the drug, taking into account the ortance of the drug to the mother.

ADVERSE EXPERIENCES: The incidence of adverse events during treatment with ADALAT CC in doses up to 90 mg daily were derived from multi-center placebo-controlled clinical trials in 370 hypertensive potients. Atenolol 50 mg once daily was used concomiantly in 187 of the 370 patients on ADALAT CC and in 64 of the 126 patients on placebo. All adverse events reported during ADALAT CC therapy were tabulated independently of their causal relationship to medication.

The most common adverse event reported with ADALAT® CC was peripheral edema. This was dose related and the frequency was 18% on ADALAT CC 30 mg daily, 22% on ADALAT CC 60 mg daily and 29% on ADALAT CC 90 mg daily versus 10% on placebo.

ADACAT CE of ing duty and 27% of in Adach CE of ing many Yearso 10% of indicesor.

Other common odverse events reported in the above placebo-controlled trials include: Headache (19%, versus 13% placebo incidence); Flushing/heat sensation (4%, versus 0% placebo incidence); Dizziness (4%, versus 2% placebo incidence); Flushing/heat sensation (4%, versus 4% placebo incidence); Nausea (2%, versus 1% placebo incidence); Constipation (1%, versus 0% placebo incidence).

Where the frequency of adverse events with ADALAT CC and placebo is similar, causal relationship cannot be established.

The following adverse events were reported with an incidence of 3% or less in daily doses up to 90 mg:

Body as a Whole/Systemic: chest pain, leg pain Central Nervous System: paresthesio, vertigo Dermatologic: rash Gastrointestinal: constipution Musculoskeletal: leg cramps Respiratory: epistaxis, rhinitis Urogenital: impotence, urinary frequency

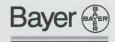
Other adverse events reported with an incidence of less than 1.0% were:

Other adverse events reported with an incidence of less than 1.0% were:

Body as a Whole/Systemic: cellulitis, chills, facial edema, neck pain, pelvic pain, pain Cardiovascular: atrial fibrillation, bradycardia, cardiac arrest, extrasystole, hypotension, polipitations, phlebitis, postural hypotension, tachycardia, cutaneous angleictaese Central Nervous Systems anxiety, confusion, decreased libid, depression, hypertonia, insomnia, somnolence Dermatologic: pruritus, sweating Gastrointestinale abdominal pain, diarrhea, dry mouh, dyspepsia, esophaglis, flatience, gastrointestinal hemorrhage, vomiting Hematologic: lymphadenopathy Metabolic: gout, weight loss Musculoskeletal: arthralgia, arthritis, myalgia Respiratory: dyspnea, increased cough, rales, pharyngitis Special Senses: abnormal vision, amblyopia, conjunctivitis, diplopia, tinnitus Uragenital/Reproductive: kidney calculus, nocturia, breast engorgement

The following adverse events have been reported rarely in patients given nifedipine in other formulations: allergenic hepatitis, alapecia, anemia, arthritis with ANA (+1), depression, erythromelalgia, exholiative dermaitis, fever, gingvid hyperplasia, guecomastia, leukopenia, mood changes, muscle cramps, nervousness, paranoid syndrome, purpura, shakiness, sleep disturbances, syncope, taste perversion, thrombacytopenia, transient blindness at the peak plasma level, tremor and urticaria.

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Pharmaceutical Division

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Real Value for Real People with Hypertension

Real Therapeutic Value

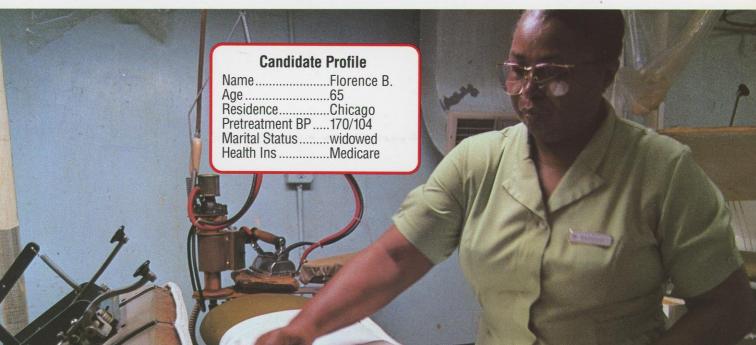
 The benefits of long-acting nifedipine therapy for hypertension*¹

Real Human Value

- · Convenient, well-tolerated therapy
- Peripheral edema and headache were the most common dose-related adverse events reported; flushing/heat sensation, dizziness, and fatigue/asthenia were all reported at an incidence of 4%

Real Economic Value

- Lower price (AWP) than Procardia XL[®] 30 mg, 60 mg and 90 mg—potential 25% savings^{†2}
- *Not indicated for angina. Take on an empty stomach. Careful titration may be necessary when switching between Procardia XL® and Adalat® CC. Procardia XL is a registered trademark of Pfizer Labs Division, Pfizer Inc.
- †Calculations based on suggested Average Wholesale Price (AWP). Please see brief summary of Prescribing Information on back of this page.



"Save up to \$192† a year? That's Sunday clothes for the grandkids."

Adalat nifedipine

30mg, 60mg & 90mg

Start with*

30mg once daily

Titrate, if necessary*

*Please see DOSAGE AND ADMINISTRATION section in brief summary of Prescribing Information below.

BRIEF SUMMARY CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION For Oral Use

P7100744BS

INDICATION AND USAGE: ADALAT CC is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents CONTRAINDICATIONS: Known hypersensitivity to nifedipine.

CONTRAINDICATIONS: Known hypersensitivity to nifedipine.

WARNINGS: Excessive Hypotension: Although in most patients the hypotensive effect of nifedipine is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients using concomitant beta-blockers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients who received immediate release capsules together with a beta-blocking agent and who underwent coronary artery bypass surgery using high dose fentanty appears to be due to the combination on infedipine and a beta-blocker, but the possibility that it may occur with nifedipine alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analogetics cannot be ruled out. In nifedipine-treated patients where surgery using high dose fentanyl anesthesia is contemplated, the physician should be allowed for nifedipine to be washed out of the body prior to surgery.

the body prior to surgery.

Increased Angina and/or Myocardial

Interessed Angina and/or Myocardial
Infarction: Rarely, patients, particularly
those who have severe obstructive coronary artery disease, have developed well documented increased frequency, duration and/or severity of angina or acute myocardial
infarction upon starting nifedipine or at the time of dosage increase. The mechanism of
this effect is not established.

this effect is not established.

Beta-Blocker Withdrawal: When discontinuing a beta-blocker it is important to taper its dose, if possible, rather than stopping abruptly before beginning nifedipine. Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased anging, probably related to increased sensitivity to catecholomines. Initiation of nifedipine treatment will not prevent this occurrence and on occasion has

Initiation of intellipine treatment will not prevent this occurrence and on occasion has been reported to increase it.

