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.

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

**References**

**Once-Daily NORVASC (amlodipine besylate)**

**Efficacy and Safety THAT'S EASY TO LIVE WITH**

**Brief Summary**
NORVASC® (amlodipine besylate) Tablets

For Oral Use

**CONTRAINDICATIONS:** NORVASC is contraindicated in patients with known sensitivity to amlodipine.

**Warnings and Precautions: Increased Angina and/or Myocardial Ischemia: Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration, and/or severity of angina or myocardial ischemia on titration to a higher dose of NORVASC.

The mechanism of this effect has not been elucidated.

**Patients with Hyperkalemia:** Since the vasodilator effect of NORVASC is gradual in onset, acute hypotension has rarely been reported after oral administration of NORVASC. Nonetheless, caution should be exercised when administering NORVASC to patients with symptomatic hypotension or in patients with high risk of hypotension. Patients with hyperkalemia should be monitored closely by serial determination of the dose of the beta-blocker or calcium channel blocker.

**Patients with Hepatic Failure:** Since NORVASC is extensively metabolized by the liver and the plasma elimination half-life (t1/2) is 6 hours in patients with impaired hepatic function, caution should be exercised when administering NORVASC to patients with severe hepatic impairment.

**Drug Interactions:** In vitro data in human plasma indicate that NORVASC has no effect on the protein binding of drugs tested (barbituates, phenytoin, warfarin, and indomethacin) and that theophylline and warfarin clearance do not significantly change in patients treated with NORVASC. However, with digoxin does not change serum digoxin levels or digoxin renal clearance in normal volunteers, that co-administration with omeprazole did not alter the pharmacokinetics of NORVASC and that co-administration with warfarin did not change the warfarin prothrombin response time.

In clinical trials, NORVASC has been safety administered to all patients during clinical studies. No new or unexpected serious adverse events have been reported. The most common (incidence >20%) side effects are headache and edema.

**Rx**

NORVASC® 5 mg

Sig: 1 tablet daily

5 mg and 10 mg tablets

5 mg and 10 mg tablets

NORVASC® (amlodipine besylate) Tablets

5 mg and 10 mg tablets

Fif: 1 tablet daily

Pfizer

Labs • NHO • Pratt • Roerig

U.S. Pharmaceuticals Group

**Efficacy and Safety THAT'S EASY TO LIVE WITH**

**References**
An injectable iron therapy
in a class of its own

Coming soon from
Schein Pharmaceutical
PhosLo® is indicated for control of hyperphosphatemia in end-stage renal disease. Patients with higher-than-normal serum calcium levels should be closely monitored and their dose adjusted or terminated to bring levels to normal.


Description: PhosLo® (Calcium Acetate) is a phosphate binder that reduces the absorption of dietary phosphate. Each white round tablet contains 667 mg of calcium acetate (anhydrous) equal to 169 mg calcium, and 10 mg of the inert binder, polyethylene glycol 8000.

Contraindications: Patients with hypercalcemia.

Indications and Usage: PhosLo® is indicated for the control of hyperphosphatemia in end-stage renal disease (ESRD) and does not promote aluminum absorption.

Warnings: Patients with ESRD may develop hypercalcemia when given calcium with meals. No other calcium supplements should be given concurrently with PhosLo®. Serum calcium levels should be monitored when PhosLo® therapy is started and periodically thereafter. Safety in the elderly: No increased incidence of adverse reactions has been noted in patients over 65 years of age.

Precautions: Serum calcium and phosphate levels should be closely monitored. PhosLo® should be taken with meals to insure the mixing of calcium with dietary phosphate.

Adverse Reactions: On occasion, patients have developed nausea while taking PhosLo®, but the relationship of the adverse reaction to the drug is unclear as nausea often occurs in patients with end-stage renal disease. Mild hypercalcemia may occur in some patients, but it is easily controlled by reduction in dose or by temporarily discontinuing therapy.

Drug Interactions: The potential for hypercalcemia is increased if the patient takes other calcium supplements or calcitriol.

Manufactured for:
Braintree Laboratories, Inc.
P.O. Box 850929, Braintree, MA
02185-0929

Binds twice as much phosphate as equivalent amounts of calcium carbonate.1,2

• Reimbursable under Medicaid and other state and private insurance programs.

