What's missing?

Perhaps it’s PLENDIL. Because of the greater rate of severe hypertension in blacks, more black patients will require multidrug therapy. What’s more, non-insulin-dependent diabetes is twice as prevalent in black patients as compared to white patients.

Often, PLENDIL is appropriate. In clinical trials, blood pressure response was similar in black and non-black patients. And, PLENDIL may be used for many hypertensive patients with or without concomitant disorders, such as: hypercholesterolemia, diabetes, impaired renal function, COPD, or asthma.

PLENDIL provides a gradual onset of action for continuous 24-hour blood pressure control with convenient once-daily dosage.

PLENDIL. A highly effective calcium channel blocker for hypertension. Alone or in combination with another antihypertensive agent.

Plendil®

(felodipine) Tablets, 5 mg, 10 mg

Because you consider the whole patient.

* Data available upon request from Medical Affairs, Astra/Merck Group of Merck & Co., Inc., 725 Chesterbrook Boulevard, Wayne, PA 19087. Please request information packet #DA-PLN4.

PLENDIL is contraindicated in patients who are hypersensitive to this product. Please see brief summary of Prescribing Information on page following next page.
References:

BRIEF SUMMARY

TABLETS
PLENDIL® (FELODIPINE)
EXTENDED-RELEASE TABLETS

INDICATIONS AND USAGE
PLENDIL® is indicated for the treatment of hypertension. PLENDIL® may be used alone or concomitantly with other antihypertensive agents.

CONTRAINDICATIONS
PLENDIL is contraindicated in patients who are hypersensitive to this product.

PRECAUTIONS
General
Hypotension: Feldilpine, like other calcium antagonists, may occasion-
ally precipitate significant hypotension and rarely syncope. It may lead to reflex tachycardia, and aortic or mitral incompetence may precipitate angina pectoris. (See ADVERSE REACTIONS.)

Heart Failure: Although acute hemodynamic studies in a small number of patients with NYHA Class I or II heart failure treated with feldilpine have not demonstrated negative inotropic effects, safety in patients with heart failure has not been established. Caution therefore should be exer-
cised when treating these patients.

Administration and Dosage
PLENDIL capsules should be removed from the bottle upon opening. It should not be used if the foil inner bridge is not intact before administration.

Pregnancy
Category C

ADVERSE REACTIONS

In clinical studies, the United States and overseas approximately 3000 patients were treated with feldilpine as either the extended-release or the immediate-release formulations.

The most common adverse experiences reported with PLENDIL® (felodipine) administered as monotherapy in all settings and with all once-daily dose regimens and doses tested were:

- Headache
- Flushing
- Nasal congestion
- Edema
- Ptosis
- Dizziness
- Rash

In long-term studies involving 10,000 patients treated with felodipine, the most frequent adverse experience observed was headache; the incidence of headache was 41%. The incidence of headache in felodipine-treated patients was not different from that observed in placebo-treated patients. The incidence of headache was not affected by the duration of treatment. The incidence of headache was not altered by the concomitant use of other antihypertensive agents, and the incidence of headache was not increased by the addition of a second anti
hypertensive agent.

It has been established that in clinical studies, the incidence of headache was not increased by the addition of a second antihypertensive agent. The incidence of headache was not increased by the addition of a second antihypertensive agent.

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Dry Nights For Good Mornings

Brief Summary

CONTINUATION: Known hydromedically to be DDAVP Nasal Spray.

Use

1. For nocturnal enuresis only.
2. Only for children and adolescents in particular, fund course should be adjusted in order to decrease the potential occurrence of water intoxication and hyponatremia. Particular attention should be paid to the possibility of the rare occurrence of an adverse decrease in renal concentrating ability.

Precautions

General: DDAVP Nasal Spray at high dosage has frequently produced a slight elevation of blood pressure, which disappeared with a reduction in dosage. This drug should be used with caution in patients with coronary artery insufficiency and/or hypertension, and cardiac disease because of possible rise in blood pressure.

DDAVP Nasal Spray should be used with caution in patients with conditions associated with fluid and electrolyte imbalance, such as osmotic diuresis, because these patients are prone to hyponatremia.

Central Urinary Diabetes Insipidus (CUDI): Since DDAVP Nasal Spray is used intranasally, changes in the nasal mucosa such as scaling, edema, or other disease may cause erosive, ulcerative absorption in which case DDAVP Nasal Spray should not be used. For such situations, DDAVP Nasal Spray should be discontinued.