Congestive Heart Failure: Rarely, patients (usually while receiving a beta-blocker) have developed heart failure after beginning intellipine. Patients with tight aortic stemosts may be at greater risk for such an event, os the unloading effect of intellipine will be expected to be of less benefit to these patients, owing to their fixed impedance to

PRECAUTIONS: General - Hypotension: Because nifedipine decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and itiration of ADAIAT Ct is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure (See WARNINGS).

WARNINGS).

Peripheral Edema: Mild to moderate peripheral edema occurs in a dose-dependent manner with ADALAT CC. The placebo subtracted rate is approximately 8% at 30 mg, 12% at 60 mg and 19% at 90 mg daily. This edema is a localized phenomenon, thought to be associated with vasodilation of dependent netretioles and small bload vessels and not due to left ventricular dysfunction or generalized fluid retention. With patients whose hypertension is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction. Information for Patients: ADALAT CL is an extended release tablet and should be saullowed whole and taken on an empty stomach. It should not be administered with food. Do not chew, divide or crush tablets.

tood. Do not chew, divide or crush tablets.

Laboratory Tests: Rare, usually transient, but occasionally significant elevations of enzymes such as alkaline phosphatase, CPK, LDH, SoDT, and SoPT have been noted. The relationship to nifedipine therapy is uncertain in most cases, but probable in mosm. These laboratory abnormalities have rarely been associated with clinical symptoms; however, cholestasis with or without jaundice has been reported. A small increase (-5%) in mean (alkaline phosphatase was noted in patients treated with ADALAT CC. This was an isolated finding and it rarely resulted in values which fell outside the normal range. Rare instances of allergic hepatitis have been reported with intelliginar treatment. In controlled studies, ADALAT CC did not adversely affect serum uric acid, glucose, cho-

In controlled studies, ADALAI CC did not adversely affect serum uric acid, glucose, cho-lesterol or potossium.
Nifedipine, like other calcium channel blackers, decreases platelet aggregation in vitro.
Limited (linical studies have demonstrated a moderate but statistically significant
decrease in platelet aggregation and increase in bleeding time in some nifedipine
patients. This is thought to be a function of inhibition of calcium transport across the
platelet membrane. No clinical significance for these findings has been demonstrated.
Positive direct (Coombs' test with or without hemolytic anemia has been reported but a
causal relationship between infedipine administration and positivity of this laboratory
test, including hemolysis, could not be determined.

Although nifedipine has been used safely in patients with renal dysfunction and has been reported to exert a beneficial effect in certain cases, crae reversible elevations in BUN and serum creatinine have been reported in patients with pre-existing chair renal insufficiency. The relationship to nifedipine therapy is uncertain in most cases but

probable in some.

Drug Interactions: Beta-adrenergic blocking agents: (See WARNINGS).

ADALAT C was well tolerated when administered in combination with a beta blocker in 187 hypertensive patients in a placebo-controlled clinical trial. However, there have been occasional literature reports suggesting that the combination of nifedipine and beta-adrenergic lookcing drugs may increase the likelihood of congestive heart failure, severe hypotension, or exacerbation of angina in patients with cardiovascular disease.

Digitalis: Since there have been isolated reports of patients with elevated digoxin levels, and there is a possible interaction between digoxin and ADALAT CC, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing ADALAT CC to avoid possible over- or under-digitalization.

Coumarin Anticoagulants: There have been rare reports of increased prothrombin time in patients taking coumarin anticoagulants to whom infedipine was administered. However, the relationship to infedipine therapy is uncertain.

Quinidine: There have been rare reports of an interaction between quinidine and nifedipine (with a decreased plasma level of quinidine).

Real People, Real Needs, Real Value

Body as a Whole/Systemic: chest pain, leg pain Central Nervous System: paresthesia, vertiga Dermatologic: rash Gastrointestinal: constipation Musculoskeletal: leg cramps Respiratory: epistaxis, rhinitis Urogenital: impotence, urinary frequency

tence, urinary frequency
Other adverse events reported with an incidence of less than 1.0% were:
Body as a Whole/Systemic: cellulitis, thills, facial edema, neck pain, pelvic pain,
pain Cardiovascular: atrial fibrillation, bradycardia, cardiac arrest, extrasystole,
hypotensian, palpitations, phlebitis, postural hypotensian, tachycardia, cutaneous angiectases Central Nervous System: anxiety, confusion, decreased libido, depressian,
hypertonia, insomnia, somnolence Dermatologic: pruritus, sweating
Gastrointestand: abdominal pain, diarrhea, dry mouth, dyspegsia, esophagitis, sweating
Metabolic: goul, weight loss Musculoskeletal: arthralgia, arthritis, myaglia
Metabolic: goul, weight loss Musculoskeletal: arthralgia, arthritis, myaglia
sion, amblyopia, conjunctivitis, diplopia, finnitus Urogenital/Reproductive:
kidney calculus, nouturiar hereat engonaement

mal vision, amblyopia, conjunctivitis, diplopin, linnitus **Urogenitai/ keproductive**: kidney calculus, nocturia, breast engorgement
The following adverse events have been reported rarely in patients given nifedipine in other formulations: allergenic hepatitis, alopecia, anemia, arthritis with AMA (+), depression, erythromelolgia, excloiditive dermatifis, fever, gingivid hyperplosia, guocomastia, leukopenia, mood changes, muscle cramps, nervousness, paranoid syndrome, purpura, shakiness, sleep disturbances, open, it is the perversion, thrombocytopenia, transient blindness at the peak plasma level,

PROBLEM TO A DAMINISTRATION:
Dosage should be adjusted according to each patient's needs. It is recommended that ADALAT CC is an actended release dosage form and toblets should be swallowed whole, not bitten or divided. In general, titration should proceed over a 7-14 day period starting with 30 mg once daily. Upward titration should be based on therapeutic efficacy and safety. The usual maintenance dose is 30 mg to 60 mg once daily. Itiration to doses above 90 mg daily is not recommended. If discontinuation of ADALAT CC is necessary, sound clinical practice suggests that the dosage should be decreased gradually with dose physician supervision.

Care should be taken when dispensing ADALAT CC to assure that the extended release dosage form has been prescribed.

P7100744BS

5/93

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3060 Printed in USA

References:
1. Data on file, Miles Inc.
2. Redbook Update. Montvale, NJ, Medical Economics Data, Inc., October 1993;p. 34.

Cimetidine: Both the peak plasma level of nifedipine and the AUC may increase in the presence of cimetidine. Ranitidine produces smaller non-significant increases. This effect of cimetidine may be mediated by its known inhibition of hepatic cytochrane P-450, the enzyme system probably responsible for the first-pass metabolism of nifedipine. If nifedipine therapy is initiated in a patient currently receiving cimetidine, cautious titra-

tion is advised non's acrivee. Carrinagenesis, Mutagenesis, Impairment of Fertility: Nifedipine was adminis-tered orally to rats for two years and was not shown to be carrinagenic. When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose. In vivo mutagenicity studies were neg-

artive.

