In hypertension or angina...
Control That's Easy to Live With

HIGH RATE OF SUCCESS IN AN NIH-SPONSORED STUDY

83% of hypertensive patients—the highest percentage—remained on initial therapy with NORVASC® (amlodipine besylate) after 4 years; nearly all patients were on the 5-mg starting dose.

LOW RATE OF DISCONTINUATION

ONLY 1.5% of patients in placebo-controlled studies (n=1730) discontinued therapy due to adverse effects.

PROVEN SAFETY

No negative inotropic effects at clinical doses in hemodynamic studies.*
No clinically significant effect on cardiac conduction or heart rate.

* Similar hemodynamic findings, however, have been observed with agents possessing significant negative inotropic effects.

Once-Daily NORVASC® (amlodipine besylate) 5-mg and 10-mg tablets

EFFICACY AND SAFETY THAT'S EASY TO LIVE WITH
In hypertension
or angina, convenient
once-daily dosing

• The usual starting dose is 5 mg in hypertension or angina

— In hypertension, small, fragile, or elderly individuals or patients with hepatic insufficiency may be started on 2.5 mg once daily.

• Titration can proceed to 10 mg

— Most angina patients will require 10 mg

• Can be taken with or without food

The most common side effects are headache and edema

Precautions:

1. In U.S. GE:

2. Use in Patients with Congestive Heart Failure: In general, cardiac channel blockers should be used with caution in patients with NYHA class III or IV heart failure.

3. Use with NSAIDs: The concurrent use of aspirin or other NSAIDs with NORVASC may be associated with an increased incidence of cardiovascular complications in patients with unstable angina pectoris or recent myocardial infarction.

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

5. Nursing Mothers: It is not known whether amlodipine is excreted in human milk. In the absence of information, it is recommended that nursing be discontinued while NORVASC is administered.

6. Pediatric Use: Safety and effectiveness of NORVASC in children have not been established.

7. ADVERSE REACTIONS: NORVASC has been evaluated for safety in more than 11,000 patients in U.S. and foreign clinical trials. In general, treatment with NORVASC was well tolerated at doses up to 10 mg daily.

8. Overdosage: There have been no documented reports of deliberate intake of NORVASC in humans. The effects of a single oral dose of 5, 10, 20, 30, 40, and 80 mg have been studied in healthy volunteers. At these dosages, adverse effects were related to dose, being more frequent and of greater severity at the higher doses. Treatment at this level is probably not justified.

9. Laboratory Tests: In vitro data in human platelets indicate that NORVASC has no effect on the protein binding of drugs tested (digoxin, phenytoin, warfarin, and indomethacin). Special studies have indicated that the co-administration of NORVASC with digoxin did not change serum digoxin levels.

10. Drugs/Laboratory Tests Interactions: None known.

11. Contraindications: Management of Patients: Rats and mice treated with amlodipine in the diet for 2 years at concentrations calculated to provide daily doses of 0.5, 1.25, and 2.5 mg/kg/day showed no evidence of carcinogenicity. The highest dose (1.25 mg/kg/day) was approximately 10 times the maximum recommended clinical dose of 10 mg on a mg/m² basis. The maximum dose (40 mg/kg/day) was approximately 100 times the maximum recommended clinical dose of 10 mg on a mg/m² basis.

12. Pregnancy: There have been no adequate and well-controlled studies in pregnant women. NORVASC should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

13. Nursing Mothers: It is not known whether amlodipine is excreted in human milk. In the absence of information, it is recommended that nursing be discontinued while NORVASC is administered.

14. Pediatric Use: Safety and effectiveness of NORVASC in children have not been established.

15. ADVERSE REACTIONS: NORVASC has been evaluated for safety in more than 11,000 patients in U.S. and foreign clinical trials. In general, treatment with NORVASC was well tolerated at doses up to 10 mg daily. Most adverse reactions reported during therapy with NORVASC were mild to moderate in severity. In controlled clinical trials directly comparing NORVASC to placebo, 7% of patients taking NORVASC did not tolerate the drug, compared to 4% of patients taking placebo. In open-label trials, 14% of patients taking NORVASC did not tolerate the drug, compared to 5% of patients taking placebo.

16. Overdosage: There have been no documented reports of deliberate intake of NORVASC in humans. The effects of a single oral dose of 5, 10, 20, 30, 40, and 80 mg have been studied in healthy volunteers. At these dosages, adverse effects were related to dose, being more frequent and of greater severity at the higher doses. Treatment at this level is probably not justified.

17. Laboratory Tests: In vitro data in human platelets indicate that NORVASC has no effect on the protein binding of drugs tested (digoxin, phenytoin, warfarin, and indomethacin). Special studies have indicated that the co-administration of NORVASC with digoxin did not change serum digoxin levels.
There’s More To EPOGEN* (Epoetin alfa) Than Epoetin Alfa.

When you specify EPOGEN* (Epoetin alfa), you get more than a product. You also get a comprehensive support system. That’s important, because the depth and quality of professional support is a significant element in long-term clinical success.

EPOGEN* support encompasses the Amgen Reimbursement Hotline, the Amgen SAFETY NET* Program, Professional Services, Professional Education Programs, and Clinical Support Services. Your Amgen Professional Sales Representative can tell you more about the ways these programs can satisfy your needs.

There simply is no comparable source of professional support. That’s not surprising, because EPOGEN* is a lot more than just a drug. It’s a way of life.

For more information, please call 1-800-77-AMGEN.
In Your Adult Predialysis and Dialysis Patients...

HELP ERADICATE HEPATITIS B

Use the only vaccine with a concentrated 40 mcg/mL dose precisely formulated for predialysis and dialysis patients

Recombivax HB
(Hepatitis B Vaccine [Recombinant])

The Vision and Precision to Help End Hepatitis B

RECOMBIVAX HB is contraindicated in the presence of hypersensitivity to yeast or to any component of the vaccine. Patients who develop symptoms suggestive of hypersensitivity after an injection should not receive further injections of the vaccine.

RECOMBIVAX HB Dialysis Formulation (40 mcg/mL) is intended only for adult predialysis/dialysis patients.

A booster dose or revaccination may be considered if the anti-HBs level is less than 10 mIU/mL 1–2 months after the third dose.

Please read the Brief Summary of the Prescribing Information accompanying this advertisement.
BRIEF SUMMARY

RECOMBIVAX HB®
HEPATITIS B VACCINE (RECOMBINANT)

Please read the full Prescribing Information for complete details.

INDICATIONS AND USAGE

RECOMBIVAX HB is indicated for vaccination against infection caused by all known subtypes of hepatitis B virus. RECOMBIVAX HB Dialysis Formulation is indicated for vaccination of adult predialysis and dialysis patients against infection caused by all known subtypes of hepatitis B virus.

CONTRAINDICATIONS

Hypersensitivity to yeast or any component of the vaccine.

WARNINGS

Patients who develop symptoms suggestive of hypersensitivity after an injection should not receive further injections of the vaccine (see CONTRAINDICATIONS).

Because of the long incubation period for hepatitis B, it is possible for unrecognized infection to be present at the time the vaccine is given. The vaccine may not prevent hepatitis B in such patients.

PRECAUTIONS

General

As with any percutaneous vaccine, epinephrine should be available for immediate use should an anaphylactoid reaction occur.

Any serious acute infection is reason for delaying use of the vaccine except when in the opinion of the physician, withholding the vaccine entails a greater risk.

Caution and appropriate care should be exercised in administering the vaccine to individuals with severely compromised cardiopulmonary status or to others in whom a febrile or systemic reaction could pose a significant risk.

Pregnancy

Pregnancy Category C: Animal reproduction studies have not been conducted with the vaccine. It is also not known whether the vaccine can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. The vaccine should be given to a pregnant woman only if clearly needed.

Nursing Mothers

It is not known whether the vaccine is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when the vaccine is administered to a nursing woman.

Pediatric Use

RECOMBIVAX HB has been shown to be usually well-tolerated and highly immunogenic in infants and children of all ages. Newborns also respond well; maternally transferred antibodies do not interfere with the active immune response to the vaccine. See DOSAGE AND ADMINISTRATION in full Prescribing Information for recommended pediatric dosage and for recommended dosage for infants born to HBsAg positive mothers.

The safety and effectiveness of RECOMBIVAX HB Dialysis Formulation in children have not been established.

ADVERSE REACTIONS

RECOMBIVAX HB and RECOMBIVAX HB Dialysis Formulation are generally well-tolerated. No serious adverse reactions attributable to the vaccine have been reported during the course of clinical trials. No adverse experiences were reported during clinical trials which could be related to changes in the titers of antibodies to yeast. As with any vaccine, there is the possibility that broad use of the vaccine could reveal adverse reactions not observed in clinical trials.

In a group of studies, 1636 doses of RECOMBIVAX HB were administered to 653 healthy infants and children (up to 10 years of age) who were monitored for 5 days after each dose. Injection site reactions (including erythema and swelling) and systemic complaints were reported following 8% and 17% of the injections, respectively. The most frequently reported systemic adverse reactions (>1% injections), in decreasing order of frequency were irritability, tiredness, fever (>101°F oral equivalent), crying, diarrhea, vomiting, diminished appetite, and insomnia.

In a group of studies, 3258 doses of RECOMBIVAX HB were administered to 1252 healthy adults who were monitored for 5 days after each dose. Injection site and systemic complaints were reported following 17% and 16% of the injections, respectively. The following adverse reactions were reported:

Incidence Equal to or Greater Than 1% of Injections

LOCAL REACTION (INJECTION SITE)

Injection site reactions consisting principally of soreness, and including pain, tenderness, pruritus, erythema, ecchymosis, swelling, warmth, and nodule formation.

BODY AS A WHOLE

The most frequent systemic complaints include fatigue/weakness; headache; fever (>100°F); and malaise.

DIGESTIVE SYSTEM

Nausea; and diarrhea

RESPIRATORY SYSTEM

Pharyngitis; and upper respiratory infection

Incidence Less Than 1% of Injections

BODY AS A WHOLE

Sweating; achiness; sensation of warmth; lightheadedness; chills; and flushing

DIGESTIVE SYSTEM

Vomiting; abdominal pains/cramps; dyspepsia; and diminished appetite

RESPIRATORY SYSTEM

Rhinitis; influenza; and cough

NERVOUS SYSTEM

Vertigo/dizziness; and paresthesia

INTEGUMENTARY SYSTEM

Pruritus; rash (non-specific); angioedema; and urticaria

MUSCULOSKELETAL SYSTEM

Arthralgia including monoarticular; myalgia; back pain; neck pain; shoulder pain; and neck stiffness

HEMIC/LYMPHATIC SYSTEM

Lymphadenopathy

PSYCHIATRIC/BEHAVIORAL

Insomnia/disturbed sleep

SPECIAL SENSORS

Earache

UROGENITAL SYSTEM

Dysuria

CARDIOVASCULAR SYSTEM

Hypotension

Marketed Experience

The following additional adverse reactions have been reported with use of the marketed vaccine. In many instances, the relationship to the vaccine was unclear.

Hypersensitivity

Anaphylaxis and symptoms of immediate hypersensitivity reactions including rash, pruritus, urticaria, edema, angioedema, dyspnea, chest discomfort, bronchial spasm, palpitation, or symptoms consistent with a hypotensive episode have been reported within the first few hours after vaccination. An apparent hypersensitivity syndrome (serum sickness-like) of delayed onset has been reported days to weeks after vaccination, including: arthralgia/arthritis (usually transient), fever, and dermatologic reactions such as urticaria, erythema multiforme, ecchymoses and erythema nodosum (see WARNINGS and PRECAUTIONS).

Digestive System

Elevation of liver enzymes; constipation.

Nervous System

Guillain-Barré Syndrome; multiple sclerosis; myelitis including transverse myelitis; peripheral neuropathy including Bell's Palsy; radiculopathy; herpes zoster; migraine; muscle weakness; hypotension.