Primary Nocturnal Enuresis: If changes in the nasal mucosa have occurred, ulcerative absorption may result. DDAVP Nasal Spray should be discontinued until the nasal problems resolve.

Information for Patients: Patients should be informed that the bottle accuracy delivers 5.0-6.0 drops of 10 mcg each. Any solution remaining after 30 drops should be discarded since the amount delivered thereafter may be substantially less than 10 mcg of drug. No attempt should be made to transfer remaining solution to another bottle. Patrons should be instructed to read accompanying directions or use of the spray pump carefully before use.

Labeled: Laboratory tests for following the patient with central diabetes insipidus or post-surgery or head trauma-related polyuria or polydipsia include urine volume and osmolality in some cases plasma osmolality may be required. For the healthy patient with primary nocturnal enuresis, serum electrolytes should be checked at least once if therapy is continued beyond 6 days.

Drug interactions: Although the pressor activity of DDAVP Nasal Spray is very low compared to the antidiuretic activity, use of large doses of DDAVP Nasal Spray with other pressor agents should only be done with careful patient monitoring.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No studies in animals have shown to be carcinogenic no teratogenic informations available.

Pregnancy: Category C: Reproduction studies performed in rats and rabbits up to 15 times the human intravenous dose (aabout 1.25 times the total adult human dose given systemically) have revealed no evidence of harm to the fetus due to developmental anomalies. There were no observations of management of diabetes insipidus in pregnant women with no harm to the fetus reported. However, no long-term studies in pregnant women have been carried out in animals. It is not known whether DDAVP or DDAVP Nasal Spray will appear in mammalian breast milk. Because of the potential for adverse effects in nursing infants, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the potential benefit of the drug to the mother.

Nursing Mothers: There have been no controlled studies in nursing mothers. A single study in a non-parturient woman demonstrated a marked decrease in lactation. It is not recommended that DDAVP Nasal Spray be used during lactation.

Central Diabetes Insipidus: DDAVP Nasal Spray has been used in children with diabetes insipidus. Chronic (6-9 weeks) daily treatment with DDAVP Nasal Spray in doses of 10 mcg (15 mcg) has been shown to be safe and in 2 of 13 patients administration was avoided.

Central Urinary Diabetes Insipidus: DDAVP Nasal Spray has been used in children with diabetes insipidus. Use in infants and children requires careful monitoring relative to possible development of signs and symptoms indicative of hyponatremia which may be due to a local activation of the hypothalamus.

ADVERSE REACTIONS

BODY AS A WHOLE: Altered taste. Headache. ACHN. Nephropathy. GENITOURINARY: Cramps. Polyuria. Urethritis. LARYNX: Hoarseness. NOSE: Rhinitis. Oral mucositis. DERM: Rash. NURSING-MOTHERS: Decrease in milk. DEHYDRATION: None. REPRODUCTIVE SYSTEM: None. RESPIRATORY SYSTEM: None. SKIN: Rash. SKIN & APPARATUS: None. SPECIAL SENSES: None. SYSTEMIC: None. CARINOSURGICAL SYSTEM: None. DENTAL: None. OVERREACTIONS: See adverse reactions above. If overzealous, the dose should be reduced frequency of administration decreased to the drug withdrawn according to the severity of the condition. There is no known specific antidote for DDAVP Nasal Spray and oral DDAVP has not been established. An intravenous dose of 2 mg/ml in most demonstrated no effect.

HOW SUPPLIED: A 0.5 mL bottle with spray pump delivers 30 doses of 10 mcg (NDC 0075-2493-02). Also available as 1 mL, oral pack, contains 10 final dose spray applications per pack (NDC 0075-2494-00). Recalculated at 2.5 mg/ml (0.4 mg/mL). When traveling, your product may contain solids (up to 10) weeks when stored at room temperature, 22°C (72°F). Cautions: FDA, U.S.A. law prohibits dispensing without prescription. Please see all prescribing information in product circular.

References:


Manufactured for: PHOENIX-POLUNCE ROYER
RHONE-POLUNCE ROYER PHARMACEUTICALS INC.
190 ROUTE 100, SUITE 301
GOLDENVALLEY, MN 55422

By Ferring Pharmaceuticals, Malmo, Sweden

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TAKE EFFECTIVE CONTROL OF BED-WETTING

- Rapid response—substantial effect seen in as little as 1 to 3 nights of therapy
- A combined 15-year record of successful and safe use in the U.S. and Europe
- May be used hand in hand with behavior modification

Nighttime fluid intake should be restricted to decrease the potential occurrence of fluid overload; serum electrolytes should be checked at least once when therapy is continued beyond 7 days.