Pregnancy: Pregnancy: Category C. In rodents, rabbits and monkeys, nifedipine has been shown to have a variety of embryotoxic, placentotoxic and festoxic effects, including stunted fetuses (rats, mice and rabbits), digital anomalies (rats and rabbits), rib deformities (mice), cleft polate (mice), small placentas and underdeveloped chroniar villi comokeys), embryonic and fetal deaths (rats, mice and rabbits), prolonged pregnancy (rats; not evaluated in other species). On a mg/kg or mg/m² basis, some of the doses sociated with these various effects are higher than the maximum recommended human dose and some are lower, but all are within an order of magnitude of it. The digital anomalies seen in infedigine-exposed rabbit pups are strikingly similar to those seen in pups exposed to phenytoin, and these are in turn similar to the phalangeal deformities that are the most common malformation seen in human children with in utera exposure to phenytoin.

There are no adequate and well-controlled studies in pregnant women. ADALAT CC should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

be used during pregnancy only if the polential benefit justifies the potential risk to the fetus.

Nursing Mothers: Nifedipine is excreted in human milk. Therefore, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE EXPERIENCES: The incidence of adverse events during treatment with ADALAT CC and boses up to 90 mg daily were derived from multi-center placebo-controlled clinical trials in 370 hypertensive patients. Atenolol 50 mg ance daily was used concomitantly in 187 of the 370 patients on ADALAT CC and in 64 of the 126 patients on placebo. All adverse events reported during ADALAT CC therapy were tabulated independently of their causal relationship to medication.

The most common adverse event reported with ADALAT® CC was peripheral edema. This was dose related and the frequency was 18% on ADALAT CC 30 mg daily, 22% on ADALAT CC 90 mg daily versus 10% on placebo. Other common adverse events reported in the above placebo-controlled trials include: Headache (19%, versus 3% placebo incidence); Dizziness (4%, versus 2% placebo incidence); Tabriang-hat essastion (4%, versus 4% placebo incidence); Nausea (2%, versus 1% placebo incidence); Onstipation (1%, versus 0% placebo incidence); Where the frequency of adverse events with ADALAT CC and placebo is similar, causal relationships cannot be established.

The following adverse events were reported with an incidence of 3% or less in daily doses up to 90 mg:



Pharmaceutical Division

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Real Value for Real People with Hypertension

Real Therapeutic Value

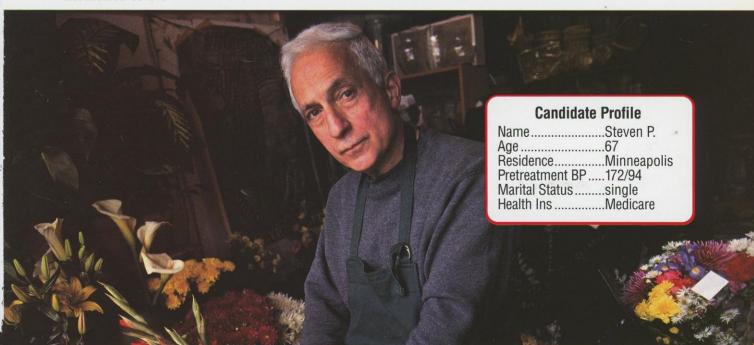
• The benefits of long-acting nifedipine therapy for hypertension*1

Real Human Value

- · Convenient, well-tolerated therapy
- Peripheral edema and headache were the most common dose-related adverse events reported; flushing/heat sensation, dizziness, and fatigue/asthenia were all reported at an incidence of 4%

Real Economic Value

- Lower price (AWP) than Procardia XL⁹ 30 mg, 60 mg and 90 mg—potential 25% savings⁺²
- *Not indicated for angina. Take on an empty stomach. Careful titration may be necessary when switching between Procardia XL® and Adalat® CC. Procardia XL is a registered trademark of Pfizer Labs Division, Pfizer Inc.
- †Calculations based on suggested Average Wholesale Price (AWP). Please see brief summary of Prescribing Information on back of this page.



"Save as much as \$111† a year? I could afford to paint the apartment."



5/93

Start with*

Adalat CC 30mg once daily

Titrate, if necessary*

Adalat CC 60mg once daily

*Please see DOSAGE AND ADMINISTRATION section in brief summary of Prescribing Information below.

BRIEF SUMMARY CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION For Oral Use

P7100744BS

INDICATION AND USAGE: ADALAT CC is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents.

CONTRAINDICATIONS: Known hypersensitivity to nifedipine.

WARNINGS: Excessive Hypotension: Although in most patients the hypotensive effect of nifedipine is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients using concomitant beta-blockers.

Severe hypotension and/or increased fluid volume requirements have been reported in the patients with a beta-blocking agent.

Severe hypotension and/or increased that volume requirements have been reported in patients who received immediate release capacites together with a beta-blocking agent and who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of nifedipine and a beta-blocker, but the possibility that it may occur with nifedipine alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analyses cannot be ruled out. In nifedipine-treat-ed patients where surgery using high dose featured are their in screen that the

ea patients where surgery using inju absetentiary lanesthesia is contemplated, the physician should be aware of these potential problems and, if the patient's condition permits, sufficient time (at least 36 hours) should be allowed for nifedipine to be washed out of the body prior to surgery.

the body prior to surgery.

Increased Angina and/or Myocardial

Infarction: Rarely, patients, particularly

those who have severe obstructive coronary artery disease, have developed well documented increased frequency, duration and/or severity of angina or acute myocardial
infarction upon starting nifedipine or at the time of dosage increase. The mechanism of
this effect is not established.

Beta-Blocker Withdrawal: When discontinuing a beta-blocker it is important to
taper its dose, if possible, rather than stopping abruptly before beginning nifedipine

Patients recently withdrawn from beta blockers may develop a withdrawal syndrome
with increased angina, probably related to increased sensitivity to catecholamines.

Initiation of nifedipine treatment will not prevent this occurrence and on occasion has
been reported to increase it. been reported to increase it.

Congestive Heart Failure: Rarely, patients (usually while receiving a beta-blocker) have developed heart failure after beginning nifedipine. Patients with tight aorts steno-sis may be at greater risk for such an event, as the unloading effect of nifedipine would be expected to be of less benefit to these patients, owing to their fixed impedance to flow across the gortic valve.

PRECAUTIONS: General - Hypotension: Because nifedipine decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and itration of ADALAT CC is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure (See WARNINGS).

ed for patients already taking medications that are known to lower alload pressure (Dee WARNINGS).