Integumentary System

Stevens-Johnson Syndrome; petechiae.

Musculoskeletal System

Arthritis.

Hematologic

Increased erythrocyte sedimentation rate; thrombocytopenia.

Immune System

Lupus-like syndrome.

Psychiatric/Behavioral

Irritability; agitation; somnolence.

Special Senses

Optic neuritis; tinnitus; conjunctivitis; visual disturbances.

Cardiovascular System

Syncope, tachycardia.

The following adverse reaction has been reported with another Hepatitis B Vaccine (Recombinant) but not with RECOMBIVAX HB: keratitis.
Now For the Treatment of Hypertension...

Bring down the pressure with ease

ONCE-DAILY 80 mg • 160 mg

Diovan valsartan capsules
For the Treatment of Hypertension...
An Angiotensin-II Receptor Blocker (ARB)

Brings down the

USE IN PREGNANCY
When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system can cause injury and even death to the developing fetus. When pregnancy is detected, DIOVAN should be discontinued as soon as possible. See WARNINGS in brief summary of Prescribing Information immediately following advertisement.

DIOVAN is contraindicated in patients who are hypersensitive to any component of this product.

*No significant differences between adverse events (AEs), DIOVAN vs placebo; AEs more frequent than placebo: viral infection (3% vs 2%), fatigue (2% vs 1%), abdominal pain (2% vs 1%); the most common AEs were headache and dizziness.
ONCE-DAILY

Diovan™
valsartan capsules

80 mg • 160 mg

NOW—

NOT ONLY the power of leading antihypertensives...

- Starting dose delivers efficacy of:
  - amlodipine 5 mg
  - enalapril 20 mg
  - lisinopril 10 mg

BUT ALSO the tolerability of placebo...

- Overall incidence of side effects comparable to placebo at both dosage strengths

PLUS convenient once-daily dosing

- Start with 80 mg qd
- Dosage can be titrated to 160 mg qd for additional antihypertensive effect at no extra cost

pressure with ease
Diovan™
valsartan
Capsules

BRIEF SUMMARY (FOR COMPLETE PRESCRIBING INFORMATION, SEE PACKAGE INSERT)

USE IN PREGNANCY
When used in pregnancy during the second and third trimesters, drugs that act directly on the renin-angiotensin system cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature in patients who were taking angiotensin-converting enzyme inhibitors. When pregnancy is detected, Diovan should be discontinued as soon as possible. See WARNINGS: Fetal/Neonatal Morbidity and Mortality.

INDICATIONS AND USAGE
Diovan is indicated for the treatment of hypertension. It may be used alone or in combination with other antihypertensive agents.

CONTRAINDICATIONS
Diovan is contraindicated in patients who are hypersensitive to any component of this product.

WARNINGS
Fetal/Neonatal Morbidity and Mortality
Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. Several dozen cases have been reported in the world literature in patients who were taking angiotensin-converting enzyme inhibitors. When pregnancy is detected, Diovan should be discontinued as soon as possible. See WARNINGS: Fetal/Neonatal Morbidity and Mortality.

The use of drugs that act directly on the renin-angiotensin system during the second and third trimesters of pregnancy has been associated with fetal and neonatal injury, including hypotension, neonatal death, and renal failure. Diovan should be discontinued as soon as possible. See WARNINGS: Fetal/Neonatal Morbidity and Mortality.

Other adverse effects have been reported, although it is not clear whether these occurrences were due to exposure to the drug.

These adverse effects do not appear to have resulted from intravenous drug exposure that has been limited to the first trimester. Mothers whose embryos and fetuses are exposed to an angiotensin II receptor antagonist only during the first trimester should be informed. Nonetheless, when patients become pregnant, physicians should advise the patient to discontinue the use of Diovan as soon as possible. Rarely (probably less often than once in every thousand pregnancies), no alternative to a drug on the national list of drugs for which the group who was exposed in utero has been reported to have adverse outcomes associated with exposure to an angiotensin II receptor antagonist should be considered.

In fetal sheep, angiotensin II receptor antagonists may reduce the potential hazards to their fetuses, and serial ultrasound examinations should be performed to assess the intrauterine growth of the fetus during gestation. Oligohydramnios and amniotic band syndrome have also been reported, although it is not clear whether these occurrences were due to exposure to the drug.

It is not known whether valsartan is excreted in human milk, but valsartan was excreted in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
In the controlled clinical trials of valsartan, 1241 (36.2%) of patients treated with valsartan were 65 years and 265 (7.9%) were 75 years or older. No overall differences in the efficacy or safety of valsartan was observed in these patient populations, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS
Diovan has been evaluated for safety in more than 4900 patients, including over 400 treated for over 6 months, and more than 160 for 1 year. Adverse experiences have generally been mild and transient in nature and have only infrequently required discontinuation of therapy. Most of the adverse experiences with Diovan were similar to placebo.

The overall frequency of adverse experiences was not dose-related nor related to gender, age, race, or regimen. Discontinuation of therapy due to side effects was required in 2.2% of valsartan patients. The most common reasons for discontinuation of therapy with Diovan were headache and dizziness.

The adverse experiences that occurred in patients controlled clinical trials in at least 1% of patients treated with Diovan and at a higher incidence in valsartan (n=2161) than placebo (n=888) patients included viral infection (2% vs. 2%), fatigue (2% vs. 1%), and abdominal pain (2% vs. 1%).

Headache, dizziness, upper respiratory infection, cough, diarrhea, rhinitis, sinalitus, nausea, pharyngitis, and gastritis were observed in 1% to 2% of the patients. Other adverse experiences were more common in patients treated with Diovan than placebo. It includes vomiting, diarrhea, and rash.

Diovan has been used concomitantly with hydrochlorothiazide without evidence of clinically important adverse interactions. Other adverse experiences that occurred in controlled clinical trials of patients treated with Diovan (≥2.0% of patients) are listed below. It cannot be determined whether these events were causally related to Diovan.

Body as a Whole: Rash, urticaria, angina, nervous system: Headache, fatigue, nervousness, dizziness, vertigo, abnormal sweating, hypotension, chest pain, syncope, anorexia, vomiting, and angina.

Cardiovascular: Palpitations, edema, postural hypotension, syncope, chest pain, palpitations, and angina.

Dermatologic: Rashes, pruritus, and hair loss.

Gastrointestinal: Abdominal pain, nausea, vomiting, diarrhea, constipation, and dyspepsia.

Genitourinary: Nausea, vomiting, anorexia, constipation, and dysuria.

Hematologic: Anemia, leukopenia, and thrombocytopenia.

Musculoskeletal: Arthralgia.

Neuromuscular and psychiatric: Anxiety, insomnia, paresthesia, and somnolence.

Respiratory: Dyspnea, sinusitis, and rhinitis.

Special senses: Tinnitus, vertigo.

Urogenital: Impotence.

Other reported events less frequently in clinical trials included chest pain, syncope, anorexia, vomiting, and angina.

Laboratory Test Results
In controlled clinical trials, clinically important changes in standard laboratory parameters were rarely associated with administration of Diovan. Serum uric acid levels were increased. Serum creatinine, total and direct bilirubin, AST and ALT levels were increased. Other changes were not significant.

In studies of ACE inhibitors in patients with unilateral or bilateral renal artery stenosis, increases in serum creatinine or blood urea nitrogen were reported. In a 4-day trial of valsartan in 12 patients with unilateral renal artery stenosis, no significant increase in serum creatinine or blood urea nitrogen was observed. There has been a long-term use of Diovan in patients with unilateral or bilateral renal artery stenosis, but an effect similar to that seen with ACE inhibitors should be anticipated.

For Pregnancy
Female patients of childbearing age should be told about the consequences of second- and third-trimester exposure to Diovan. Pregnancy Registry: The number of women exposed to Diovan in pregnancy is not available. Diovan should be given to pregnant women only if the potential benefit justifies the potential risk to the fetus.

Drug Interactions
No clinically significant pharmacokinetic interactions were observed when valsartan was coadministered with atorvastatin, amiodarone, digoxin, furosemide, glibenclamide, hydrochlorothiazide, or indomethacin. The valsartan-atenolol combination was more antihypertensive than either component, but it did not alter the heart rate more than alone. Simultaneous ingestion of Diovan and warfarin did not change the pharmacokinetics of valsartan or the time-course of the anticoagulant properties of warfarin.

Drug/Laboratory Interactions: The (S)-enantiomer of valsartan is responsible for valsartan metabolism and has been identified but do not seem to be CYP 450 inhibitors. The induction or inhibition potential of CYP 450 enzymes by valsartan has not been evaluated.

Carcinogenesis, Mutagenesis, Impairment of Fertility
The carcinogenic potential of carcinogen when was administered in the diet to mice and rats for up to 2 years at doses up to 150 and 200 mg/kg/day, respectively. These doses in mice and rats are about 2.6 and 6 times, respectively, the maximum recommended human dose on a mg/m² basis. (Calculations assume an oral dose of 320 mg/day and a 60-kg patient.)

Muta
genicity assays did not reveal any valsartan-related effects at either the gene or chromosome level. These assays included bacterial mutagenicity tests (Salmonella Ames) and an in vitro gene mutation test with Chinese hamster V79 cells, a clastogenic test with Chinese hamster ovary cells, and a rat micronodose test.

Valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses up to 100 mg/kg/day. This dose is 6 times the maximum recommended human dose on a mg/m² basis. (Calculations assume an oral dose of 320 mg/day and a 60-kg patient.)

Preparation Categories C (first trimester) and D (second and third trimesters) See WARNINGS: Fetal/Neonatal Morbidity and Mortality.

Nursing Mothers
It is not known whether valsartan is excreted in human milk, but valsartan was excreted in the milk of lactating rats. Because of the potential for adverse effects on the nursing infant, a decision should be made whether to discontinue nursing or discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

Geriatric Use
In the controlled clinical trials of valsartan, 1241 (36.2%) of patients treated with valsartan were 65 years and 265 (7.9%) were 75 years or older. No overall difference in the efficacy or safety of valsartan was observed in these patient populations, but greater sensitivity of some older individuals cannot be ruled out.
Chromagen Forte Liquid-Iron Gelcaps

- Contains 151 mg of elemental iron—the most elemental iron available in an oral hematinic today

- Supplies the essential amount of iron for successful Epogen therapy

- Reduces the need for and risks associated with IV iron

- Delivers liquid iron to the site of optimal absorption for enhanced GI tolerability and excellent patient compliance

The most solid choice is liquid

Chromagen Forte

The strength of liquid iron in a soft gelcap

Please see full prescribing information adjacent to this ad.
© 1998 Savage Laboratories

*Based on a nationwide survey of nephrologists. Data on file, Savage Laboratories.
Epogen (epoetin alfa) is a registered trademark of Amgen Inc.
*Based on IMS National Prescription Audit, September 1997.
DESCRIPTION

CONTENTS: Each brown soft gelatin capsule contains: ferrous fumarate USP, 400 mg (151 mg elemental iron), ascorbic acid USP, 60 mg, folic acid USP, 1 mg, cyanocobalamin USP, 10 mcg.

DISCUSSION: The amount of elemental iron and the absorption of the iron components of commercial iron preparations varies widely. It is further established that certain "accessory components" may be included to enhance absorption and utilization of iron. Chromagen® Forte Capsules are formulated to provide the essential factors for a complete, versatile hematinic.

INSTRUCTIONS: For the treatment of all anemias responsive to oral iron therapy, such as hypochromic anemia associated with pregnancy, chronic or acute blood loss, dietary restriction, metabolic disease and post-surgical convalescence.

CONTRAINDICATIONS

Hemochromatosis and hemosiderosis are contraindications to iron therapy. Folic acid is contraindicated in patients with pernicious anemia (see PRECAUTIONS).