DDAVP® Nasal Spray
(desmopressin acetate) 5mL
DRY NIGHTS FOR GOOD MORNINGS

Please see brief summary of prescribing information on adjacent page.
Nonconventional Therapies
Roger O. Lütge, MD, MSPH

You Can Be Both Conventional and Nonconventional
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Hisham Barakat, PhD; John Bray, PhD;
Christy Whitley, PharmD; Ronnie D. Horner, PhD

American Medical Association
Physicians dedicated to the health of America

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A Little Means A Lot To The Older Hypertensive

Comparable antihypertensive efficacy to 2.5 mg* with the safety profile of a lower once-daily dose

Favorable metabolic profile—no adverse effect on lipids; only 2% incidence of clinical hypokalemia†

Safe and effective for step-down therapy

Side-effect profile compatible with other antihypertensive agents

LOZOL 1.25 mg once daily is now the recommended starting dose for indapamide in hypertension

LOW-DOSE ONCE-DAILY

INDICATIONS: LOZOL® (indapamide) is indicated for the treatment of hypertension, alone or in combination with other antihypertensive drugs, and for the treatment of salt and fluid retention associated with congestive heart failure.

Usual In Pregnancy See PRECAUTIONS.

CONTRAINDICATIONS: Anuria, hypersensitivity to indapamide or other sulfonamides-derived drugs.

WARNINGS: In a small number of cases, severe hypokalemia, accompanied by hypokalemia, has been reported with 2.5 mg and 5.0 mg indapamide primarily in elderly females. Serum potassium levels were not corrected by electrolyte replacement. Hypokalemia occurred more commonly with the higher dose (5 mg) of indapamide. However, serum concentrations of potassium increased only slightly with indapamide. Hypokalemia may decrease serum PTH levels without signs of hypocalcemia. Combinations of hypokalemic and/or diuretics have not been seen. Discourage before tests of potassium function are performed.

Thiazides have shown to have consistent type I renin-mediated hypertension. Consider this possibility with indapamide.

DRUG INTERACTIONS: LOZOL may add to or potentiate the action of other antihypertensive drugs. The antihypertensive effect of the drug may be enhanced in the post-synaptic/alpha-adrenergic blocker patient. Indapamide may decrease antral responsiveness to nonepostricta, noradrenaline, and this may decrease the use of these drugs.

In Ministry and life lifetime oncogenesis studies, there were no significant differences in the incidence of tumors between the indapamide-treated animals and the control groups.

Preparatory Category B: Diuretics over the course of a placentate barrier in and out of children. Indapamide should be used during pregnancy only if clearly needed. Use may be associated with fetal or neonatal juxta, throracic, and possibly other adverse effects that have occurred in adults. It is not known whether this drug is excreted in human milk. If the use of this drug in a breast-fed patient.

ADVERSE REACTIONS: Most adverse effects have been mild and transient. From Phase III placebo-controlled studies with indapamide 1.25 mg, adverse reactions with 5% cumulative incidences include headache, infection, pain, back pain, abnormality, edema, -5% cumulative incidence; reticulum, fever, diarrhea, respiratory tract, allergic; 3% cumulative incidence; reticulum, fever, herpes simplex, abdominal pain, chest pain, constipation, diarrhea, nausea, peripheral edema, hypotension, nausea, syncope, rhynogia, urticaria, conjunctivitis, photophobia, conjunctivitis, allergic contact dermatitis, headaches, urticaria.


Indapamide has been shown to be a renin-dependent inhibitor of angiotensin II production.

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While every precaution is taken to ensure accuracy, we cannot guarantee against the possibility of an occasional change or omission in the preparation of this index.
One in three adults say they occasionally have trouble sleeping.

Now you can help with...
More sleep, better sleep, through the night

AMBien
(Zolpidem Tartrate)®
5-mg & 10-mg tablets

©1994 Searle
From a unique class of non-benzodiazepine sleep agents

More sleep
Total sleep time significantly increased compared with placebo. Patients fall asleep quickly; generally within 20 to 30 minutes.²⁴

Better sleep
Awakenings were reduced, compared to placebo.

Through the night
No evidence of increased wakefulness during the last third of the night. Normal sleep stages are generally preserved (clinical significance unknown).