Peripheral Edema: Mild to moderate peripheral edema occurs in a dose-dependent manner with ADALAT (C. The placebo subtracted rate is approximately 8% at 30 mg, 12% at 60 mg and 19% at 90 mg daily. This edema is a localized phenomenon, thought to be associated with vasodilation of dependent arterioles and small blood vessels and not due to left ventricular dysfunction or generalized fluid retention. With patients whose hypertension is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction. Information for Patients: ADALAT (C is an extended release tablet and should be swallowed whole and taken an an empty stomach. It should not be administered with lood. Do not chew, divide or crush tablets.

Laboratory Tests: Rare, usually transient, but accasionally significant elevations of enzymes such as alkaline phosphatase, (PK, LDH, SGOT, and SGPT have been noted. The relationship to nifedipine therapy is uncertain in most cases, but probable in some. These laboratory abnormalities have rarely been associated with clinical symptoms; however, cholestasis with or without jaundice has been reported. A small increase (<5%) in mean alkaline phosphatase (PK to the constitution of the patients treated with ADALAT (C this was an isolated finding and it rarely resulted in values which fell outside the normal range. Rare instances of allergic hepatitis have been reported with infieldipine treatment. In controlled studies, ADALAT (C did not adversely affect serum uric acid, glucose, cholesterol or potassium.

lesterol or potassium. lesterol or potassium.

Mifeldpine, like other calcium channel blockers, decreases platelet aggregation in vitro. Limited clinical studies have demonstrated a moderate but statistically significant decrease in platelet aggregation and increase in bleeding time in some nitediprine patients. This is thought to be a function of inhibition of calcium transport across the platelet membrane. No clinical significance for these findings has been demonstrated. Positive direct Combs' test with or without hemolytic anemia has been reported but a causal relationship between nifedigine administration and positivity of this laboratory test, including hemolysis, could not be determined.

Although nifedipine has been used safely in patients with renal dysfunction and has been reported to exert a beneficial effect in certain cases, rare reversible elevations in BUN and serum creatinine have been reported in patients with pre-existing chronic renal insufficiency. The relationship to nifedipine therapy is uncertain in most cases but probable in come

probable in some.

Drug Interactions: Beta-adrenergic blocking agents: (See WARNINGS).

ADAIAT CC was well tolerated when administered in combination with a beta blocker in 187 hypertensive patients in a placebo-controlled clinical trial. However, there have been occasional literature reports suggesting that the combination of nitedipine and beta-adrenergic blocking drugs may increase the likelihood of congestive heart failure, severe hypotension, or exacerbation of angina in patients with cardiovascular disease. Digitalis: Since there have been isolated reports of patients with elevated digoxin levels, and there is a possible interaction between digoxin and ADAIAT CC, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing ADAIAT (Ct no ravial rossible overe or under-distributations).

mar algoxin levels be monitored with miniming, Journally, and assonitioning subsect (C to avoid possible over- or under-digitalization. Coumarin Anticoagulants: There have been rare reports of increased prothrombin time in patients taking coumarin anticoagulants to whom nifedipine was administered. However, the relationship to infedipine therapy is uncertain. Quinidine: There have been rare reports of an interaction between quinidine and

nifedipine (with a decreased plasma level of quinidine).

Real People, Real Needs, Real Value

Gimetidine: Both the peak plasma level of nifedipine and the AUC may increase in the presence of cimetidine. Rantitdine produces smaller non-significant increases. This effect of cimetidine may be mediated by its known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of nifedipine. If nifedipine therapy is initiated in a patient currently receiving cimetidine, cautious fitration is advised.

non's advised.

Carcinagenesis, Mutagenesis, Impairment of Fertility: Nifedipine was administered arally to rats for two years and was not shown to be carcinagenic. When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose. In vivo mutagenicity studies were neg-

Body as a Whole/Systemic: chest pain, leg pain Central Nervous System: paresthesia, vertigo Dermatologic: rash Gastrointestinal: constipation Musculoskoletal: leg cramps Respiratory: epistaxis, rhinitis Urogenital: impo tence, urinary frequency

tence, urinary frequency
Other adverse events reported with an incidence of less than 1.0% were:
Body as a Whole/Systemic cellulitis, chills, facial edema, neck pain, pelvic pain,
pain Cardiovascular: atrial fibrillation, bradycardia, cardiac arrest, extrasystole,
typolension, polipations, phelbisitis, postural hypotension, tardycardia, cutaneous angiectoses Central Nervous System: anxiety, confusion, decreased libido, depression,
hypertonia, insomnia, somnolence Dermatologis: pruritus; sweating
Gastrointestand: abdominal pain, diarrhea, dry mouth, dyspessia, esophagiis, flatulence, gostrointestinal hemorrhage, vomiting Hematologic: lymphadenopathy
Metabolic: gout, weight loss Musculoskeletal: arthralgia, arthritis, myalgia
Respiratory: dyspnea, increased cough, rales, pharyngiis Special Senses: abnormal vision, amblyopia, conjunctivitis, diplopia, funnitus Urogenital/Reproductive:
kidney rafalus, nacturia bresst enoorgement

mal vision, amblyopia, conjunctivitis, alipopia, lininius uragentral / Reproductive: kidney calculus, nocturia, breast engargement |
The following adverse events have been reported rarely in patients given infedipine in other formulations: allergenic hepatitis, alopecia, anemia, arthritis with AMA (+), depression, erythromelalgia, extoliative dermatitis, lever, gingival hyperplasia, gynecomastia, leukopenia, mood changes, muscle cramps, nervousness, paranaid syndrome, purpura, shakiness, siepe disturbances, syncope, taste perversion, thromborytopenia, transient hindesc, at the peak alternal level.

transient blindness at the peak plasma level,

Peal Value

Termor and uritoria.

Dosage should be adjusted according to each patient's needs. It is recommended that ADALAT CC is an early stamach. ADALAT CC is an extended release dosage form and tablets over a 7-14 day period starting with 30 mg once daily. Upward titration should proceed over a 7-14 day period starting with 30 mg once daily. Upward titration should be based on therapeutic efficacy and safety. The usual maintenance dose is 30 mg to 60 mg once daily. Ilitration to doses above 90 mg daily is not recommended. If discontinuation of ADALAT CC is necessary, sound clinical practice suggests that the dosage should be decreased gradually with dose physician supervision.

Care should be taken when dispensing ADALAT CC to assure that the extended release dosage form has been prescribed.

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1. Data on file, Miles Inc. 2. Redbook Update. Montvale, NJ, Medical Economics Data, Inc., October 1993:p. 34.

Pregnancy: Pregnancy (alegary C In rodents, rabbits and mankeys, nifedipine hosens shown to have a variety of embryotoxic, placentotoxic and fetotoxic effects, including stunted fetuses (rats, mice and rabbits), digital anomalies (rats and rabbits), rib deformities (mice), delt polate (mice), small placentos and underdeveloped chorionic villi (mankeys), embryonic and fetal deaths (rats, mice and rabbits), prolonged pregnancy (rats; not evaluated in other species) and decreased neonatal survival (rats; not evaluated in other species). On a mg/kg or mg/m² basis, some of the dosea associated withese various effects are higher than the maximum recommended human dose and some are lower, but all are within an order of magnitude of it.