PRECAUTIONS

Folic acid should not be prescribed unless the diagnosis of pernicious anemia has been eliminated, since it can alleviate the hematologic manifestations, while allowing neurological damage to continue undetected.

ADVERSE REACTIONS

Average capsule doses in sensitive individuals or excessive dosage may cause nausea, skin rash, vomiting, diarrhea, precordial pain, or flushing of the face and extremities.

DOSEAGE AND ADMINISTRATION

Usual adult dose is 1-2 soft gelatin capsules daily, or as directed by a physician.

HOW SUPPLIED

Capsules: NDC 0281-0262-18, Unit Dose Box 100

CAUTION: Federal law prohibits dispensing without prescription.

BIBLIOGRAPHY


REFERENCES


Manufactured for: SAGE LABORATORIES®

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by: R.P. Scherer Corporation, St. Petersburg, Florida 33702
Raise calcitriol therapy to a higher level.
Drive down elevated PTH with enhanced Calcijex® therapy.
(Calcitriol Injection)

Raising the level of calcitriol therapy.
For optimal patient management, enhanced Calcijex therapy...

- Represents a major change in initial and titration dosing guidelines.
- Provides an opportunity to intervene more aggressively in mild to severe secondary hyperparathyroidism.
- Significantly reduces morbidity caused by undertreated renal osteodystrophy... a therapeutic approach that is truly enhanced.\(^1,3\)
- Broadens your dosing range, allowing you to provide treatment commensurate with PTH levels.
- Corresponds to the practice of nephrology thought leaders for patients with markedly elevated PTH.

### Dosing highlights

<table>
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<th>Enhanced therapy</th>
<th>Previous guidelines</th>
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<tr>
<td><strong>Initial dose</strong></td>
<td>1-2 mcg q dialysis</td>
<td>0.5 mcg q dialysis</td>
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<tr>
<td><strong>Titration dose</strong></td>
<td>0.5-1 mcg q 2-4 weeks</td>
<td>0.25-0.5 mcg q 2-4 weeks</td>
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Enhanced Calcijex\(^\circ\) (Calcitriol Injection) therapy refers to changes in dosing guidelines to encourage therapy commensurate with PTH level. Calcijex has not changed, only the suggested dosing guidelines as reflected in the accompanying brief disclosure.

A pattern of success.

Representative patient with severe hyperparathyroidism: Initial 2 mcg calcitriol dose, 3 x per week increased incrementally to 6 mcg, 3 x per week. PTH decreased dramatically.\(^4\)

Measures to control calcium intake, including a low-calcium dialysate and strict control of phosphorus levels, limited hypercalcemia.
CALCIJEX®
CALCIUM INJECTIONS
1 mcg and 2 mcg/mL

BRIEF SUMMARY
INDICATIONS AND USAGE
CalciJex® calcium injections are indicated in the management of hypercalcemia in patients undergoing chronic renal dialysis. It has been shown to significantly reduce elevated parathyroid hormone levels. Reduction of PTH has been shown to result in an improvement in renal osteodystrophy.

CONTRAINDICATIONS
CalciJex® (calcitriol injection) should not be given to patients with hypercalcemia or evidence of vitamin D toxicity.

HARMFULNESS
Since calciJex® is the most potent metabolite of vitamin D available, vitamin D and its derivatives should be withheld during treatment.

A non-aluminum phosphate-binding compound should be used to control serum phosphorus levels in patients undergoing dialysis.

Overdosage of any form of vitamin D is dangerous (see also OVERDOSE). Progressive hypercalcemia due to overdosage of vitamin D and its metabolites may be so severe as to require emergency attention. Chronic hypercalcemia can lead to generalized vascular calcification, nephrocalcinosis and other soft tissue calcification. The serum calcium times phosphate (Ca x P) product should not be allowed to exceed 70. Radiographic evaluation of suspect anatomical regions may be useful in the early detection of this condition.

PRECAUTIONS
1. General
Excessive dosage of CalciJex® (calcitriol injection) induces hypercalcemia and in some instances hypercalcemic renal failure. Early in treatment during dosage adjustment, serum calcium and phosphorus should be determined at least twice weekly. Should hypercalcemia develop, the drug should be discontinued immediately.

2. Information for the Patient
The patient and his or her parents should be informed about adherence to instructions about diet and calcium supplementation and avoidance of the use of unapproved non-prescription drugs, including magnesium-containing antacids. Patients should also be carefully informed about the symptoms of hypercalcemia (see ADVERSE REACTIONS).

3. Essential Laboratory Tests
Serum calcium, phosphorus, magnesium and alkaline phosphatase and 24-hour urinary calcium and phosphorus should be determined periodically. During the initial phase of the medication, serum calcium and phosphorus should be determined more frequently (twice weekly).

Adynamic bone disease may develop if PTH levels are suppressed to abnormal levels. If biopsy is not being done, a diagnostic bone biopsy may be used to indicate the rate of bone turnover. If PTH levels fall below recommended target range (15.0 to 3.0 times the upper limit of normal), in patients treated with CalciJex, the CalciJex dose should be reduced or therapy discontinued. Discontinuation of CalciJex therapy may result in relevant, therefore, appropriate titration downward in a matter of days to a maintenance dosage that is recommended.

4. Drug Interactions
Magnesium-containing antacid and CalciJex® should not be used concomitantly, because use may lead to the development of hypermagnesemia.

5. Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate the carcinogenic potential of CalciJex® (calcitriol injection). There was no evidence of mutagenicity as studied by the Ames Method. No significant effects of calciJex on fertility were reported using oral calciJex.

6. Use in Pregnancy: Pregnancy Category C
CalciJex® given early in pregnancy has been reported to be teratogenic in rabbits when given in doses 4 and 15 times the dose recommended for human use.

All 11 fetuses in 3 litters at doses shown normal and skeletal abnormalities. However, none of the other 22 litters (158 fetuses) showed significant abnormalities compared with controls.

7. Teratogenic Effects
No teratogenic pathology was noted in these studies in rats and mice. CalciJex® should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8. Nursing Mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from calcitriol, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

9. Patients with Impaired Renal Function
Safety and efficacy of calciJex in pediatric patients have not been established.

ADVERSE REACTIONS
Adverse effects of CalciJex® (calcitriol injection) are, in general, similar to those encountered with excessive vitamin D intoxication. The early and late signs and symptoms of vitamin D intoxication associated with hypercalcemia include:

- Early:
  Weakness, headache, somnolence, nausea, vomiting, dry mouth, constipation, muscle pain, bone pain and metallic taste.

- Late:
  Polyuria, polydipsia, anorexia, weight loss, nocturia, conjunctivitis (calcific), pancreatitis, lipoatrophy, hypercalcemia, hiccups, nausea and vomiting, xerostomia, alopecia, edema, hypercalcemia, elevated SGOT and alkaline phosphatase, calcification, hypercalcemia, cardiac arrhythmias and, rarely, overt psychosis.

Occasional mild pain on injection has been observed.

OVERDOSE
Administration of CalciJex® (calcitriol injection) to patients in excess of their requirements can cause hypercalcemia, hypercalciuria and hyperphosphatemia. High intake of calcium and phosphate concomitant with CalciJex may lead to similar abnormalities.

Temperature, blood pressure and pulse rate may be monitored in patients on hemodialysis.

General treatment of hypercalcemia (greater than 1 mg/dL above the upper limit of normal range) consists of immediate discontinuation of CalciJex therapy, institution of a low calcium diet and withdrawal of calcium supplements. Serum calcium levels should be determined daily until normocalcemia ensues. Hypercalcemia usually resolves in two to seven days. When serum calcium levels have returned to within normal limits, CalciJex therapy may be re instituted at a dose of 0.5 mcg less than prior therapy. Serum calcium levels should be obtained at least twice weekly after dosage changes.

Parenteral or intravenous calcium serum calcium levels may be corrected by dialysis against a calcium-free dialysate.

Treatment of acute accidental overdose of CalciJex should consist of general supportive measures. Serial serum electrolyte determinations (especially calcium), rate of urinary calcium excretion and assessment of electrolyte abnormalities due to hypercalcemia should be obtained. Such monitoring is critical in patients receiving digitals. Discontinuation of supplemental calcium and low calcium diet are also indicated in such situations. Due to the relatively short duration of the pharmacological action of calcitriol, further measures are probably unnecessary. Should, however, persistent and markedly elevated serum calcium levels occur, calcitriol may be a victim of therapeutic alternatives which may be considered, depending on the patient's underlying condition. These include the use of drugs such as phosphates and corticosteroids as well as measures to induce an appropriate forced diuresis. If necessary, a peritoneal dialysis against a calcium-free dialysate has also been reported.

HOW SUPPLIED
CalciJex® (calcitriol injection) is supplied in 1 mL ampules containing 1 mcg (Lot No. 1200) and 2 mcg (Lot No. 1210). Parenteral use.

Store at controlled room temperature 15° to 30°C (59° to 86°F).

Caution: Federal (USA) law prohibits dispensing without prescription.

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For documented iron-deficiency anemia not amenable to oral therapy

A CRUCIAL LINK

INFeD® AND EPO

in the treatment of iron-deficiency anemia for most ESRD patients

Please see references and prescribing information including the boxed WARNING on following page.

Copyright © 1996 by Schein Pharmaceutical, Inc. All rights reserved.
INFeD® and EPO for target HCT range of 30% to 36%

■ Treatment is currently targeted to a hematocrit range of 30% to 36%

INFeD® for effective erythropoiesis

■ Erythropoiesis can rapidly mobilize iron reserves and deplete even ample iron stores

INFeD® for rapid iron repletion

■ IV iron should be considered for all patients with low iron stores requiring a rapid EPO response

■ In dialysis patients receiving EPO:
  “The efficacy of oral iron is variable in these patients, and many require the use of intravenous iron dextran to maintain adequate iron levels...”

INFeD® evaluated for safety in hemodialysis patients

■ After reviewing the charts of 573 patients treated with INFeD® from four hemodialysis centers, Fishbane et al concluded: “We found serious adverse reactions with IVFe in hemodialysis patients to be uncommon.”

The parenteral use of complexes of iron and carbohydrates has resulted in anaphylactic-type reactions. Deaths associated with such administration have been reported. Therefore, INFeD® should be used only in those patients in whom the indications have been clearly established and laboratory investigations confirm an iron-deficient state not amenable to oral iron therapy.

Please see complete prescribing information under WARNINGS, PRECAUTIONS and ADVERSE REACTIONS including boxed WARNING for a complete listing of side effects.

*A study of 46 recombinant human erythropoietin-treated patients who were randomized to 4 groups to receive 4 different oral iron preparations demonstrated the following: in the short term oral iron was adequate to maintain iron status, but the downward trend in ferritin in 3 of the 4 groups indicated that eventually intravenous iron dextran would likely be required.

For documented iron-deficiency anemia not amenable to oral therapy

INFeD®
Iron Dextran Injection, USP 50 mg/mL
Replaces Iron Rapidly
DESCRIPTION: Iron (dextran) injection, USP is a dark brown, slightly viscous sterile liquid complex of ferric hydroxide and dextran. Each mL contains 50 mg of elemental iron as an iron-dextran complex, approximately 0.5% sodium citrate in water. Sodium citrate and/or hydrochloric acid may have been used to adjust pH. The pH of the solution is between 5.2 and 5.6.

The concentration of iron (dextran) injection, USP has an average apparent molecular weight of 165,000.

Therapeutic Class: Hematinics.

CLINICAL PHARMACOLOGY: After intravenous injection, iron dextran is absorbed from the injection site into the capillaries and the lymphatic system. Circulating iron dextran is removed from the plasma by cells of the reticuloendothelial system. The iron is then transported through the bloodstream and deposited in the reticuloendothelial tissues, including the bone marrow, liver, lung, and spleen. The major portion of intravenous iron dextran is absorbed within 72 hours; most of the remaining iron is absorbed in 5 to 10 days. Various studies involving intravenously administered iron dextran in deficient subjects, some of which had discontinued iron therapy, have demonstrated retention of iron for as long as 14 months. The iron content of iron dextran from a study used laboratory methods to separate the circulating iron dextran from the transfusion-bound iron. The iron retention during the initial 14 months of the study was 51%. Thus, the body may still be capable of using the iron dextran for a longer period.