Mean percent of time in each sleep stage²

<table>
<thead>
<tr>
<th>Stage 2</th>
<th>Stage 3 &amp; 4</th>
<th>REM</th>
</tr>
</thead>
<tbody>
<tr>
<td>56.7%</td>
<td>19.1%</td>
<td>16.5%</td>
</tr>
</tbody>
</table>

In this multicenter, double-blind, randomized, controlled study of 631 healthy volunteers, no significant differences were found between the durations of sleep stages.

Short half-life
Mean 2.5-hour half-life, with no active metabolites.

With no objective evidence of tolerance or rebound insomnia
In studies of up to 35 consecutive nights at recommended doses.²³

Favorable safety and tolerability profile
Adverse events with dosages of ≤ 10 mg that were statistically significant vs placebo

<table>
<thead>
<tr>
<th></th>
<th>Short-term: ≤10 nights</th>
<th>Long-term: 28 to 35 nights</th>
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</thead>
<tbody>
<tr>
<td>drowsiness</td>
<td>2%</td>
<td>5%</td>
</tr>
<tr>
<td>dizziness</td>
<td>1%</td>
<td>drugged</td>
</tr>
<tr>
<td>diarrhea</td>
<td>1%</td>
<td>feelings</td>
</tr>
</tbody>
</table>

Recommended dosage

For adults: one 10-mg tablet
Patients should take AMBIEN right before going to bed and when ready for sleep.

For elderly/debilitated patients: one 5-mg tablet

AMBIEN is indicated for the short-term treatment of insomnia. Prescriptions should not exceed a 1-month supply. Hypnotics should generally be limited to 7 to 10 days of use. Reevaluation of the patient is recommended if they are taken for more than 2 to 3 weeks.
In patients with hepatic dysfunction, treatment should be initiated with a 5-mg dose and patients closely monitored.
INDICATIONS AND USAGE
Ambien (zolpidem tartrate) tablets are indicated for the short-term treatment of insomnia. Hypnagogic should generally be limited to 7 to 10 days of treatment. Treatment beyond 10 days has not been evaluated. Ambien should be administered for no more than 2 months.
Full text Practice Parameters at your fingertips.

New Practice Parameters on CD-ROM 1994 Edition gives you the convenience of having full text practice parameters at your fingertips whenever you need them, at a cost that's far less than you'd pay to purchase them separately.

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Physicians dedicated to the health of America
ONCE-A-DAY

CARDIZEM CD
(diltiazem HCl) 120-, 180-, 240-, 300-mg Capsules

IN HYPERTENSION OR ANGINA
IN HYPERTENSION OR ANGINA

CARDIZEM CD
(diltiazem HCl)

FOR EFFECTIVE
24-HOUR CONTROL

ONCE A DAY
HEMODYNAMIC EFFECTS

In hypertension

- The magnitude of blood pressure reduction is related to the degree of hypertension
- Low incidence of vasodilatory side effects
- No reflex tachycardia is associated with chronic antihypertensive effects

In angina

- Potent dilator of coronary arteries* and reduces vasospasm
- Appropriate decrease in heart rate with a low incidence (<1%) of reflex tachycardia
- Little or no negative inotropic effect in patients with normal ventricular function†

WELL-TOLERATED CONTROL REGARDLESS OF AGE OR GENDER‡

- A side-effect discontinuation rate comparable to placebo in both hypertension and angina trials²
- Most commonly reported side effects are headache (5.4%), bradycardia (3.3%), first-degree AV block (3.3%), dizziness (3.0%), edema (2.6%), ECG abnormality (1.6%), and asthenia (1.8%)¹

* Demonstrated in patients with vasospastic angina.
† See Warnings and Clinical Pharmacology sections in prescribing information.
‡ In clinical trials with Cardizem CD.

Please see brief summary of prescribing information on next page.
Brief Summary of Prescribing Information as of April 1993

CARDIZEM® CD (diltiazem HCl)

Capsules

**INDICATIONS:**

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker; (2) patients known to be hypersensitive to diltiazem; (3) patients with AV block except in the presence of a functioning ventricular pacemaker; (5) patients with hypotension (less than 90 mm Hg systolic); (4) patients who have demonstrated hypersensitivity to the drug; and (5) patients with acute myocardial infarction and pulmonary congestion documented by X-ray on admission.

**WARNINGS:**

1. **Cardiac Conduction:** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in an abnormally slow heart rate (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (13 of 3250 patients [0.40%]). Concomitant use of diltiazem with beta-blockers or digoxin may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed prolonged asystole (2 to 5 seconds) during concomitant administration of CARDIZEM and digoxin.