The digital anomalies seen in infeligine-exposed rabbit pups are strikingly similar to those seen in pups exposed to phenytoin, and these are in turn similar to the phalangeal deformities that are the mast common malformation seen in human children with in utero exposure to phenytoin.

There are no adequate and well-controlled studies in pregnant women. ADALAT CC should be used during pregnancy only if the potential benefit justifies the potential risk to the letus. Nursing Mothers: Nifedipine is excreted in human milk. Therefore, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the

importance of the drug to the mother. ADVERSE EXPERIENCES: The incidence of adverse events during treatment with

ADVERSE EXPERIENCES: The incidence of adverse events during treatment with ADALAT CC in doses up to 90 mg daily were derived from multi-center placebo-constituted in trail trails in 370 hypertensive patients. Atenolo 50 mg once daily was used concomitantly in 187 of the 370 patients on ADALAT CC and in 64 of the 126 patients on placebo. All adverse events reported during ADALAT CC therapy were tobulated independently of their causal relationship to medication.

The most common adverse event reported with ADALAT CC was peripheral edema. This was dose related and the frequency was 18% on ADALAT CC 30 mg daily, 22% on ADALAT CC 40 mg daily ond 29% on ADALAT CC 90 mg daily versus 10% on placebo. Other common adverse events reported in the above placebo-controlled trials include: Headache (19%, versus 13% placebo incidence); Fushing/heat sensation (4%, versus 0% placebo incidence); Hushing/heat sensation (4%, versus 0% placebo incidence); Wischen (1%, versus 0% placebo incidence); Constipation (1%, versus 0% placebo incidence). Where the frequency of adverse events with ADALAT CC and placebo is similar, causal relationship cannot be established.

The following adverse events were reported with an incidence of 3% or less in daily doses up to 90 mg:

The following adverse events were reported with an incidence of 3% or less in daily doses up to 90 mg:



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Real Value for Real People with Hypertension

Real Therapeutic Value

• The benefits of long-acting nifedipine therapy for hypertension*1

Real Human Value

- · Convenient, well-tolerated therapy
- Peripheral edema and headache were the most common dose-related adverse events reported; flushing/heat sensation, dizziness, and fatigue/asthenia were all reported at an incidence of 4%

Real Economic Value

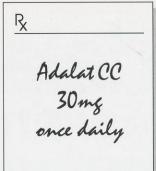
- Lower price (AWP) than Procardia XL[®] 30 mg, 60 mg and 90 mg—potential 25% savings⁺²
- *Not indicated for angina. Take on an empty stomach. Careful titration may be necessary when switching between Procardia XL® and Adalat® CC. Procardia XL is a registered trademark of Pfizer Labs Division, Pfizer Inc.
- †Calculations based on suggested Average Wholesale Price (AWP). Please see brief summary of Prescribing Information on back of this page.



"Save as much as \$111† a year? I could replace the worn linoleum."



Start with*



Titrate, if necessary*

60mg once daily

*Please see DOSAGE AND ADMINISTRATION section in brief summary of Prescribing Information below.

BRIEF SUMMARY CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

PZ100744BS

INDICATION AND USAGE: ADALAT CC is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents

soon. It may be used olone or in combination with other antihypertensive agents.

CONTRAINDICATIONS: Known hypersensitivity to nifedipine.

WARNINGS: Excessive Hypotension: Although in most patients the hypotensive effect of nifedipine is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients using concomitant beta-blockers. Severe hypotension and/or increased fluid volume requirements have been reported in patients who received immediate release capsules together with a beta-blocking agent and who underwent concorny arterly bytoss surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of infedipine and a beta-blocker, but the possibility that it may occur with nifedipine alone, with low doses of fentanyl, in other surgical procedures, or with other narrotic analogesic cannot be ruled out. In nifedipine-treated patients where surgery using high dose fentanyl anesthesia is contemplated, the physician should be aware of these potential problems and, if the patient's condition permits, sufficent time (al least 36 hours) should be allowed for nifedipine to be washed out of the body prior to surgery.

Increased Angina and/or Myocardial Infarction: Rarely, patients, particularly those who have severe obstructive acronary artery disease, have developed well documented increased frequency, duration and/or severity of angina or acute myocardial infarction: Rarely, patients, particularly those who have severe obstructive acronary artery disease, have developed well documented increased frequency, duration and/or severity of angina or acute myocardial infarction upon starting infedipine or at the time of dosage increase. The mechanism of this effect is not established.

Beta-Blocker Withdrawal: When discontinuing a beta-blocker it is important to taper its dose,

this effect is not established.

Beta-Blocker Withdrawal: When discontinuing a beta-blocker it is important to taper its dose, if possible, rather than stopping abruptly before beginning infedipine. Patients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased angina, probably related to increased sensitivity to catecholamines. Initiation of infedipine treatment will not prevent this occurrence and on occasion has

inination of integipine treatment will not prevent this occurrence and on occasion has been reported to increase it.

Congestive Heart Failure: Rarely, patients (usually while receiving a beta-blocker) have developed heart failure after beginning infedipine. Potients with light oortic stenosis may be at greater risk for such an event, as the unloading effect of infedipine would be expected to be of less benefit to these patients, owing to their fixed impedance to flow across the aortic valve.

PRECAUTIONS: General - Hypotension: Because nifedipine decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administration and litration of ADALAT CC is suggested. Close observation is especially recommended for patients already taking medications that are known to lower blood pressure (See WARNINGS).

WARNINGS).

Peripheral Edema: Mild to moderate peripheral edema occurs in a dose-dependent manner with ADALAT CC. The placebo subtracted rate is approximately 8% at 30 mg, 12% at 60 mg and 19% at 90 mg daily. Nis edema is a localized phenomenon, thought to be associated with vasodilation of dependent netroloss and small blood vessels and not due to left ventricular dysfunction or generalized fluid retention. With patients whose hypertension is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction. Information for Patients: ADALAT Ct. is an extended release tablet and should be swallowed whole and taken on an empty stomach. It should not be administered with food. Do not chew, divide or crush tablets.

food. Do not chew, divide or crush tablets.

Laboratory Tests: Rare, usually transient, but occasionally significant elevations of enzymes such as alkaline phosphatase, CPK, LDH, S60T, and S6PT have been noted. The relationship to nifedipine therapy is uncertain in most cases, but probable in some. These laboratory abnormalities have rarely been associated with clinical symptoms; however, cholestasis with or without jounditie has been reported. A small increase (<5%) in mean alkaline phosphatase was noted in patients treated with ADALAT CC. This was an isolated finding and it rarely resulted in values which fell outside the normal range. Rare instances of allergic hepatilis have been reported with nifedipine treatment. In controlled studies, ADALAT CC did not adversely affect serum uric acid, glucose, cho-

In controlled studies, JAUAH LC did not adversely affect serum unc acid, gutose, cinclesterol or potassium.