INDICATIONS AND USES: Intravenous or intramuscular iron dextran are indicated for treatment of patients with documented iron deficiency in whom administration is unreliable or impossible.

CONTRAINdications: Iron dextran is contraindicated in patients with histories of severe immediate or anaphylactic reactions to iron or its salts.

Anaphylactic and other hypersensitivity reactions have been reported after unsterilized test doses as well as therapeutic doses of iron dextran. Aseptic meningitis, typically described as fever lasting 24 to 48 hours, has been reported following administration of iron dextran. Patients with hemolytic anemia may have an acute exacerbation of joint pain and swelling following the administration of iron dextran. Reports of blood dyscrasias (e.g., aplastic anemia, PEL, hemorrhagic, and neoplastic) in patients administered iron dextran have been associated with an increased incidence of granulocyte and platelet abnormalities in children. Children with pre-existing hemoglobinopathies are at increased risk for such abnormalities. Large doses of iron dextran have been associated with an increased incidence of adverse effects. The adverse effects frequently are delayed (1-5 days) reactions: hypotension, hypoxia, respiratory distress, vomiting, diarrhea, and seizures. The onset is usually 24-48 hours after administration and symptoms generally subside within 3-4 days. These symptoms have also been reported in patients given single doses of 25 mg/kg or more in 3-4 days. The clinical significance is not known. The potential for a delayed reaction must be considered when estimating the risk/benefit of the treatment.

The iron content of iron dextran is 1% by weight. 2 mL of iron dextran contains 62 mg of iron. This preparation should be used with extreme caution in patients with serious impairment of liver function. It should be used with extreme caution in patients with significant infection. Adverse reactions following administration of iron dextran may exacerbate cardiovascular complications in patients with pre-existing cardiovascular disorders.

PRECAUTIONS: Seebeck: Unwarrented therapy with parental iron will cause excessive storage of iron with the possiblility of further iron overload. Such accumulation of iron has been observed in patients with hemochromatosis and other iron storage diseases that might be erroneously diagnosed as iron deficiency anemia. Iron (dextran) injection, USP is not to be used with other iron compounds, iron preparations of different strength or iron preparations of different concentration.

Dosage and Administration:

Iron dextran is supplied in single-use containers of 100 mL. It is formulated as a 5% colloidal suspension in sodium chloride injection, USP. Iron dextran is administered by intravenous injection. Iron dextran may be administered by the intravenous route, the intramuscular route, or the intradermal route. Intravenous administration should be used whenever feasible. The intravenous rate should be such that the patient will not experience undue discomfort or marked flushing of the skin. The usual dosage schedule is 50 to 150 mg/kg as a single dose, or 25 to 75 mg/kg on 2 consecutive days. Intramuscular injection should be given slowly and at a recommended rate not to exceed 10 mL/min to each site. The necessary number of injections is determined by the patient’s iron deficiency and the expected need for future iron administration. Intradermal injection is the site of choice for the administration of test dose of 2 mL of iron dextran. Injections should not be made into areas that have been previously irradiated by cobalt-60 or other types of radiation.

Pregnancy: Category C: Iron dextran has been shown to be teratogenic and embryotoxic in mice, rats, rabbits, dogs, and monkeys. It was not teratogenic in rats at a dose of 200 mg/kg and monkeys at 30 mg/kg. The maximum dose used in the tests in monkeys was 30 mg/kg. The tests were conducted in two different laboratories using different test systems. Similar effects were observed in mice and rats on administration of a single dose of 150 mg/kg iron (as iron). Toxic abnormalities at dosages 5 to 10 times the normal daily oral iron dosages have been reported in pregnant rats and rabbits. Iron dextran, total iron loading capacity (TLC) and percent saturation of the iron by the intravenous route.

Hemorrhagic: Ulcers, purpura, purpura, rash.

Renal: Glomerular: Nephritis, nephrotic syndrome.

Hematological: Lymphadenopathy, Leukopenia, lymphoid hyperplasia.

Gastrointestinal: Arthritis, arthritis (may represent reactive arthritis in patients with quiescent rheumatoid arthritis).

Respiratory: Arteritis, arterial lesions, interstitial fibrosis, lymphoid hyperplasia.

Cardiovascular: Chest pain, chest tightness, shock, hypotension, hypertension, tachycardia, flushing, arrhythmias. (Flushing usually correlates with the intravenous route.)

Hepatic: Ulcers, portal, mesenteric, peritoneal, portal.

Respiratory: Acute respiratory distress syndrome.

Iron dextran is administered to a nursing woman. Traces of unabsorbed iron dextran are excreted in human milk.

PEDIATRIC USE: Use in infants under 4 months of age (See Precautions). Adverse Reactions: Anaphylactic reactions have been reported with the use of iron dextran injection; on occasion fatal reactions have been reported. There have been reports of hypertensive reactions following intravenous iron dextran injection. In clinical studies, 208 (4.2%) patients with a history of allergic reactions exhibited a decrease in blood pressure of 50 to 100 mm Hg for 3 to 5 minutes following the injection of iron dextran. The decrease in blood pressure was usually transient and not associated with symptoms. There were 14 patients who exhibited a decrease in blood pressure of 150 mm Hg for 5 to 30 minutes following the injection of iron dextran. There were no reactions in patients without a history of allergic reactions.

Cardiovascular: Chest pain, chest tightness, shock, hypotension, hypertension, tachycardia, flushing, arrhythmias. (Flushing usually correlates with the intravenous route.)

Hepatic: Ulcers, portal, mesenteric, peritoneal, portal.

Gastrointestinal: Abdominal pain, nausea, vomiting, diarrhea, ulcerative colitis, hemorrhoids, hepatitis, pancreatitis.

Hematological: Convulsions, seizures, syncope, headache, weakness, anorexia, anorexia, anemia, thrombocytopenia, ecchymosis, clots, discr., pain, tenderness, gouty arthritis.

Renal: Respiratory: Arteritis, nephritis, renal failure.

Iron toxicity may be seen in patients with severe iron overload, following parenteral iron therapy. Severe iron toxicity may be associated with severe anemia, jaundice, hepatomegaly, and death. Iron toxicity may be associated with severe anemia, jaundice, hepatomegaly, and death.

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When a hypertensive patient doesn’t adequately respond to any Ca blocker* or any ACE inhibitor . . .

Simplify your next choice

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Lotrel is a single therapy with complementary CCB/ACEI actions, resulting in superior control and an excellent side effect profile

**LOTREL**
amlodipine/benazepril HCl
2.5/10 • 5/10 • 5/20-mg capsules

- Patients with congestive heart failure (with or without associated renal insufficiency) should be monitored for the first 2 weeks whenever Lotrel therapy is started or the dosage is changed
- In non-African-American patients, the complementary mechanisms of action of Lotrel produce a BP-lowering effect that is additive and in some cases synergistic

*In African-American patients, virtually all of the antihypertensive effect could be attributed to the amlodipine component, but all patient groups benefit from the reduction in amlodipine-induced edema.

**Pregnancy Warning:** ACE inhibitors should be discontinued as soon as pregnancy is detected (see Warnings).

Angioedema and cough have been reported in patients receiving ACE inhibitors. Headache and edema are the most common side effects in patients receiving amlodipine. Please consult the brief summary of Prescribing Information on next page.
Lotrel®
amlodipine and benazepril hydrochloride Combination Capsules

2.5 mg/5 mg
5 mg/10 mg

BRIEF SUMMARY (FOR COMPLETE PRESCRIBING INFORMATION, SEE FULL PRESCRIBING INFORMATION ATTACHED)

USE IN PREGNANCY
When used during pregnancy the second and third trimesters, ACE inhibitors should be avoided (see Precautions)

If pregnancy is detected, Lotelect should be discontinued as soon as possible. See Warnings, Fetal/Neonatal Mortality and Morbidity.

INDICATIONS AND USAGE
Lotrel is indicated for the treatment of hypertension. This fixed combination dose is indicated for the initial therapy of hypertension in patients whose blood pressure is not adequately controlled with amlodipine or benazepril alone.

In using Lotelect, consideration should be given to the fact that an ACE inhibitor should not be used during the second and third trimesters of pregnancy (see Precautions). If pregnancy is detected, Lotelect should be discontinued as soon as possible.

CONTRAINDICATIONS
Lotrel is contraindicated in patients who are hypersensitive to amlodipine, or to any other member of the dihydropyridine class.

WARNINGS
Hypersensitivity and Possible Reactions Related to Hypersensitivity
Preferably because angiotensin-converting enzyme inhibitors affect the function of the renin-angiotensin system, angiotensin-converting enzyme inhibitors may also be expected to reduce aldosterone secretion, resulting in a reduction of extracellular fluid and blood volume. The effect of these changes on renal function and to recommend the use of ACE inhibitors for the purpose of reducing aldosterone secretion, resulting in a reduction of extracellular fluid and blood volume. The effect of these changes on renal function and to recommend the use of ACE inhibitors for the purpose of reducing aldosterone secretion, resulting in a reduction of extracellular fluid and blood volume. The effect of these changes on renal function and to recommend the use of ACE inhibitors increases in blood pressure may be small or may not occur. Therefore,

Most patients who have been receiving a diuretic agent, in particular those with a reduced sodium intake, may be hypotensive from the very first dose of the ACE inhibitor, but they do not usually experience acute hypotension. Patients receiving ACE inhibitors have been reported to have a higher incidence of angioedema compared to non-black.

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\[
\begin{align*}
\text{CH}_3 & \quad \text{N} \quad \text{O} \\
\text{O} & \quad \text{O} \\
\text{CH} & \quad \text{OH} \\
\text{COOH} & \quad \text{OH}
\end{align*}
\]

Formulas: C20H33ClN2O5 \quad \text{Molecular Weight: 512.10}

Each CARNITOR® (Levocarnitine) Tablet contains 330 mg of levocarnitine and the inactive ingredients magnesium stearate, microcrystalline cellulose and polyethylene glycol.

Each 18 ml container of the CARNITOR® (Levocarnitine) Oral Solution contains 1 g of levocarnitine/10 ml. Also contains: Flavored Berry Flavor, D&C Red No. 33, D&C Blue Acid, FD&C Red No. 40, Purified Water, Sucrose Syrup, Methylparaben NF and Propylparaben NF are added as preservatives. The pH is approximately 5.

CARNITOR® (Levocarnitine) Injections is a sterile aqueous solution of levocarnitine 1 mg/ml, for injection, for intramuscular injection in single doses not to exceed 60 mg.

CARNITOR® (Levocarnitine) is a naturally occurring sub-
stance required in normal energy metabolism. It has been shown to affect energy metabolism in certain cellu-
lar mitochondria, therefore delivering substrate for oxidation and subsequent energy production. Fatty acids are utilized as an energy substrate in all tissues except the brain, skeletal and cardiac muscle as they serve as major fuel. Primary sys-
temic carnitine deficiency is characterised by low plasma, RBC and tissue levels which have not been possible to de-
mine which symptoms are due to carnitine deficiency and which are due to the underlying organic acidemia, as symp-
toms of both abnormalities may be expected to improve with carnitine. The literature does not confirm or deny the possibility to concomitantly improve carnitine deficiency and correct organic acidemia.