2. **Congestive Heart Failure:** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index or consistent negative effects on contractility (see CLINICAL PHARMACOLOGY). An acute study of 15 patients with impaired ventricular function (ejection fraction 24% to 45%) showed improvement in indices of ventricular function (ejection fraction). Worsening of clinical signs of congestive heart failure has been reported in patients with precluding impairment of ventricular function. Experience with the use of CARDIZEM in patients with congestive heart failure in combination with beta-blockers in patients with impaired ventricular function is limited. Caution should be exercised when using this combination.

3. **Hypotension:** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.

4. **Acute Hepatic Injury:** Mild elevations of transaminases without and with concurrent elevation in alkaline phosphatase and bilirubin have been observed in clinical studies. These abnormalities have been generally reversible and sustained during CARDIZEM dose reductions or discontinuation. Do not discontinue therapy without consultation with a physician. If ALT, AST, or bilirubin abnormalities persist or worsen, or if new clinical symptoms suggestive of acute hepatitis appear, discontinue therapy and evaluate patient for further treatment. Patients with preexisting hepatic abnormalities should be carefully monitored.

**PRECAUTIONS:**

General

CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidney and bile. As with any drug given over prolonged periods, laboratory parameters of renal and hepatic function should be monitored at regular intervals. The drug should be used with caution in patients with renal impairment or hepatic function. In subjects with advanced liver disease, drug levels may be increased.

Cardiac Conduction: Studies indicating that there may be additive effects in prolonging AV conduction when using beta blockers or digoxin concomitantly with CARDIZEM. (See WARNINGS.)

As with other calcium channel blockers, patients should be closely monitored when starting or stopping concomitantly administered diltiazem to maintain optimum therapeutic blood levels.

Beta-blockers: Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers is usually well tolerated, but available data are not sufficient to predict the effects of concomitant treatment in patients with left ventricular dysfunction or cardiac conduction abnormalities.

Administration of CARDIZEM (diltiazem hydrochloride) concomitantly with propafenone in five volunteers resulted in increased propafenone plasma levels in all subjects and increased creatinine clearance. Propafenone is a competitive antagonist, but no data are available to predict the effects of diltiazem on propafenone metabolism. Propranolol plasma levels were not increased.

Cimetidine: A study in six healthy volunteers showed a significant increase in peak diltiazem plasma levels (50%) and an increase in the half-life of diltiazem. The effects may be mediated by cimetidine's known inhibition of hepatic cytochrome P450. Enzyme systems responsible for the first-pass metabolism of diltiazem may be affected by cimetidine. Further studies are needed to confirm these findings.

Digitalis: Administration of CARDIZEM with digitalis in 24 healthy male subjects increased plasma digoxin concentrations approximately 20%. Another investigator found no increase in digoxin levels in 12 patients with coronary artery disease on diltiazem while on digoxin. Cardiac monitoring revealed no predictable increase in digoxin toxicity. Effects of diltiazem on digoxin levels may need to be monitored. Patients with renal failure or hepatic dysfunction may be more susceptible to the effects of diltiazem.

Cyclosporine: A pharmacokinetic interaction between diltiazem and cyclosporine has been observed during studies involving concomitant administration. Cyclosporine concentrations were reduced, and diltiazem concentrations were increased. The effect of diltiazem on cyclosporine concentration may be of clinical importance, especially in patients on cyclosporine therapy who are also provided with other drugs that may affect cyclosporine metabolism. The effects of cyclosporine on diltiazem concentrations have not been evaluated.

Carbamazepine: Concomitant administration of diltiazem with carbamazepine has been reported to result in elevated serum levels of carbamazepine (40% to 72%), resulting in toxicity in some cases. Patients

**SIDE EFFECTS:**

In clinical trials of CARDIZEM CD capsules, CARDIZEM tablets, and CARDIZEM SR capsules involving over 3500 patients, the most common adverse events (i.e., greater than 1%) were edema (4%), palpitations (4.6%), headache (4.6%), dizziness (3.5%), asthenia (2.8%), first-degree AV block (2.4%), bronchitis (1.7%), flushing (1.5%), nausea (1.5%), and pruritus (1.5%).

The following postmarketing adverse events have been reported infrequently in patients receiving CARDIZEM: angioedema, asthma, and urticaria. Patients should be closely monitored when starting or stopping concomitantly administered diltiazem to maintain optimum therapeutic blood levels.

**ADVERSE REACTIONS:**

In controlled clinical trials with CARDIZEM CD capsules, adverse reactions occurred in a total of 8% of patients. The incidence of adverse reactions was similar for patients receiving CARDIZEM CD capsules and placebo. The most common adverse reactions were edema (4%), palpitations (4.6%), headache (4.6%), and dizziness (3.5%).