• Tablets are swallowed, not chewed.

• No threat of aluminum toxicity1,3,4

PhosLo® (Calcium Acetate Tablets)
667 mg Tablets
Medicaid-approved.
Dialysis keeps her going.
Today, a growing consensus supports managing ESRD patients in the upper half of the 30–36% hematocrit range.

- New NKF-DOQI guidelines recommend hematocrits of 33–36%.¹

- Two new studies suggest an association between hematocrits of 33–36% and reduced hospitalization.²³ Reduced hospitalization may reduce the cost of care.

The future? Hematocrits higher in the target range mean more dialysis patients can be feeling better. Doing better. And going stronger.

Let's keep it up.

Recommended Hematocrit Ranges

**EPOGEN®**

**(EpOetin ALFA)**

**Higher Hematocrits Lead to Better Outcomes.**

*The EPOGEN® package insert recommends a target hematocrit range of 30% to 36%.

EPOGEN® is indicated for the treatment of anemia in dialysis patients with chronic renal failure. Patients who receive EPOGEN® may experience adverse effects such as hypertension or flu-like symptoms.

Please see brief summary of prescribing information on following page.

**BRIEF SUMMARY OF PRESCRIBING INFORMATION**

**INDICATIONS AND USAGE** — EPOGEN® is contraindicated in patients with: 1) uncomplicated hypertension; 2) known hypersensitivity to mammalian cell-derived products; or 3) known hypersensitivity to the ingredients of EPOGEN®. (See WARNINGS — Pediatric Use.

**CONTRAINDICATIONS** — EPOGEN® is contraindicated in patients with: 1) uncomplicated hypertension; 2) known hypersensitivity to mammalian cell-derived products; or 3) known hypersensitivity to the ingredients of EPOGEN®. (See WARNINGS — Pediatric Use.

**WARNINGS** — Pediatric Use: The multidose preserved formulation contains benzyl alcohol. Benzyl alcohol has been reported to cause gas production and death in premature and newborn infants. Therefore, the safety and effectiveness of EPOGEN® in pediatric patients have not been established.

Thrombotic Thrombolytic Activity: A randomized, prospective trial of 1356 hemodialysis patients with clinically evident cardiac disease ischemic heart disease or congestive heart failure were treated with EPOGEN® with a target HCT of either 42 ± 3% or 30 ± 3%. Increased mortality was observed in 634 patients randomized to the higher HCT target compared to 722 patients randomized to a target HCT of 30% (185 deaths vs 292 mortality). The reason for the increased mortality observed in the original trial was not always clear in the either of these interventions: vascular access thrombosis (39% vs 29%) or all other thrombotic events (22% vs 18%) were also lower in the patients randomized to achieve a target HCT of 42 ± 3%.

Hypertension: Patients with uncomplicated hypertension should not be treated with EPOGEN® before initiation of therapy. Up to 80% of patients with CRI have a history of hypertension. Although there does not appear to be any direct presevence of EPOGEN® BP may rise during EPOGEN® therapy. During the early phase of treatment, transient hypertension may occur in up to 30% of patients. Thereafter, the incidence of hypertension was reduced to less than 20% in most patients. In the hypertensive patients, the mean increase in blood pressure was approximately 25% of patients as compared with baseline.

**DISCLAIMER**

There is no evidence that use of EPOGEN® in the treatment of anemia associated with chronic renal failure (CRF), including patients on dialysis (end stage renal disease) and patients not on dialysis (all causes), maintains or returns the red blood cell level (as measured by the hematocrit (HCT) or hemoglobin determination) and to decrease the need for transfusions in these patients.

**Hypertension** — In the EPOGEN® trials, approximately 25% of patients experienced increases in blood pressure (BP). The BP was controlled adequately before initiation of therapy. Up to 80% of patients with CRF have a history of hypertension. Although there does not appear to be any direct presevence of EPOGEN® BP may rise during EPOGEN® therapy. During the early phase of treatment, transient hypertension may occur in up to 30% of patients. Thereafter, the incidence of hypertension was reduced to less than 20% in most patients. In the hypertensive patients, the mean increase in blood pressure was approximately 25% of patients as compared with baseline.