Secondary levocarnitine deficiency can be a consequence of infant carnitine deficiency, which may lead to the metabolic abnormalities of patients with inborn errors that result in accumulation of toxic organic acids. Conditions for which this effect was demonstrated are glutaric aciduria type II, methyl malonic aciduria, propionic acidemia, and medium-chain fatty acyl-CoA dehydrogenase deficiency.1,2 Auton-
loadation occurs in patients due to the accumula-
tions of fatty acids which cause the development of conditions that impair intermediary metabolism. The subsequent hydrolysis of the acyl-CoA compound to free fatty acid results in acids that can be the substrate for energy production or stored in the fat cells. Secondary carnitine deficiency is characterised by low plasma, RBC and tissue levels which have not been possible to de-
mine which symptoms are due to carnitine deficiency and which are due to the underlying organic acidemia, as sympt-
toms of both abnormalities may be expected to improve with carnitine. The literature does not confirm or deny the possibility to concomitantly improve carnitine deficiency and correct organic acidemia.

Carnitine deficiency is defined biochemically as abnor-
malities of the major long-chain acyl-CoA dehydrogenase enzyme. It is an inherited metabolic disorder and is transmitted as an autosomal recessive trait. Affected infants are born with normal plasma carnitine levels but subsequently develop clinical symptoms of carnitine deficiency as a consequence of the enzyme deficiency. The clinical presentation is variable and may include failure to thrive, hypermetabolism, developmental delay and cardiomyopathy. The diagnosis of secondary carnitine deficiency is made by demonstrating a decreased level of carnitine in body fluid such as serum or urine, usually obtained by venous puncture or catheterization. The diagnosis is confirmed by investigation of the patient for other conditions that may cause secondary carnitine deficiency. In the case of untreated patients, the level of carnitine may be normal or decreased due to the underlying organic acidemia. In the case of treated patients, the level of carnitine may be normal or decreased as a result of the treatment. The diagnosis of secondary carnitine deficiency is usually made by measuring the level of carnitine in body fluid such as serum or urine, usually obtained by venous puncture or catheterization. The diagnosis is confirmed by investigation of the patient for other conditions that may cause secondary carnitine deficiency. In the case of untreated patients, the level of carnitine may be normal or decreased due to the underlying organic acidemia. In the case of treated patients, the level of carnitine may be normal or decreased as a result of the treatment.

CARNITOR® (Levocarnitine) Tablets are intended for use for oral use only. Not for parenteral use. CARNITOR® (Levocarnitine) Oral Solution is for oral use only. Not for parenteral use.

Gastrointestinal reactions may result from too rapid consump-
tion of levocarnitine. CARNITOR® (Levocarnitine) Oral Solution should be consumed alone or may be added to other liquid foods to reduce taste tastes. It should be con-
sumed slowly and doses should be spaced evenly throughout the day to maintain tolerance. CARNITOR® (Levocarnitine) Tablets should be consumed slowly and doses should be spaced evenly throughout the day to maintain tolerance. CARNITOR® (Levocarnitine) Injection is for intramuscular use only.
Reduce the Pressure of Hypertension

- Effective as monotherapy¹
- Effective in combination with other antihypertensive agents²,³

Well Tolerated

- Like other α₁-blockers, HYTRIN can cause marked lowering of blood pressure, especially postural hypotension and syncope.¹
- Caution should be observed when HYTRIN is administered concomitantly with other antihypertensive agents, especially the calcium channel blocker verapamil, to avoid the possibility of developing significant hypotension. Dosage reduction and retitration of either agent may be necessary.¹
- Adverse events occurring significantly more often than placebo in hypertension clinical trials were dizziness, asthenia, nasal congestion, peripheral edema, somnolence, nausea, palpitations and blurred vision.¹

HYTRIN FREE START™ PROGRAM

Free patient samples available.
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for more information.

References:

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HYTRIN* (terazosin hydrochloride) Capsules

INDICATIONS AND USAGE: HYTRIN is indicated for the treatment of hypertension. It can be used alone or in combination with other antihypertensive agents such as diuretics or beta-adrenergic blocking agents.

CONTRAINDICATIONS: HYTRIN capsules are contraindicated in patients with a history of systemic allergic reactions due to terazosin, syncope, and in association with the first dose or first few days of therapy. A similar effect can be seen in patients with a history of syncope even when the dosage is increased only slightly, then restarted. Syncope has also been reported with other alpha-adrenergic blocking agents, can occur within the first 24 hours after starting the therapy, and may be associated with cardiovascular collapse, cardiac arrest, or death. In rare cases, syncope, in association with the first dose or first few days of therapy, may occur before the onset of hypotension due to the antihypertensive effect of terazosin. Syncope may also occur when the dosage is increased only slightly, then restarted. Syncope is believed to be due to an excessive postural decrease in blood pressure, although the postural hypotension in these episodes has been preceded by a bout of severe supraventricular or ventricular tachycardia. Syncope has also been noted after up to 4 weeks of use. Additionally, the possibility of the contribution of hormonal modulation to the symptoms of postural hypotension should be considered.

To decrease the likelihood of syncope or excessive hypotension, HYTRIN should be initiated with a 1 mg dose of terazosin, given at bedtime. The 2 mg, 5 mg and 10 mg capsules are not indicated as initial therapy. Dosage modification should be based on clinical response and should be individualized for each patient. Additional dosage adjustment should be made with caution in patients who are concurrently receiving drugs such as diuretics, which may reduce the effective circulating blood volume due to either reduced intake or increased losses, or antihypertensive agents, which may increase the effective circulating blood volume. In early investigational studies, where increasing single doses up to 7.5 mg were given at 3 day intervals, tolerance to the first dose was more common than tolerance to subsequent doses. The usual effective syncope for HYTRIN was 4.5 mg.

In multiple dose clinical trials involving nearly 2000 hypertensive patients, syncope was reported in about 1% of patients. Syncope did not occur with the first dose.

In multiple dose clinical trials involving nearly 2000 hypertensive patients, syncope was reported in about 1% of patients. Syncope did not occur with the first dose.

PRECAUTIONS: General: Prostate Cancer: Carcinoma of the prostate and BPH cause many of the same symptoms. These two diseases might coexist in an individual. Thus, a positive response to HYTRIN therapy may not rule out the presence of carcinoma of the prostate.

Orthostatic hypotension: This is the most severe orthostatic effect of terazosin (see Warnings). Other symptoms of lower blood pressure, such as dizziness, lightheadedness and palpitations, are more common and occurred in some 28% of patients in clinical trials of hypotension. In BPH clinical trials, 21% of the patients experienced dizziness. Dizziness, hypotension, postural hypotension, syncope, and vertigo. Patients with occupations in which such events represent potential hazards should be treated with particular caution.

Laboratory Tests: Small but statistically significant decreases in hematocrit, hemoglobin, white blood cells, total protein and albumin were observed in controlled clinical trials. These laboratory findings suggested the possibility of hemodilution. Treatment with terazosin for up to 24 months had no significant effect on prostate specific antigen (PSA) levels.

Drug Interactions: In controlled trials, terazosin has been added to diuretics, and several beta-adrenergic blockers; no unexpected interactions were observed. Terazosin has also been used in patients with cardiac disease. While these patients were not formal interaction studies, no interactions were observed. In studies involving at least 50 patients on the following drugs or drug classes: 1) analgesics/anti-inflammatory drugs, 2) angiotensin converting enzyme inhibitors, 3) beta blockers, 4) calcium channel blockers, 5) dopamine antagonists, 6) digitalis, 7) diuretics, 8) hypnotics (1.3% - 0.4%), tachycardia (1.9% - 1.2%), nausea (0.5% - 0.1%), headache (1.3% - 2.4%), weight gain (0.6% - 0.4%), pain (5% - 3.6%), diarrhea (1.9% - 2.6%), dizziness (1.9% - 2.6%), syncope (0.5% - 0.1%), sensation (3% - 2.4%), somnolence (2.6% - 2.4%), anemia (1% - 0.1%), nausea, peripheral edema, palpitations, and somnolence were the only symptoms that were significantly (p < 0.05) more common in patients receiving the combination than in patients receiving placebo. Similar adverse reaction rates were observed in placebo-controlled monotherapy trials. Additional adverse reactions and reports have been seen, but these are, in general, not distinguishable from symptoms that might have occurred in the absence of treatment. The following additional adverse reactions were reported by at least 1% of U.S. patients who received terazosin in controlled or open, short- or long-term clinical trials or have been reported during marketing experience: Body as a Whole: chest pain, facial edema, abdominal pain, paresthesia; Cardiovascular System: arrhythmia, vasodilation; Digestive System: constipation, diarrhea, dry mouth, dysphagia, flatulence, vomiting; Genito-Urinary System: impotence; Skin: rash; Eye: photophobia; Other: tiredness, decreased libido, dry mouth, vertigo, abnormal dreams, sweating, postural hypotension, syncope; postural hypotension may be marked in the supine position. Post-marketing experience indicates that in rare instances patients may develop allergic reactions, including anaphylaxis, following administration of terazosin hydrochloride. There have been reports of priapism during post-marketing surveillance. Although priapism can occur without warning, its presence i
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DEXFERRUM®
(IRON DEXTRAN INJECTION, USP)

For effective intravenous treatment of iron deficiency anemia, it positively delivers.
Decreases total iron binding capacity.
Increases transferrin saturation.
For your patients with documented iron deficiency in whom oral administration is unsatisfactory or impossible, depend on DEXFERRUM for quality intravenous treatment. Here's why:

- A recent study demonstrated that rapid iron utilization to replete iron stores and produce new hemoglobin takes place soon after DEXFERRUM administration.¹
- The study noted that DEXFERRUM significantly decreases total iron binding capacity and increases transferrin saturation.

<table>
<thead>
<tr>
<th></th>
<th>Pre-study</th>
<th>Week 1</th>
<th>Day 30</th>
<th>Effect of Iron Dextran (probability value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum TIBC (µg/dl)</td>
<td>221.2 ± 40.9</td>
<td>201.3 ± 51.6</td>
<td>183.2 ± 48.6</td>
<td>0.0061</td>
</tr>
<tr>
<td>Transferrin saturation (%)</td>
<td>14.3 ± 2.8</td>
<td>32.3 ± 13.6</td>
<td>22.9 ± 3.3</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Study was conducted to determine the rate and extent of iron utilization after administration of intravenous iron dextran and to compare the efficacy of iron dextran of different molecular weights. Twenty patients were randomized to receive either a 500 mg dose of DEXFERRUM (267,000 daltons) or INFeD® (96,000 daltons) administered in five sequential 100 mg doses. Indices of iron status were examined before treatment and at weekly intervals up to four weeks later.

- The safety and efficacy of DEXFERRUM have been confirmed through clinical trials in end-stage renal disease (ESRD) patients on epoetin alfa.²

For more information, or to order DEXFERRUM, call us toll-free at 1-800-645-1706.

Call our Reimbursement Hotline at 1-800-282-7712 regarding DEXFERRUM reimbursement issues or our Patient Assistance Program. In the Washington, D.C., metropolitan area call 1-202-942-2453.

**Warning**

The parenteral use of complexes of iron and carbohydrates has resulted in anaphylactic-type reactions. Deaths associated with such administration have been reported. Therefore, DEXFERRUM should be used only in those patients in whom the indications have been clearly established and laboratory investigations confirm an iron-deficient state not amenable to oral iron therapy.

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2. Data on file at American Regent Laboratories, Inc.

Please see brief summary of the prescribing information on the following page.
**WARNING**

THE PARENTERAL USE OF COMPLEXES OF IRON AND CARBOHYDRATES HAS RESULTED IN ANAPHYLACTOID-TYPE REACTIONS. DEATHS ASSOCIATED WITH SUCH ADMINISTRATION HAVE BEEN REPORTED. THEREFORE, DEXFERRUM SHOULD BE USED ONLY IN THOSE PATIENTS IN WHOM THE INDICATIONS HAVE BEEN CLEARLY ESTABLISHED AND LABORATORY INVESTIGATIONS CONFIRM AN IRON DEFICIENT STATE NOT AMENABLE TO ORAL IRON THERAPY.