In placebo-controlled studies, the most common adverse reactions reported in patients receiving CARDIZEM CD capsules were edema (4%), palpitations (4.6%), headache (4.6%), and dizziness (3.5%).

References:

2. Data on file, Marion Merrell Dow Inc.

Marion Merrell Dow Inc.
Kansas City, MO 64114

Contact:

CVM94021201

RX

Cardizem CD

Start with one 180-mg capsule daily
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Real Value for Real People with Hypertension

Real Therapeutic Value
• The benefits of long-acting nifedipine therapy for hypertension

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

*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.

Candidate Profile
Name: Florence B.
Age: 65
Residence: Chicago
Pretreatment BP: 170/104
Marital Status: Widowed
Health Ins: Medicare

“Save up to $217† a year?
That’s Sunday clothes for the grandkids.”
**Once-A-Day**

**Adalat CC**

**EXTENDED RELEASE TABLETS**

30mg, 60mg & 90mg

Start with*

![Rx]

Tritrate, if necessary*

![Rx]

*Please see DOSAGE AND ADMINISTRATION section in brief summary of prescribing information below.

**Real People, Real Needs, Real Value**

**Adalat CC**

30mg, 60mg & 90mg

**Extended Release Tablets**

**Adalat CC**

30mg once daily

**Adalat CC**

60mg once daily

**Body as a Whole/Systemic**: chest pain, leg pain
**Central Nervous System**: paraesthesia, vertigo
**Cardiovascular**: hypotension, convulsions
**Musculoskeletal**: leg cramps, Raynaud's phenomena, thrombophlebitis

**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, pain, rash
**Cardiovascular**: atrial fibrillation, bradycardia, cardiac arrest, ventricular arrhythmia, hypotension, palpitations, phlebitis, peripheral hypotension, tachycardia, urticaria, angioedema
**Central Nervous System**: anxiety, confusion, delirium, dizziness, depression, hyperventilation, insomnia, manic-depressive state, drowsiness
**Gastrointestinal**: abdominal pain, diarrhea, dyspepsia, dysphagia, flatulence, indigestion, nausea, vomiting, Hematemesis, tachyphylaxis
**Metabolic, weight loss**: Musculoskeletal: arthritis, arthralgia, Respiratory, dyspnea, increased cough, nose, pharyngitis, *SpecialSes: abnormal vision, epistaxis, conjunctivitis, dizziness, photosensitivity, Urogenital/Reproductive: testicular atrophy, increased breast enlargement*

The following adverse events have been reported rarely in patients given nifedipine in other formulations: cholestatic hepatitis, alopecia, anemia, arthritis with ARA (++)

Distribution and availability: Adalat CC is an extended release dosage form and tablet.

**Dosage and Administration**: Should be adjusted according to each patient's needs. It is recommended that Adalat CC be administered once daily on an empty stomach. Adalat CC is an extended release dosage form and tablet.

**Concomitant Use**: Treatment should be initiated within 2-14 days of starting therapy.

**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 REACTIONS**: 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 1904 hypertensive patients. Nifedipine 50 to 90 mg daily was used comparably in 167 of the 379 patients on Adalat CC and in 64 of the 717 patients on placebo. All adverse events reported during Adalat CC therapy were tabulated independently of their suspected relationship to medication.

**Contraindications**: Patients with a history of angina pectoris, hypertension, or other cardiovascular disease, are at increased risk of exacerbating angina pectoris, especially if they are taking beta blockers or digitalis. In these patients, the use of nifedipine may be contraindicated. In patients with severe left ventricular failure, nifedipine should be used cautiously.

**Warnings**: Nifedipine should be used with caution in patients with a history of cardiac disease, especially angina pectoris, or recent myocardial infarction. In patients with severe hypertension or severe angina pectoris, nifedipine may produce a decrease in coronary perfusion resulting in unstable angina pectoris, particularly in patients with coronary artery disease or a history of myocardial infarction. Nifedipine should be used with caution in patients with diabetes mellitus. In patients with a history of heart failure, nifedipine may produce a decrease in cardiac output, which may be exacerbated by the use of other vasodilators.

**Precautions**: Nifedipine should be used with caution in patients with a history of gastrointestinal disease, which may be exacerbated by the use of other vasodilators.