Nifedipine, like other calcium channel blockers, decreases platelet aggregation in vitro. Limited clinical studies have demonstrated a moderate but statistically significant decrease in platelet aggregation and increase in bleeding time in some nifedipine patients. This is thought to be a function of inhibition of calcium transport across the platelet membrane. No clinical significance for these findings has been demonstrated. Positive direct (combs' test with or without hemolytic anemia has been reported but a causal relationship between infedipine administration and positivity of this laboratory test, including hemolysis, could not be determined.

Although nifedipine has been used safely in patients with renal dysfunction and has been reported to exert a beneficial effect in certain cases, crae reversible elevations in BUN and serum creatinine have been reported in patients with pre-existing chronic renal insufficiency. The relationship to nifedipine therapy is uncertain in most cases but

BUM and serum retainine nave been reported in patients with pre-existing circonic renal insufficiency. The relationship to nifedipine therapy is uncertain in most cases but probable in some.

Drug Interactions: Beta-adrenergic blocking agents: (See WARNINGS).

ADALAT CC was well tolerated when administered in combination with a beta blocker in 187 hypertensive patients in a placebo-controlled clinical trial. However, there have been occasional literature reports suggesting that the combination on infedipine and beta-adrenergic blocking drugs may increase the likelihood of congestive heart failure, severe hypotension, or exacerbation of angina in patients with cardiovoscular disease.

Digitalis: Since there have been isolated reports of patients with elevated digoxin levels, and there is a possible interaction between digoxin and ADALAT CC, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing ADALAT CC to avoid possible over- or under-digitalization.

Coumarin Anticogulants: There have been rare reports of increased prothrombin time in patients taking coumarin anticoagulants to whom nifedipine was administered. However, the relationship to nifedipine therapy is uncertain.

Quinidine: There have been rare reports of an interaction between quinidine and nifedipine (with a decreased plasma level of quinidine).

Real People, Real Needs, Real Value

Body as a Whole/Systemic: chest pain, leg pain Central Nervous System: paresthesia, vertigo Dermatologic: rash Gastrointestinal: constipution Musculoskeletal: leg cramps Respiratory: epistaxis, rhinitis Urogenital: impotence, urinary frequency
Other adverse events reported with an incidence of less than 1.0% were:

tence, urnary trequency
Other adverse events reported with an incidence of less than 1.0% were:
Body as a Whole/Systemic cellulitis, chills, facial edema, neck pain, pelvic pain, pain Cardiovascular: atrial fibrillation, bradyardia, cardiac arrest, extracystole, hypotensian, polalitations, phlebitis, postural hypotension, tochyvardia, culaneous angiectases Central Nervous System: anxiety, confusion, decreased libido, depression, hypotensian, insommia, somolence Dermatologic: purifus, sweating Gastrointestinal: abdominal pain, diarrhea, dry mouth, dyspepsia, esophagitis, flatuence, gastrointestinal hemorrhage, womiting. Hematologic: lymphadenopathy Metabolic: gout, weight loss Musculoskeletal: arthralgia, arthritis, myalgia Respiratory: dyspnea, increased cought, tales, pharyngitis Special Senses: abnormal vision, amblyopia, conjunctivitis, diplopia, tinnitus Uragential/Reproductive: kidney calculus, nocturio, breast engorgement
The following adverse events have been reported rarely in patients given nifedipine in other formulations: allergenic hepatitis, alopecia, anemia, arthritis with ANA (+), depression, erythromelalgia, extoliative dermatitis, fever, gingival hyperplosia, gyramomatic, leukopenia, mood changes, muscle cramps, nervousness, paranoid syndrome, purpura, shakiness, sleep disturbances, yerupura, shakiness, sleep d

tremor and urticaria.

Dosage should be adjusted according to each patient's needs. It is recommended that ADALAT (C be administered orally once daily on an empty stomach. ADALAT (C is an should be swallowed whole, not biten or divided. In general, titration should proceed over a 7-14 day period starting with 30 mg once daily. Upward titration should proceed based on therapeutic efficacy and safety. The usual maintenance dose is 30 mg to 60 mg once daily. Itiration to doses above 90 mg daily is not recommended. It discontinuation of ADALAT (C is necessary, sound clinical practice suggests that the dosage should be decreased gradually with dose physician supervision.

Care should be taken when dispensing ADALAT (C to assure that the extended release dosage form has been prescribed.

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1. Data on file, Miles Inc.
2. Redbook Update. Montvale, NJ, Medical Economics Data, Inc., October 1993;p. 34.

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Gimelidine: Both the peak plasma level of nifedipine and the AUC may increase in the presence of cimelidine. Ranitidine produces smaller non-significant increases. This effect of cimelidine may be mediated by its known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of nifedipine. If nifedipine therapy is initiated in a patient currently receiving cimelidine, cautious titra-tions is advised.

Intedipine therapy is initiated in a patient currently receiving cimeliane, contious titration is advised.

Carcinagenesis, Mutagenesis, Impairment of Fertility: Nifedipine was administered arally to rats for two years and was not shown to be carcinagenic. When given to rats prior to mating, nifedipine caused reduced fertility at a dose approximately 30 times the maximum recommended human dose. In vivo mutagenicity studies were negative.

ative.

Pregnancy: Pregnancy Category C. In rodents, rabbits and monkeys, nifedipine has been shown to have a variety of embryotoxic, placentotoxic and fetotoxic affects; including stunted fetuses (rats, mice and rabbits), digital anomalies (rats and rabbits), rib detarmilies (mice), elfe placite (mice), small placentas and underdeveluped chroinciv till (mankeys), embryonic and fetal deaths (rats, mice and rabbits), prolonged pregnancy (rats, not evaluated in other species). On a mg/kg or mg/m² basis, some of the doses associated with these various effects are higher than the maximum recommended human dose and some are lower, but all are within an order of magnitude of it.

The digital anomalies seen in infedigine-exposed rabbit pups are strikingly similar to those seen in pups exposed to phenytoin, and these are in turn similar to the planaged deformities that are the most common malformation seen in human children with in utero exposure to phenytoin.

with *in utero* exposure to phenytoin.

There are no adequate and well-controlled studies in pregnant women. ADALAT CC should be used during pregnancy only if the potential benefit justifies the potential risk to the

be used during pregnancy only if the potential benefit justifies the potential risk to the feture.

Nursing Mothers: Nifedipine is excreted in human milk. Therefore, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE EXPERIENCES: The incidence of adverse events during treatment with ADALAT CC in doses up to 90 mg adily were derived from multi-center placebo-controlled clinical trials in 370 hypertensive politients. Atenolol 50 mg ance daily was used concomitantly in 187 of the 370 patients on ADALAT CC and in 64 of the 126 patients on placebo. All adverse events reported during ADALAT CC therapy were tabulated independently of their causal relationship to medication.