DESCRIPTION: DEXFERRUM is a dark brown, slightly viscous sterile liquid complex of ferric oxyhydroxide and a low molecular weight dextran derivative for intravenous use. Each mL contains 50 mg elemental iron as an iron dextran complex. Sodium chloride may have been added for tonicity. Water for injection q.s. pH adjusted to 5.2 - 6.5 with hydrochloric acid and, if necessary, sodium hydroxide. Sterile, nonpyrogenic.

Therapeutic Class: Hematologic

INDICATIONS AND USAGE: DEXFERRUM is indicated for treatment of patients with documented iron deficiency in whom oral administration is unfeasible or impossible.

CONTRAINDICATIONS: Hypersensitivity to the product. All anemias not associated with iron deficiency.

WARNINGS: See BOXED WARNING.

A risk of carcinogenesis may attend the intravenous injection of iron-carbohydrate complexes. Such complexes have been found under experimental conditions to produce tumors when large doses or small doses injected repeatedly at the same site were given to rats, mice, and rabbits, and possibly in hamsters. The long latent period between the injection of a potential carcinogen and the appearance of a tumor makes it impossible to measure accurately the time this in man. There have, however, been several reports in the literature describing tumors at the injection site in humans who had previously received intravenous injections of iron-carbohydrate complexes.

Large intravenous doses, such as used with total dose infusions (TDI), have been associated with an increased incidence of adverse effects. The adverse effects frequently are delayed (1-2 days) reactions typified by one or more of the following symptoms: anaphylactic, urticarial, rash, pruritus, flushing, malaise, myalgia, nausea, and vomiting. The onset is usually 24-48 hours after administration and symptoms generally subside within 3-4 days. The etiology of these reactions is not known. The potential for a delayed reaction must be considered when estimating the risk/benefit of treatment.

The maximum daily dose should not exceed 2 mL undiluted iron dextran.

This preparation should be used with extreme care in patients with serious impairment of liver function. It should not be used during the acute phase of infectious kidney disease. Adverse reactions experienced following administration of DEXFERRUM may exacerbate cardiovascular complications in patients with pre-existing cardiovascular disease.

PRECAUTIONS: General: Uncommon therapy with parenteral iron will cause excess storage of iron with the consequent possibility of exogenous hemosiderosis. Such iron overload is particularly apt to occur in patients with hemoglobinopathies and other refractory anemias that might be erroneously diagnosed as iron deficiency anemias. DEXFERRUM should be used with caution in individuals with histories of significant allergies and/or asthma.

Anaphylactic and other hypersensitivity reactions have been reported following parenteral iron therapy. Pre-existing anaphylactic and other hypersensitivity anaphylactic reactions may occur and cause death if there is no immediate treatment. Therefore, administration of subsequent test doses during therapy should be considered. See BOXED WARNING AND ADMINISTRATION (ADMINISTRATION).

Eosinophilia should be immediately available in the event of acute hypersensitivity reactions. (Usual adult dose: 0.5 mL or a 1:1,000 dilution, by subcutaneous or intramuscular injection.) Note: Patients using beta-blocking agents may not show these signs and symptoms.

Patients with iron deficiency anemia may have an acute exacerbation of joint pain and swelling following the administration of DEXFERRUM.

Information For Patients: Patients should be advised of the potential adverse reactions associated with the use of iron dextran complex.

Drug/Laboratory Test Interactions: Large doses of iron dextran (5 mL or more) have been reported to give a brown color to serum from a blood sample drawn 4 hours after administration. The drug may cause falsely elevated values of serum bilirubin and falsely decreased values of serum calcium.

Serum iron determinations (especially by colorimetric assays) may not be meaningful for 3 weeks following the administration of iron dextran.

Serum ferritin peaks approximately 7 to 9 days after an intravenous dose of DEXFERRUM and slowly returns to baseline over about 3 weeks. Examination of the bone marrow for iron stores may not be meaningful for prolonged periods following iron dextran therapy because residual iron dextran may remain in the reticuloendothelial cells.

Bone scans with 99mTc labeled bone seeking agents, in the presence of high serum ferritin levels or following iron dextran infusions, have been reported to show reduction of bony uptake, marked renal activity, and excessive blood pool and soft tissue accumulation.

Carcinogenesis. Mutagenesis. Impairment Of Fertility: See WARNINGS.

Pregnancy: Teratogenic Effects. Pregnancy Category C: Iron dextran has been shown to be teratogenic and embryocidal in mice, rats, rabbits, dogs, and monkeys when given in doses of about 3 times the maximum human dose.

No consistent adverse maternal effects were observed in mice, rats, rabbits, dogs and monkeys at doses of 50 mg/kg or less. Fetal and maternal toxicity has been reported in monkeys at a total intravenous dose of 90 mg/kg over a 14 day period. Similar effects were observed in mice and rats at an administration of a single dose of 125 mg/kg. Fetal abnormalities in rats and dogs were observed at doses of 250 mg/kg or higher. The animals used in these tests were not iron deficient. There are no adequate and well-controlled studies in pregnant women. DEXFERRUM should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Placental Transfer: Various animal studies and studies in pregnant humans have demonstrated non-toxic results with respect to the placental transfer of iron dextran as iron dextran. It appears that some iron does reach the fetus, but the form in which it crosses the placenta is not clear.

Nursing Mothers: Caution should be exercised when DEXFERRUM is administered to a nursing woman. Traces of unmetabolized iron dextran are excreted in human milk.

Pediatric Use: Not recommended for use in infants under 4 months of age (See DOSAGE AND ADMINISTRATION).

ADVERSE REACTIONS: General: Anaphylactic reactions have been reported with the use of iron dextran injection; on occasion these reactions have been fatal. Such reactions, which occur most often within the first several minutes of administration, have been generally characterized by sudden onset of respiratory difficulty and/or cardiovascular collapse. (See Boxed WARNING and PRECAUTIONS: General, pertaining to immediate availability of emergency equipment.)

Cardiovascular: Chest pain, chest tightness, shock, hypotension, hypertension, tachycardia, flushing, arrhythmias. (Flushing and hypotension may occur from too rapid injections by the intravenous route.)

Dermatologic: Urticaria, pruritus, purpura, rash.

Gastrointestinal: Abdominal pain, nausea, vomiting, diarrhea.

Hematologic: Leukocytosis, thrombocytosis.

Miscellaneous: Arthralgia, arthralgia, myalgia, anaphylactic reaction, vasculitis, dermatomyositis, rashes.

Respiratory: Respiratory arrest, dyspnea, bronchospasm.

Urologic: Hematuria.

Dilated reaction: Anaphylaxis, backache, chest pain, chest tightness, fever, headache, malaise, myalgia, nausea, vomiting (See WARNINGS).

Serious: Anaphylaxis, backache, chest pain, chest tightness, fever, headache, malaise, myalgia, nausea, vomiting (See WARNINGS).

Miscellaneous: Faintness, episodes, sweating, shivering, chills, malaise, altered taste.

DOSAGE AND ADMINISTRATION: One iron should be administered prior to administration of DEXFERRUM.

Intravenous Injection: PRIOR TO RECEIVING THEIR FIRST DEXFERRUM THERAPEUTIC DOSE, ALL PATIENTS SHOULD BE GIVEN AN INTRAVENOUS TEST DOSE OF 0.5 mL. (See PRECAUTIONS: General) THE TEST DOSE SHOULD BE ADMINISTERED AT A GRADUAL RATE OVER AT LEAST 5 MINUTES. If anaphylactic reactions known to occur following DEXFERRUM administration are usually evident within a few minutes, or sooner, it is recommended that a period of 15 minutes before the remainder of the initial therapeutic dose is given. If no alleviation of symptoms of 2 mL or less may be given on a daily basis until the calculated total amount required has been reached. DEXFERRUM is given undiluted at a slower gradual rate not to exceed 50 mg (1 mL) per minute.

If anaphylactic reactions are observed, DEXFERRUM can be given according to the following schedule until the calculated total amount required has been reached. Each day's dose should ordinarily not exceed 5.5 mL (25 mg of iron) for infants under 10 kg (22 lb) and 2 mL (50 mg of iron) for children under 10 kg (22 lb) and 2 mL (100 mg of iron) for other patients.

NOTE: Do not mix DEXFERRUM with other medications or add to parenteral nutrition solutions for intravenous infusion.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever the solution and container permit.

HOW SUPPLIED: DEXFERRUM (Iron Dextran Injection, USP) containing 50 mg of elemental iron per mL, is available in 2 mL single-dose vials (for intravenous use) in cartons of 10 (NDC 0071-0024-10) and individually packaged (NDC 0071-0024-91). Store at controlled room temperature 15° - 30°C (59° - 86°F).

CAUTION: Federal law prohibits dispensing without prescription.

This is a brief summary; see product package insert for full prescribing information.

BS0234
Rev 2/97

AMERICAN REGENT LABORATORIES, INC.
SHIRLEY, NY 11967
The only liquid growth hormone.

Eliminates the need for reconstitution.

Nutropin AQ is indicated for the treatment of growth failure due to a lack of adequate endogenous growth hormone secretion, growth failure associated with chronic renal insufficiency up to the time of renal transplantation, and short stature associated with Turner syndrome.

Important safety information

Growth hormone should not be used in patients with closed epiphyses or active neoplasia. Growth hormone therapy should be discontinued if evidence of neoplasia develops.

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For more information, call 1-800-530-3083.

Please see brief summary of prescribing information for Nutropin AQ on adjacent page.

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**BRIEF SUMMARY**

Nitropin AG

Nitropin AG (somatropin [GHD origin] injection) is indicated for the long-term treatment of growth failure due to a lack of adequate endogenous growth hormone secretion.

Nitropin ADP (somatropin [GHD origin] injection) is also indicated for the treatment of growth failure associated with chronic renal insufficiency up to the time of renal transplantation. Nitropin AG therapy should be used in conjunction with optimal management of chronic renal insufficiency.

Nitropin AG (somatropin [GHD origin] injection) is also indicated for the long-term treatment of short stature associated with Turner syndrome.

**CONTRAINdications**

Nitropin AG should not be used in subjects with closed epiphyses.

Nitropin AG should not be used in patients with active neoplasia. Growth hormone (GH) therapy should be discontinued if evidence of neoplasia develops.

**WARNINGS**

None.

**PRECAUTIONS**

General. Nitropin AG should be prescribed by physicians experienced in the diagnosis and management of patients with growth failure due to GH deficiency (GHD), Turner syndrome, or chronic renal insufficiency (CR). No studies have been completed of Nitropin AG therapy in patients who have received renal transplants. Currently, treatment of patients with functioning renal allografts is not indicated.

Because Nitropin AG may reduce insulin sensitivity, patients should be monitored for evidence of glucose intolerance.

Patients with a history of an intracranial lesion should be examined frequently for progression or recurrence of the lesion.

Patients with growth failure secondary to CRI should be examined periodically for evidence of progression of renal osteodystrophy. Slipped capital femoral epiphysis or avascular necrosis of the femoral head may be seen in children with advanced renal osteodystrophy, and it is uncertain whether these problems are affected by GH therapy. X-rays of the hips should be obtained prior to initiating therapy for CRI patients. Physicians and parents should be alert to the development of a limp or complaints of hip or knee pain in patients treated with Nitropin AG.

Slipped capital femoral epiphysis may also occur more frequently in patients with endocrine disorders or in patients undergoing rapid growth.

Progression of scoliosis can occur in patients who experience rapid growth. Because GH increases growth rate, patients with a history of scoliosis who are treated with GH should be monitored for progression of scoliosis. Growth hormone has not been shown to increase the incidence of scoliosis. Skeletal abnormalities including scoliosis are commonly seen in untreated Turner syndrome patients. Physicians should be alert to these abnormalities, which may manifest during GH therapy.