**Lilly**: Other calcium antagonist channel blockers, decreases platelet aggregation in vitro.

**Limited Data**: Limited data does not indicate any potential for drug interactions with nifedipine.

**Pharmacology Division**

Manufactured by:

**AstraZeneca Pharmaceutical Division**

Distributed by:

16470 Morgan Lane

West Haven, CT 06516 USA

Made in Germany

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Because it is non sedating.

SUBCUTANEOUS
IMITREX®
SUMATRIPTAN SUCCINATE

MIGRAINE RELIEF THAT CAN CHANGE PATIENTS' LIVES

Please consult Brief Summary of Prescribing Information on last page of this advertisement.
Imitrex® (sumatriptan succinate) Injection

For Subcutaneous Use Only.

The following is a brief summary only. Before prescribing, see complete prescribing information in Immitrex® injection product labeling.

INDICATIONS AND USAGE: Immitrex® injection is indicated for the acute treatment of migraine headache (with or without aura) in adults.

In a 78-week study in which mice received sumatriptan continuously in drinking water, there was no evidence for an increase in tumors considered related to sumatriptan administration. That study, however, did not use the maximum tolerated dose and therefore did not fully explore the carcinogenic potential of Immitrex® (sumatriptan succinate) Injection in the mouse.

A Segment I rat toxicity study by the subcutaneous route has shown no evidence of impaired fertility.

Pregnancy: Pregnancy Category C: Sumatriptan has been shown to be embryotoxic in rabbits when given in daily doses producing plasma levels 3-5 fold higher than those attained following a 4 mg/kg subcutaneous injection (i.e., recommended dose) to humans. There is no evidence of teratogenic effects associated with sumatriptan in rats. However, there are no adequate and well-controlled studies in pregnant women. Immitrex injection should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

In assessing this information, the following additional findings should be considered:

Em搏phythelial: When given intravenously to pregnant rabbits daily throughout the period of organogenesis, sumatriptan produced maternal toxicity. The mechanism of the embryopathy is not known. At these doses, peak concentrations of drug in plasma were more than 3-fold greater than the range observed in humans after the recommended subcutaneous dose of 6 mg.

The intravenous administration of sumatriptan to pregnant rats through organogenesis produced plasma concentrations more than 50 times those seen after the recommended subcutaneous human dose did not cause embryofetotoxicity. In a study of pregnant rats given subcutaneous sumatriptan daily prior to and throughout pregnancy, there was no evidence of increased embryofetal toxicity.

Zawarung: The 14-day subcutaneous implant of 5mg rats caused during organogenesis with oral sumatriptan exhibited an increased incidence of cardiovascular, renal and minor skeletal abnormalities. The functional significance of these observations is unknown.

In a study in rats dosed daily with subcutaneous sumatriptan prior to and throughout organogenesis, studies on rats and rabbits evaluating the teratogenic potential of sumatriptan administered subcutaneously only during organogenesis (standard legend) and studies not done, were not done.

Nursing Mothers: Sumatriptan is excreted in breast milk in amounts that are not biologically significant. Studies in rats and rabbits suggest that the potential for adverse effects to the human infant has not been adequately assessed. Use in the Elderly: The safety and effectiveness of Immitrex injection in individuals over age 65 has not been systematically evaluated. Although elderly patients (aged 65 and older) were not substantially represented in the clinical trials conducted, the general incidence of adverse reactions in the elderly is similar to that seen in younger adults. No unusual adverse, age-related phenomena have been identified in patients over the age of 65 who participated in clinical trials.

ADVERSE REACTIONS: (see also PRECAUTIONS) Sumatriptan may cause vasospasm in patients with a history of coronary artery disease, known to be susceptible to coronary artery vasospasm, and, very rarely, without prior history suggestive of coronary artery disease. The possibility of cerebral or coronary vasospasm could be increased in patients with hypertension, diabetes, obesity, or a family history of ischemic heart disease. In this regard, it should be noted that migrainers may be at increased risk of certain cerebrovascular events (e.g., cerebrovascular accident, transient ischemic attack).

Although written instructions are supplied with the attendant, patients who are advised to self-administer Immitrex injection in medically unsupervised situations should receive instruction on the proper use of the product from the physician or other qualified health care provider as their first line of information for Patients: See Patient INFORMATION at the end of the product package insert for the test of the separate booklet provided for patients.

Laboratory Tests: No specific laboratory tests are recommended for monitoring patients prior to and after treatment with Immitrex injection.