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INSTRUCTIONS TO AUTHORS

Send manuscripts to the Editor:

C. Craig Tisher, M.D.
J. Am. Soc. Nephrol.
Division of Nephrology
Box 100224
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University of Florida
Gainesville, Florida 32610

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5. Designate a corresponding author and provide a telephone number, fax number and address.

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Carnitine deficiency may be more serious than you think for your patients.

Carnitine plays a vital role in energy production. Typically, 75% of a patient's carnitine needs are met through dietary intake. And healthy patients depend on proper liver and kidney function to maintain adequate carnitine status. Carnitine functions by binding with fatty acids so they can be transported into the mitochondria for energy production and also binds with metabolic waste products so they can be transported out of the body.

Carnitine deficiency is hard to detect and is often overlooked. Patients who exhibit findings consistent with carnitine deficiency should be evaluated for treatment with Carnitor®.

Clinical findings associated with carnitine deficiency may be as subtle as any of the following:
- cardiomyopathy
- muscle weakness
- lethargy
- poor muscle tone
- seizures
- low levels of activity
- developmental delay
- slow growth

Carnitor® is the only treatment for carnitine deficiency.

For Carnitor® Medicare reimburse assistance, call 1-800-490-3262.

For any other questions, call 1-800-447-0169.

Transient nausea and vomiting have been observed. Please see prescribing information.

800 S. Frederick Avenue · Suite 300 · Gaithersburg, MD 20877
FAX: (301) 948-3194 · EMAIL: info@sigmatau.com · WEB: www.sigmatau.it/na
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Clinical Findings Associated with Carnitine Deficiency:

- cardiomyopathy
- muscle weakness
- lethargy
- poor muscle tone
- seizures
- low levels of activity
- developmental delay
- slow growth

Conditions Associated with Increased Risk for Developing Carnitine Deficiency:

- fatty acid oxidation defects
- mitochondrial myopathy
- dialysis
- premature birth
- administration of carnitine-free TPN
- treatment for HIV—especially administration of zidovudine (AZT)
- administration of valproic acid
- administration of pivalate derivatives
- administration of emetine
- administration of sodium benzoate

CARNITOR® (Levocarnitine)
Brief Summary of Prescribing Information
(Please see package insert for full prescribing information)

Indications and usage
CARNITOR® (Levocarnitine) Tablets and Oral Solution are indicated in the treatment of primary systemic carnitine deficiency. In the reported cases, the clinical presentation consisted of recurrent episodes of Reye-like encephalopathy, hypoketotic hypoglycemia, and/or cardiomyopathy. Associated symptoms included hypotonia, muscle weakness and failure to thrive. A diagnosis of primary carnitine deficiency requires that serum, red cell and/or tissue carnitine levels be low and that the patient does not have a primary defect in fatty acid or organic acid oxidation (see Clinical Pharmacology). In some patients, particularly those presenting with cardiomyopathy, carnitine supplementation rapidly alleviates signs and symptoms. Treatment should include, in addition to carnitine, supportive and other therapy as indicated by the condition of the patient. CARNITOR® (Levocarnitine) Tablets and Oral Solution are also indicated for acute and chronic treatment of patients with an inborn error of metabolism that results in a secondary carnitine deficiency.

CARNITOR® (Levocarnitine) Injection is indicated for the acute and chronic treatment of patients with an inborn error of metabolism that results in secondary carnitine deficiency.

Contraindications
None known.

Warnings
None.

Precautions
General
CARNITOR® (Levocarnitine) Oral Solution is for oral/internal use only.

Not for parenteral use.

Gastrointestinal reactions may result from too rapid consumption of oral levocarnitine. CARNITOR® (Levocarnitine) Oral Solution may be consumed alone or dissolved in drinks or other liquid foods to reduce taste fatigue. It should be consumed slowly and doses should be spaced evenly throughout the day to maximize tolerance.

CARNITOR® (Levocarnitine) Injection is for intravenous use only.

Carcinogenesis, mutagenesis, impairment of fertility
Mutagenicity tests performed in Salmonella typhimurium, Saccharomyces cerevisiae, and Schizosaccharomyces pombe indicate that CARNITOR® (Levocarnitine) is not mutagenic. Long-term animal studies have not been conducted to evaluate the carcinogenic potential of levocarnitine.