Patients with Turner syndrome should be evaluated carefully for uterine media and other end organ systems since these patients have an increased risk of ear or hearing disorders. In a randomized, controlled trial, there was a statistically significant increase, as compared to untreated controls, in otitis media (43% vs. 26%) and ear disorders (18% vs. 5%). Patients receiving GH. In addition, patients with Turner syndrome should be monitored closely for cardiovascular disorders (e.g., stroke, aortic aneurysms, hypertension) as these are also at risk for these conditions.

Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea and/or vomiting has been reported in a small number of patients treated with GH products. Symptoms usually occurred within the first eight (8) weeks of the initiation of GH therapy. In all reported cases, IH-associated signs and symptoms resolved after termination of therapy or reduction of the GH dose. Funduscopic examination of patients is recommended at the initiation and periodically during the course of GH therapy. Patients with CRI and Turner syndrome may be at increased risk for development of IH.

As for any protein, local and systemic allergic reactions may occur. Parents/ Patient should be informed that such reactions are possible and that prompt medical attention should be sought if allergic reactions occur.

Laboratory Tests: Serum levels of inorganic phosphorus, alkaline phosphatase, and parathyroid hormone (PTH) may increase with Nitropin AG therapy.

Unrestrained hypoglycemia prevents optimal response to Nitropin AG. Patients with Turner syndrome have an inherently increased risk of developing autoimmune thyroid disease. Changes in thyroid hormone laboratory measurements may develop during Nitropin AG treatment. Therefore, patients should have periodic thyroid function tests and should be treated with thyroid hormone when indicated.

Drug interaction. The use of Nitropin AG in patients with CRI receiving glucocorticosteroid therapy has not been evaluated. Concurrent glucocorticosteroid therapy may inhibit the growth-promoting effect of Nitropin AG. If glucocorticosteroid replacement is required, the glucocorticosteroid dose should be carefully adjusted.

There was no evidence in the controlled studies of somatropin's interaction with drugs commonly used in CRI patients. Limited published data indicate that GH treatment increases cholesterol (P<0.05) and triglycerides (P<0.05). Adverse effects associated with these changes are not known.

Carcinogenesis. Mutagenesis, Impairment of Fertility: Carcinogenicity, mutagenicity, and reproduction studies have not been conducted with Nitropin AG.

Pregnancy. Pregnancy Category Cl. Animal reproduction studies have not been conducted with Nitropin AG. It is also not known whether Nitropin AG can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Nitropin AG should be given to a pregnant woman only if clearly needed.

Hemodialysis. It is not known whether Nitropin AG is secreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Nitropin AG is administered to a nursing mother.

Information for Patients: Patients being treated with GH and/or their parents should be informed of the potential benefits and risks associated with treatment. If home use is determined to be desirable by the physician, instructions on appropriate use should be given, including a review of the contents of the Patient Information Insert. This information is intended to aid in the safe and effective administration of the medication. It is not a discourse of all possible adverse or intended effects.

If home use is prescribed, a puncture resistant container for the disposal of used syringes and needles should be recommended to the patient. Patients and/or parents should be thoroughly instructed in the importance of proper disposal and cautioned against any reuse of needles and syringes (see Patient Information Insert).

**ADVERSE REACTIONS**

As with all protein pharmaceuticals, a small percentage of patients may develop antibodies to the protein. Growth hormone increases binding capacities below 2 mg/L have not been associated with growth attenuation, in some cases when binding capacity exceeds 2 mg/L, growth attenuation has been observed. In clinical studies of patients that were treated with Nutropin (somatropin [GHD origin] injection) for the first time, 1/25 (4%) GH patients, 1/20 (5%) CRI patients, and 1/12 Turner syndrome patients screened for antibody production developed antibodies with binding capacities >2 mg/L, at six months. In a clinical study of patients that were treated with Nutropin ADP (somatropin [GHD origin] injection) for the first time, 6/38 (16%) GH patients screened for antibody production, for up to 15 months, developed antibodies with binding capacities >2 mg/L.

Additional short-term immunologic and renal function studies were carried out in a group of patients with CRI after approximately one year of treatment to detect other potential adverse effects of antibodies to growth hormone. Testing included measurements of Clq, C3, C4, rheumatoid factor, creatinine clearance, and BUN. No adverse effects of growth hormone antibodies were noted.

In addition to an evaluation of compliance with the prescribed treatment program and thyroid status, testing for antibodies to human growth hormone should be carried out in any patient who fails to respond to therapy. Injection site discomfort has been reported. This is more commonly observed in children switched from another GH product to Nutropin AG.

Lymphoma has been reported in a small number of GH-treated patients with CRI. It is uncertain whether this increased risk is related to the pathology of CRI itself, GH therapy, or other associated treatments such as radiation therapy for intracranial tumors. On the basis of current evidence, experts cannot conclude that GH therapy is responsible for these occurrences. The role in CRI, CRI, or Turner syndrome patients, if any, remains to be established.

Other adverse drug reactions that have been reported in GH-treated patients include the following: 1) Metabolic: Infrequent, mild, and transient peripheral edema. 2) Musculoskeletal: Arthralgias, rarer capsular tunnel syndrome. 3) Skin: Rare increased growth of pre-existing neo: some patients should be monitored carefully for malignant transformation. 4) Endocrine: Rare gynecomastia. Rare pancreatitis.
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The Standard of Care in Vitamin Replacement Therapy for Renal Patients

Write Nephro-Vite® Rx Do not substitute To assure your patients get the renal vitamin standard of care.

Rembursable in 43 States, by Medicaid, and by most private insurance plans.

Nephro-Vite® Rx

Indications: Nephro-Vite® Rx is a vitamin B complex and C supplement for vitamin deficiencies.

Precaution: Folic acid may partially correct the hematological damage due to vitamin B12 deficiency of pernicious anemia, while the associated neurological damage progresses.

Warning: Folic acid alone is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where Vitamin B12 is deficient. Keep out of reach of children.

Adverse Reaction: Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

Dosage: One tablet daily or as prescribed by physician. For patients on hemodialysis, Nephro-Vite®Rx should be taken after treatment on daily eight days.

How Supplied: Round, yellow tablet, film coated. NDC 5439-1000-01. Tablets in plastic bottles of 100. A child proof safety cap is standard on each 100 tablet bottle as a safeguard against accidental ingestion by children. Store at controlled room temperature 15-30°C (59-86°F). The most recent revision of this labeling is July, 1994.

Nephro-Vite® Pe

Warning: Accidental overdoses of iron-containing products is a leading cause of fatal poisoning in children under 6. Keep this product out of reach of children. In case of accidental overdose, call a doctor or poison control center immediately.

Indications: For any patient needing vitamin and iron supplementation for documented iron deficiency. Suitable for persons with end stage renal disease, certain patients undergoing therapy with arthrosis or iron deficiency anemia.

Precautions: Folic acid may partially correct the hematological damage due to vitamin B12 deficiency of pernicious anemia while the associated neurological damage progresses. Folic acid is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where vitamin B12 is deficient.

Adverse Reaction: Allergic sensitization has been reported following both oral and parenteral administration of folic acid. Iron sensitivity to low doses of iron has been reported and high doses result in iron toxicity, which is characterized by: transient bloating, flatulence, constipation, and diarrhea. Ingestion of greater than 400 mg per day of elemental iron can result in nausea and vomiting.

Dosage: One tablet daily between meals or as prescribed by the attending physician.

How Supplied: Film coated, oval tablets marked “N359” and “5439” on both sides. Tablets in blister package, sealed in foil. Ten tablets per card, 3 cards total. Store at controlled room temperature, 15-30°C (59-86°F). The most recent revision of this labeling is July, 1997.


Providing Leadership in the Nutritional and Pharmaceuetical Management of Kidney Disease

R&D Laboratories, Inc.
4840 Admiralty Way, Suite 710, Marina del Rey, CA 90292
(310) 358-4588 • (310) 358-4589 • FAX (310) 358-8135
E-Mail: rdalab@jiool.com • Internet: www.rdalab.com

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Patency... The STRETCH Advantage

The overall stretch graft survival at 2 and 3 years equals or exceeds the best results reported in the literature with regular PTFE grafts.¹

Cumulative survival of 420 GORE-TEX® STRETCH VASCULAR GRAFTS, 1991-1995²

<table>
<thead>
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<th>Measure</th>
<th>1 Year</th>
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<th>3 Years</th>
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<td>Secondary Patency</td>
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<tr>
<td>Primary Patency</td>
<td>76%</td>
<td>72%</td>
<td>71%</td>
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<tr>
<td>(Clot-free Survival)</td>
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W. L. Gore & Associates, Inc. • Flagstaff, Arizona 86004-3200 • 800-528-8783
*GORE-TEX is a registered trademark of W. L. Gore & Associates
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A972642-1/MMI
ANG91-1997
CellCept®
(mycophenolate mofetil)
250 mg capsules and 500 mg tablets

Reduces the incidence of treatment failure and organ rejection.
CellCept in combination with cyclosporine and corticosteroids reduced the incidence of treatment failure (statistically significant at the <0.05 level) over azathioprine (AZA) or placebo within the first 6 months post-transplant.*
CellCept substantially reduced the incidence of organ rejection within the first 6 months post-transplantation.

Implements combination drug protocols.
CellCept 1 g twice a day, with cyclosporine and corticosteroids, with or without antithymocyte globulin induction therapy.

Available in 250 mg capsules and 500 mg tablets.

*Data from three randomized, double-blind, multicenter trials of newly transplanted patients.

Roche Laboratories
A Member of the Roche Group
A safety profile proven in patients worldwide.

No incremental increase in nephrotoxicity, hepatotoxicity, hypertension or neurotoxicity was reported with CellCept when used with cyclosporine and corticosteroids.

The principal adverse events associated with CellCept administration include diarrhea, leukopenia, sepsis (generally CMV viremia), vomiting and a higher frequency of certain types of infections.

CellCept should not be used in pregnant women unless the potential benefit justifies the potential risk to the fetus. Women of childbearing potential should use effective contraception prior to, during and for 6 weeks after CellCept has been stopped. (See WARNINGS, PRECAUTIONS: Pregnancy and Information for Patients in brief summary of product information.)

WARNING: Increased susceptibility to infection and the possible development of lymphoma may result from immunosuppression. Only physicians experienced in immunosuppressive therapy and management of renal transplant patients should use CellCept®. Patients receiving the drug should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for maintenance therapy should have complete information requisite for the follow-up of the patient.

*Patients should be monitored for neutropenia. If neutropenia develops (ANC <1.5 x 10^9/L), dosing with CellCept should be interrupted or the dose reduced. See brief summary of product information.

Please see brief summary of product information on following pages.

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CellCept. Making every kidney count.
**CellCept**

**CellCept (mycophenolate mofetil capsules)**

**mycophenolate mofetil tablets**

**WARNING** — Increased susceptibility to infection and the possible development of lymphoma may result from immunosuppression. Only physicians experienced in immunosuppressive therapy, particularly in its management of renal allograft recipients, should administer CellCept. Patients receiving the drug should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources. The physician responsible for immunosuppressive therapy should be accessible for the follow-up of the treated patients.

**INDICATIONS AND USAGE:** CellCept is indicated for the prophylaxis of organ rejection in patients undergoing allogenic renal transplants. CellCept should be used concomitantly with corticosteroids and, in some circumstances, with other immunosuppressive agents.

**CONTRAINDICATIONS:** Allergic reactions to CellCept have been observed; therefore, CellCept is contraindicated in patients with a hypersensitivity to mycophenolate mofetil, mycophenolic acid or any component of the drug product.