Drug Interactions: There is no evidence that concurrent use of migraine prophylactic medications has any effect on the efficacy or unwanted effects of sumatriptan. In two Phase III trials in the US, a retrospective analysis of 282 patients who had been using prophylactic drugs (verapamil + 61, amitriptyline n-57, propranolol n-58, for 45 other drugs n-51) with those who had not used prophylaxis (n=452). There were no differences in relief at 60 minutes posdose for Immitrex injection, whether or not prophylactic medications were used. These data are not only of interest to adverse event rates between the two groups.

Ergot-containing drugs should not be used to cause prolonged vasospastic reactions. Because there is a theoretical basis that these effects may be additive, use of ergotamine and sumatriptan within 24 hours of each other should be avoided (see CONTRAINDICATIONS).

Drug/Laboratory Test Interactions: Immitrex injection is not known to interfere with commonly used laboratory tests.

Cardiovascular: Maintenance of Fertility: In a 104-week lifetime study in rats given sumatriptan by oral gavage, serum concentrations achieved were dose-related, ranging at the low dose from approximately twice the peak concentration of the drug after the recommended human subcutaneous dose of 6 mg to more than 100 times this concentration at the high dose. There was no evidence of an increase in tumors considered related to sumatriptan administration. In a 78-week study in which mice received sumatriptan continuously in drinking water, there was no evidence for an increase in tumors considered related to sumatriptan administration. That study, however, did not use the maximum tolerated dose and therefore did not fully explore the carcinogenic potential of Immitrex® (sumatriptan succinate) Injection in the mouse.

In this study, no evidence of increased tumor or malignancy that could be attributed to Immitrex was seen. In sumatriptan-treated rats and mice, there was an increase in the number of animals with neoplasms when compared to placebo. However, the increase was not statistically significant.

The results of the present study are not consistent with the tendency to increase the risk of neoplasms in rats and mice observed with certain other drugs (such as antiinflammatory drugs) that can cause signs of vascular insufficiency (such as oedema, wasting, scurvy, and loss of teeth and与此相关的下列表明。...

Percent of Patients Reporting

Table 1: Percent of Patients Reporting Adverse Events by Adverse Event Type

<table>
<thead>
<tr>
<th>Adverse Event Type</th>
<th>Percent of Patients Reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>13.5</td>
</tr>
<tr>
<td>Tension</td>
<td>13.5</td>
</tr>
<tr>
<td>Throat discomfort</td>
<td>13.5</td>
</tr>
<tr>
<td>Discomfort: nasal cavity/sinusitis</td>
<td>13.5</td>
</tr>
<tr>
<td>Eye</td>
<td>2.5</td>
</tr>
<tr>
<td>Vision alterations</td>
<td>1.1</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>1.1</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>1.1</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>1.1</td>
</tr>
<tr>
<td>Injection reaction</td>
<td>1.1</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Table 2: Placebo-controlled Clinical Trials: The following Table lists adverse events that occurred in 2 large US, Phase III, placebo-controlled clinical trials following either a single dose of Immitrex injection or placebo. Only events associated with a frequency of 1% or more in Immitrex injection treatment groups and were at least as frequent in the placebo group are included in Table 2.

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo</th>
<th>Immitrex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tinnitus</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Skin</td>
<td>0.5</td>
<td>0.5</td>
</tr>
<tr>
<td>Other</td>
<td>0.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Table 3: Treatment-emergent nerve and muscle pain: In the 78-week study in which mice received sumatriptan continuously in drinking water, there was no evidence for an increase in nerve and muscle pain considered related to sumatriptan administration. That study, however, did not use the maximum tolerated dose and therefore did not fully explore the potential for nerve and muscle pain.

Table 4: Placebo-controlled Clinical Trials: The following Table lists adverse events that occurred in 2 large US, Phase III, placebo-controlled clinical trials following either a single dose of Immitrex injection or placebo. Only events associated with a frequency of 1% or more in Immitrex injection treatment groups and were at least as frequent in the placebo group are included in Table 4.

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo</th>
<th>Immitrex</th>
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</thead>
<tbody>
<tr>
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<tr>
<td>Other</td>
<td>0.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>
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The recommended starting dosage for Calan SR is 180 mg once daily. Dose titration will be required in some patients to achieve blood pressure control. A lower starting dosage of 120 mg/day may be warranted in some patients (e.g., the elderly, patients of small stature). Dosages above 360 mg daily should be administered in divided doses. Calan SR should be administered with food. Constipation, which is easily managed in most patients, is the most commonly reported side effect of Calan SR. Verapamil should be administered cautiously to patients with impaired renal function.

Please see following page for brief summary of complete prescribing information.

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