The most common adverse event reported with ADALAT CC So mg daily, 22% on ADALAT CC 60 mg daily, 22% o



Real Value for Real People with Hypertension

Real Therapeutic Value

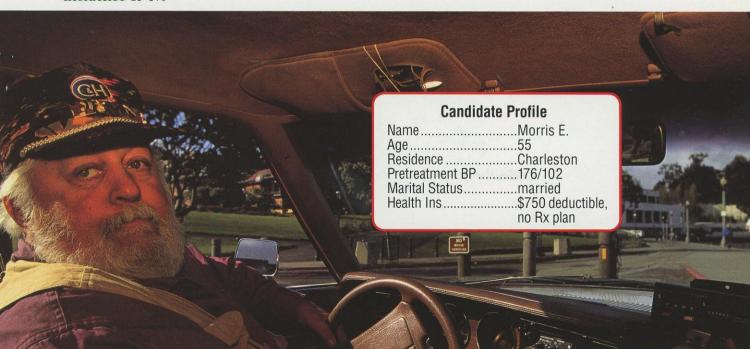
• The benefits of long-acting nifedipine therapy for hypertension*1

Real Human Value

- · Convenient, well-tolerated therapy
- Peripheral edema and headache were the most common dose-related adverse events reported; flushing/heat sensation, dizziness, and fatigue/asthenia were all reported at an incidence of 4%

Real Economic Value

- Lower price (AWP) than Procardia XL® 30 mg, 60 mg and 90 mg—potential 25% savings^{†2}
- *Not indicated for angina. Take on an empty stomach. Careful titration may be necessary when switching between Procardia XL® and Adalat® CC. Procardia XL is a registered trademark of Pfizer Labs Division, Pfizer Inc.
- †Calculations based on suggested Average Wholesale Price (AWP). Please see brief summary of Prescribing Information on back of this page.



"Save up to \$192† a year? That's the next payment on my insurance."



30ma, 60ma & 90ma

Start with*

Ŗ

Adalat CC 30mg once daily

Titrate, if necessary*

Adalat CC 60mg once daily

*Please see DOSAGE AND ADMINISTRATION section in brief summary of Prescribing Information below.

BRIEF SUMMARY CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATION AND USAGE: ADALAT CC is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents. CONTRAINDICATIONS: Known hypersensitivity to nifedipine.

CONTRAINDICATIONS: Known hypersensitivity to nifedipine.

WARNINGS: Excessive Hypotension: Although in most patients the hypotensive effect of nifedipine is modest and well tolerated, occasional patients have had excessive and poorly tolerated hypotension. These responses have usually occurred during initial titration or at the time of subsequent upward dosage adjustment, and may be more likely in patients using concomitant beta-folkers.

Severe hypotension and/or increased fluid volume requirements have been reported in patients who received immediate release capsules together with a beta-folkering agent and who underwent coronary ratery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of miledipine and a beta-folker, but the possibility that it may occur with infedipine alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analogesics cannot be ruled out. In nifedipine-treated patients where surgery using high dose fentanyl anesthesia is contemplated, the physician should be aware of these potential problems and, if the patient's condition permits, sufficient time (at least 36 hours) should be aware of these potential problems and, if the patient's condition permits, sufficient time (at least 36 hours) should be aware for the body prior to surgery.

be allowed for nitedipine to be washed out of the body prior to surgery.

Increased Angina and/or Myocardial Infraction: Rarely, patients, particularly those who have severe obstructive coronary artery disease, have developed well documented increased frequency, duration and/or severity of angina or acute myocardial infraction upon starting nifedipine or at the time of dosage increase. The mechanism of this effect is not established.

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Beta-Blocker Withdrawal: When discontinuing a beta-blocker it is important to toper its dose, if possible, rather than stopping abruptly before beginning nifedipine. Potients recently withdrawn from beta blockers may develop a withdrawal syndrome with increased anging, probably related to increased sensitivity to catecholomines. Initiation of nifedipine treatment will not prevent this occurrence and on occasion has

Initiation of integuiphe rearment will not prevent this occurrence and on occasion has been reported to increase it.

Congestive Heart Failure: Rarely, patients (usually while receiving a beta-blocker) have developed heart failure after beginning integlipine. Patients with tight nortic stenosis may be at greater risk for such an event, as the unloading effect of integlipine would be expected to be of less benefit to these patients, owing to their fixed impedance to flow cross the nortic valve.

PRECAUTIONS: General - Hypotension: Because nifedipine decreases peripheral vascular resistance, careful monitoring of blood pressure during the initial administra-tion and fitration of ADALATCC is suggested. Close observation is especially recommend-ed for patients already taking medications that are known to lower blood pressure (See WARNINGS).

ed for potients already taking medications that are known to lower blood pressure (See WARNINGS).

Peripheral Edema: Mild to moderate peripheral edema occurs in a dose-dependent manner with ADALAT CC. The placebo subtracted rate is approximately 8% at 30 mg, 12% at 60 mg and 19% at 90 mg daily. This edema is a localized phenomenon, thought to be associated with vasodilation of dependent arterioles and small blood vessels and rot due to left ventricular dysfunction or generalized fluid retention. With patients whose hypertension is complicated by congestive heart failure, care should be taken to differentiate this peripheral edema from the effects of increasing left ventricular dysfunction. Information for Patients: ADALAT CC is an extended release tablet and should be swallowed whole and taken on an empty stomach it should not be administered with food. Do not chew, divide or crush tablets.

Laboratory Tests: Rare, usually transient, but occasionally significant elevations of enzymes such as alkaline phosphatase, CPK, LDH, SGOT, and SGPT have been noted. The relationship to nifedipine therapy is uncertain in most cases, but probable in some. These laboratory abnormalities have rarely been associated with clinical symptoms; however, cholestasis with or without joundice has been reported. A small increase (<5%) in mean alkaline phosphatase was noted in patients received with ADALAT CC. This may not the proposed of the proposed of the proposed of the patients received with faired pine treatment. In controlled studies, ADALAT CC did not adversely affect serum uric acid, glucose, cholesterol or potassium.

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Although nifedipine has been used safely in patients with renal dysfunction and has been reported to exert a beneficial effect in certain cases, rare reversible elevations in BUN and serum creatinine have been reported in patients with pre-existing chronic renal insufficiency. The relationship to nifedipine therapy is uncertain in most cases but

probable in some.

Drug Interactions: Beta-adrenergic blocking agents: (See WARNINGS).