**WARNINGS:** Patients may develop immunosuppressive regimens involving combinations of drugs, including CellCept, as part of an immunosuppressive regimen at risk of developing lymphomas and other malignancies, particularly of the skin. The risk of malignancies may increase with the duration and intensity of immunosuppression rather than to the use of any specific agent. Overexpression of the immune system can also induce neoplastic alterations in bone marrow. It has been observed in anti-neoplastic agents in clinical trials: anthracycline globulin (ATGAM®), OKT3 (Orthoclone OKT-3), cyclosporine (Sandimmune®), and corticosteroids. The efficacy and safety of the use of CellCept in combination with other immunosuppressive agents have not been determined.

Lymphoproliferative disease or lymphoma developed in patients receiving CellCept with other immunosuppressive agents in approximately 1% of patients in the controlled studies of prevention of rejection. (See Adverse Reactions.)

Effective contraception must be used before beginning CellCept therapy, during therapy, and for at least 6 months after the completion of therapy. The presence of lupus-like symptoms has been reported in CellCept patients; however, the relationship of these symptoms to CellCept administration is not well known. Lupus-like symptoms may include swelling, muscle weakness, and/or malaise. In rare cases, lupus-like symptoms may become severe, and in some patients, the symptoms have subsequently been diagnosed as systemic lupus erythematosus, unless due to heterotaxy. Two relapsing forms of contraception must be used simultaneously (e.g., oral contraceptives, one oral contraceptive plus barrier method, or barrier method plus injectable method). It is recommended that the physician and patient discuss the desirability of continuing the pregnancy. (See Precautions: Pregnancy and Information for Patients.)

**ADVERSE REACTIONS:** The adverse reactions are divided into those related to the integrase inhibitor activity and those related to the mycophenolic acid (MPA) activity. Some patients have developed neutropenia and anemia, with responses usually occurring at the beginning of treatment. Neutropenia was observed in patients when CellCept was administered before or concomitantly with corticosteroids, and it is recommended that the physician and patient discuss the desirability of continuing the pregnancy. (See Precautions: Pregnancy and Information for Patients.)

**DOSE AND ADMINISTRATION:** CellCept has been administered as a single dose of 1.5 g/m² twice daily for 14 days, followed by a maintenance dose of 1.5 g/m² twice daily. For patients with renal insufficiency, CellCept should be dosed as follows: dosage should be reduced to 1.0 g/m² twice daily in patients with a creatinine clearance of 50 ml/min or less; and to 0.5 g/m² twice daily in patients with a creatinine clearance of 25 ml/min or less. If renal function improves, the dosage may be increased to 1.5 g/m² twice daily. In patients with severe renal impairment, the dosage should be reduced to 1.0 g/m² twice daily. In patients with moderate renal impairment, the dosage should be reduced to 0.5 g/m² twice daily. In patients with mild renal impairment, the dosage should be reduced to 1.0 g/m² twice daily. In patients with normal renal function, the dosage should be reduced to 0.5 g/m² twice daily. In patients with normal renal function, the dosage should be reduced to 0.5 g/m² twice daily. In patients with normal renal function, the dosage should be reduced to 0.5 g/m² twice daily. In patients with normal renal function, the dosage should be reduced to 0.5 g/m² twice daily.

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### Adverse Events in Prevention of Renal Allograft Rejection

<table>
<thead>
<tr>
<th>CellCept</th>
<th>Azathioprine</th>
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<tbody>
<tr>
<td>2 g/day</td>
<td>3 g/day</td>
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<tr>
<td>(n=530)</td>
<td>(n=330)</td>
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</table>

#### Body as a Whole

- **Pan**: 33.0% (31.2%)
- **Abdominal pain**: 24.7% (27.6%)
- **Fever**: 21.4% (23.3%)
- **Headache**: 11.1% (16.1%)
- **Infection**: 16.2% (20.9%)
- **Sepsis**: 17.6% (19.7%)
- **Anemia**: 13.7% (16.1%)
- **Chest pain**: 13.4% (13.3%)
- **Back pain**: 11.6% (12.1%)

#### Hematologic and Lymphatic

- **Anemia**: 25.6% (25.8%)
- **Leukopenia**: 23.2% (24.5%)
- **Thrombocytopenia**: 10.1% (12.2%)
- **Hypochromic anemia**: 7.4% (11.5%)
- **Leukocytosis**: 7.1% (10.9%)

#### Urinary Tract Infection

- **Hematuria**: 14.0% (12.1%)
- **Kidney tubular necrosis**: 6.3% (10.0%)

#### Cardiovascular System

- **Hypertension**: 32.4% (28.2%)

#### Metabolic and Nutritional

- **Peripheral edema**: 28.6% (27.0%)
- **Hypercholesterolemia**: 12.8% (8.5%)
- **Hypophosphatemia**: 12.5% (15.8%)
- **Edema**: 12.5% (13.8%)
- **Hypokalemia**: 10.4% (10.0%)
- **Hyperkalemia**: 8.9% (10.3%)
- **Hyperglycemia**: 8.6% (12.4%)

#### Digestive System

- **Diarrhea**: 31.0% (36.1%)
- **Constipation**: 22.9% (18.5%)
- **Nausea**: 19.9% (23.5%)
- **Vomiting**: 17.6% (13.6%)
- **Liver function tests abnormal**: 15.5% (13.3%)
- **Pharyngitis**: 9.5% (11.2%)

#### Skin and Appendages

- **Acne**: 10.1% (9.7%)
- **Rash**: 7.7% (6.4%)

#### Nervous System

- **Tremor**: 11.0% (11.8%)
- **Insomnia**: 8.9% (11.8%)
- **Dizziness**: 5.7% (11.0%)

#### Europe Study

<table>
<thead>
<tr>
<th>CellCept</th>
<th>Azathioprine</th>
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<tr>
<td>2 g/day</td>
<td>3 g/day</td>
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<tr>
<td>(n=105)</td>
<td>(n=105)</td>
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</table>

#### Body as a Whole

- **Sepsis**: 21.8% (15.7%)
- **Infection**: 12.7% (15.6%)
- **Abdominal pain**: 12.1% (11.9%)

#### Hematologic and Lymphatic

- **Leukopenia**: 11.5% (16.3%)

#### Urinary Tract Infection

- **Urinary tract disorder**: 45.5% (44.4%)

#### Cardiovascular System

- **Hypertension**: 17.6% (15.9%)

#### Digestive System

- **Diarrhea**: 16.4% (18.8%)

#### Respiratory System

- **Infection**: 15.8% (13.1%)
- **Bronchitis**: 8.5% (11.9%)
- **Pneumonia**: 3.6% (10.6%)

---

The above table shows the incidence of adverse events in the CellCept treatment group compared to the placebo group. The data includes patients receiving 2 g of CellCept and 3 g of CellCept, respectively. The table also compares these incidences to those of Azathioprine (1-2 mg/kg/day or 100-150 mg/day). The table highlights the incidence of adverse events across different body systems, including hematologic, cardiovascular, digestive, and respiratory systems.

---

The above data demonstrate that in three controlled trials for prevention of rejection, patients receiving 2 g of CellCept had an overall better safety profile than did patients receiving 3 g of CellCept. Sepsis, which was generally GvHD-related, was slightly more common in patients treated with CellCept, with an incidence of 15-22%, compared to 16% in patients receiving azathioprine and 14% in patients receiving placebo. In the digestive system, diarrhea was the most clearly increased in patients receiving CellCept, with an incidence of up to 36%, compared to 21% for patients receiving azathioprine and 14% for patients receiving placebo. The incidence of malignancies among the 1,453 patients enrolled in controlled trials for the prevention of rejection who were followed for 21 years was similar to the incidence reported in the literature for renal allograft recipients. There was a slight increase in the incidence of lymphoproliferative disease in the CellCept treatment groups compared to the placebo group. (See WARNINGS.) The following table summarizes the incidence of malignancies observed in the prevention of rejection trials.
A Special Conference Sponsored by the:
American Society of Nephrology
National Institutes of Health
National Kidney Foundation
Renal Physicians Association

Strategies for Influencing Outcomes in Pre-ESRD and ESRD Patients

June 12–14, 1998 • Sheraton Washington Hotel • Washington, D.C.

What have we learned since the 1989 Dallas Conference and what should we do now to improve morbidity and mortality?

Key Questions

- What changes in practice have occurred over the past nine years?
- Have the changes had a measurable effect on patient outcomes – morbidity, mortality, hospitalization, cost, quality of life...?
- Can any conclusions be drawn as to why that trend has occurred?
- What questions remain and how will answers to these questions be expected to influence patient outcomes?
- Based on current knowledge, what should we do now to further improve patient outcomes?

Sessions

Global Trends in Outcome: 1989 to the Present Morbidity and Mortality in Patients on Dialysis
Trends in the Quantity of Dialysis, Solute Removal, Time and Membrane: Impact on Outcomes (HD and PD)
Trends, Interventions, and Outcomes in Nutrition
Trends in Cardiovascular Disease, Interventions, and Outcomes
Trends in Anemia Control, Practices, and Outcomes
Pre-ESRD Care, Risk Factors and Initiation of Renal Replacement Therapy
Quality Improvement

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Joel D. Kopple, M.D.
Robert G. Narins, M.D.

Allen R. Nissenson, M.D.

Registration Information

Charlene Murphy
“Strategies”
6010 Forrest Park
Dallas, Texas 75235

FAX: 214-358-0486
Telephone: 214-358-2300
E-mail: murphyc@dneph.com
# Application for Active and Corresponding Membership

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<th>Last Name</th>
<th>First Name</th>
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**Preferred Mailing Address**

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**Business Address (if not listed above)**

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**Business Telephone**

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**Business Fax**

**E-mail Address**

Date of Birth______________ Sex______________ Country of Citizenship________________________________

If you reside in the U.S., but are not a U.S. citizen, please provide visa status________________________________

*(Individuals residing in the U.S. with temporary visa status will apply for corresponding membership.)*

**Academic Appointment:**

- Full Time
- Part Time
- None

**Primary Professional Interest** *(e.g., Adult Nephrology, Pediatric Nephrology, Pathology, Urology, Physiology, etc.)*

**Primary Institutional Affiliation** *(e.g., Medical School-Faculty/Clinical Dept., Medical School-Faculty/Research Dept., Hospital-Staff/Clinical Staff, Private Practice, Armed Forces or Other Federal Services, etc.)*

**Present Hospital/University Appointments** *(titles and departmental affiliations)*

**Please indicate the amount of time spent on the following. Your total should amount to 100%.*

- Clinical
- Research
- Teaching
- Administration
- Other

**Professional Education and Training** *(To qualify for active and corresponding membership you must have an M.D., Ph.D. or equivalent, such as D.O., D.V.M., F.R.C.P., M.B.B.S., Pharm.D., etc.)*

**Institutional Name/Address**

**Degree**

**Dates**

**For office use only:**

- ID#: ____________________ Date entered: ____________________ Check#: ____________________ Check name: ____________________
Training in Nephrology  *(Give inclusive dates for residences, fellowships, other relevant postgraduate education.)*

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<th>Inclusive Dates</th>
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List your five most significant publications.

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<th>Publication 1</th>
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<th>Publication 4</th>
<th>Publication 5</th>
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Describe your clinical experiences as a specialist and consultant in kidney disease and related conditions that would provide basis for qualification of membership.

List other societies to which you belong.

Provide names and addresses of three persons from whom letters of reference may be requested if needed.

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<th>Name 1</th>
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Please return your completed application with the first year’s dues (see below) payable to the ASN in U.S. funds.

- **$125**—ACTIVE MEMBERSHIP for residents of North or Central America.
- **$140**—CORRESPONDING MEMBERSHIP for those who meet the qualifications for Active Membership, but are not residents of North or Central America. Corresponding Members will receive all Society mailings and member discounts, but do not have the right to vote or hold office.

If you would like to pay by Visa or MasterCard, please list the cardholder’s name, number and expiration date below:

- [ ] Visa
- [ ] MasterCard

---

CARDHOLDER’S NAME (PLEASE PRINT OR TYPE)  

SIGNATURE

---

CARD NUMBER  

EXPIRATION DATE