ADALAT Cx wow well tolerated when administered in combination with a beta blocker in 187 hypertensive patients in a placebo-controlled clinical trial. However, there have been occasional literature reports suggesting that the combination of nifedipine and beta-adrenergic blocking drugs may increase the likelihood of congestive heart failure, severe hypotension, or exacerbation of angina in patients with cardiovascular disease. Digitalis: Since there have been isolated reports of patients with elevated digoxin levels, and there is a possible interaction between digoxin and ADALAT CC, it is recommended that digoxin levels be monitored when initiating, adjusting, and discontinuing ADALAT CC to avoid possible over- or under-digitalization.

Coumarin Anticoagulants: There have been rare reports of increased prothrombin time in patients taking coumarin anticoagulants to whom nifedipine was administered. However, the relationship to infedigine therapy is uncertain.

Quinidine: There have been rare reports of an interaction between quinidine and nifedipine (with a decreased plasma level of quinidine).

Real People, Real Needs, Real Value

Body as a Whole/Systemic: chest pain, leg pain Central Nervous System: paresthesia, vertigo Dermatologic: rash Gastrointestinal: constipution Musculoskeletal: leg cramps Respiratory: epistaxis, rhinitis Urogenital: impotence, urinary frequency

Musculoskeletal: leg cramps Respiratory: epistoxis, rhinitis Uragenital: impotence, urinary frequency
Other adverse events reported with an incidence of less than 1.0% were:
Body as a Whole/Systemic: cellulitis, chills, facial edema, neck pain, pelvic pain,
pain (ardiovascular: atrial fibrillation, bradycardia, cardiac arrest, extrasystole,
hypotension, polpitations, phlebilis, postural hypotension, tachycardia, cutaneous angiectases Central Nervous Systems anxiety, contusion, decreaced libido, depression,
hypertonia, insomnia, somnolence Dermatologic: pruritus, sweating
Gastrointestinal: adeominal pain, diarrhea, dry mouth, dyspegaia, esophaghis, flatulence, gastrointestinal hemorrhage, vomiting Hematologic: lymphadenopathy
Metabolic: goul, weight loss Musculoskeletal: arthraligia, arthritis, myalgia a
Kidney calculus, nacturia, breast engargement
The following adverse events have been reported rarely in patients given nifedipine in
the formulations: allergenic hepatitis, alopecia, anemia, arthritis with AMA (+),
depression, erythromelolgia, exfoliative dermatitis, fever, gingival hyperplasia, gynecomaslia, leukopenia, mood changes, muscle cramps, nervousness, paraniol syndrome,
puprura, shakiness, sleep disturbances, syncope, taste perversion, thrombocytopenia,
transient blindness at the peach plasma level,
termor and uritaria.

tremor and urticaria

Itemor and urticaria.

DoSAGE AND ADMINISTRATION:
Dosage should be adjusted according to each
patient's needs. It is recommended that
ADALAT CC to administered orally one delivery
on an empty stomach. ADALAT CC is an
extended release dosage form and tablets
should be swallowed whole, not bitten or divided. In general, litration should proceed
over a 7-14 day period starting with 30 mg once daily. Upward titration should proceed
over and over a 1-14 day period starting with 30 mg once daily. Upward titration should be
based on theropeutic efficary and safety. The usual maintenance dose is 30 mg to 60
mg once daily. Titration to doses above 90 mg daily is not recommended. If discontinuation of ADALAT CC is necessary, sound clinical practice suggests that the
dosage should be decreased gradually with dose physician supervision.
Care should be taken when dispensing ADALAT CC to assure that the extended release
dosage form has been prescribed.

dosage form has been prescribed

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References:

1. Data on file, Miles Inc.

2. Redbook Update. Montvale, NJ, Medical Economics Data, Inc., October 1993;p. 34.

Cimelidine: Both the peak plasma level of nifedipine and the AUC may increase in the presence of cimelidine. Ranitidine produces smaller non-significant increases. This effect of cimelidine may be mediated by its known inhibition of hepatic cytochrome P-450, the enzyme system probably responsible for the first-pass metabolism of nifedipine. If nifedipine therapy is initialed in a patient currently receiving cimetidine, cautious titra tion is advised.

norts auviseu. Carcinagenesis, Impairment of Fertility: Nifedipine was adminis-tered orally to rats for two years and was not shown to be carcinagenic. When given to rats prior to matring, nifedipine caused reduced fertility at a dose approximately 30 finnes the maximum recommended human dose. In vivo mulagenicity studies were neg-

ative.

Pregnancy: Pregnancy Category C. In rodents, rabbits and monkeys, nifedipine has been shown to have a variety of embryotoxic, placentotoxic and fetotoxic effects, including stunted fetuses (rats, mice and rabbits), digital anomalies (rats and rabbits), rib detormities (mice), cleft palate (mice), small placentas and underdevelaged chronici villi (monkeys), embryonic and fetal deaths (rats, mice and rabbits), prolonged pregnancy (rats; not evaluated in other species). On a mg/kg or mg/m² basis, some of the doses associated with these various effects are higher than the maximum recommended human dose and some are lower, but all are within an order of magnitude of it.

The digital anomalies seen in intelliginie-exposed rabbit pups are strikingly similar to those seen in pups exposed to phenytoin, and these are in turn similar to the phalangeal deformities that are the most common malformation seen in human children with in utere accounter to hardworkin.

with in utera exposure to phenytoin.

There are no adequate and well-controlled studies in pregnant women. ADALAT CC should be used during pregnancy only if the potential benefit justifies the potential risk to the

Nursing Mothers: Nifedipine is excreted in human milk. Therefore, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

ADVERSE EXPERIENCES: The incidence of adverse events during treatment with ADALAT CC in doses up to 90 mg daily were derived from multi-center placebo-controlled clinical trials in 370 hypertensive patients. Atenolol 50 mg once daily was used concomitantly in 187 of the 370 patients on ADALAT CC and in 64 of the 126 patients on placebo. All adverse events reported during ADALAT CC therapy were tabulated independently of their causal relationship to medication.

The most common adverse event reported with ADALAT CC Cwas peripheral edema. This was dose related and the frequency was 18% on ADALAT CC 30 mg daily versus 10% on placebo. Other common adverse events reported in the above placebo-controlled trials include: Headache (19%, versus 13% placebo incidence); Flushing/heat sensation (4%, versus by a placebo incidence); Puzziness (4%, versus 2% placebo incidence); Puzziness (4%, versus 1% placebo incidence); Oscipiotion (1%, versus 0% placebo incidence); Oscipiotion (1%, versus 0% placebo incidence). Musen (2%, versus 1% placebo incidence); Constipotion (1%, versus 0% placebo incidence). Musen (2%, versus 1% placebo incidence); Where the frequency of adverse events with ADALAT CC and placebo is similar, causal relationship cannot be established. ADVERSE EXPERIENCES: The incidence of adverse events during treatment with

relationship cannot be established. The following adverse events were reported with an incidence of 3% or less in daily doses up to 90 mg:

Pharmaceutical Division

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