Pregnancy
Pregnancy Category B.

Reproductive studies have been performed in rats and rabbits at doses up to 3.8 times the human dose on the basis of surface area and have revealed no evidence of impaired fertility or harm to the fetus due to CARNITOR®. There are, however, no adequate and well controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing mothers
It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, 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.

Pediatric use
See Dosage and Administration.

Adverse reactions
Various mild gastrointestinal complaints have been reported during the long-term administration of L- or D,L-carnitine; these include transient nausea and vomiting, abdominal cramps, and diarrhea. Less frequent adverse reactions are body odor, nausea, and gastritis. An incidence for these reactions is difficult to estimate due to the confounding effects of the underlying pathology. Mild myasthenia has been described only in neonatal patients receiving D,L-carnitine.

Decreasing the dosage often diminishes or eliminates drug-related patient body odor or gastrointestinal symptoms when present. Tolerance should be monitored very closely during the first week of administration, and after any dosage increases. Gastrointestinal adverse reactions with CARNITOR® (Levocarnitine) Oral Solution dissolved in liquids might be avoided by a slow consumption of the solution or by a greater dilution.

Caution
Federal (U.S.A.) law prohibits dispensing without prescription.

References
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 strength of liquid iron in a soft gelcap
DESCRIPTION

Each brown soft gelatin capsule contains: ferrous fumarate USP, 460 mg (151 mg elemental iron), ascorbic acid USP, 60 mg, folic acid USP, 1 mg, cyanocobalamin USP, 10 mg.

DISCUSSION: The amount of elemental iron and the absorption of the iron components of commercial iron preparations vary 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 hematocinetic.

ACtIONS

HIGH ELEMENTAL IRON CONTENT: Ferrous fumarate, used in Chromagen Forte Capsules, is an organic iron complex which has the highest elemental iron content of any hematonic salt - 33%. This compares with 25% for ferrous sulfate (hephatehydrate) and 13% for ferrous gluconate. Chromagen Forte contains 151 mg of elemental iron.

MORE COMPLETE ABSORPTION: It has been repeatedly shown that ascorbic acid, when given in sufficient amounts, can increase the absorption of ferrous iron from the gastrointestinal tract. The absorption-promoting effect is mainly due to the reducing action of ascorbic acid within the gastrointestinal lumen, which helps to prevent or delay the formation of insoluble, less dissociated ferro compounds.

PROMOTES MOVEMENT OF PLASMA IRON: Ascorbic acid also plays an important role in the movement of plasma iron to storage depots in the tissues. The action, which leads to the transport of plasma iron to ferritin, presumably involves its reducing effect, converting transferrin iron from the ferric to the ferrous state. There is also evidence that ascorbic acid improves iron utilization, presumably as a further result of its reducing action, and some evidence that it may have a direct effect upon erythropoiesis. Ascorbic acid is further alleged to enhance the conversion of folic acid to a more physiologically active form, folic acid, which would make it even more important in the treatment of anemia since it would aid in the utilization of dietary folic acid.

EXCELLENT ORAL TOLERATION: Ferrous fumarate is used in Chromagen Forte Capsules because it is less likely to cause the gastrointestinal disturbances so often associated with oral iron therapy. Ferrous fumarate has a low ionization constant and high solubility in the entire pH range of the gastrointestinal tract. It does not precipitate proteins or have the astringency of more ionizable forms of iron, and does not interfere with proteolytic or diastatic activities of the digestive system. Because of excellent oral tolerance, Chromagen Forte Capsules can be usually administered between meals when iron absorption is maximal.

FOLIC ACID SUPPLEMENTATION: The use of supplemental folic acid may be indicated in patients with increased requirements for this vitamin, such as iron deficiency anemia. Folic acid administration may reduce the risk of neural tube defects in the developing fetus. Folic acid has also been shown to reduce circulating homocysteine levels in the blood. Folate as 5-methyltetrahydrofolate and B12 as methylcobalamin are involved in the remethylation reaction of homocysteine to methionine.

Elevated homocysteine plasma levels are associated with increased risk of preclampsia, neural tube defects, myocardial infarction and arteriosclerosis. 

TOXICITY: Ferrous fumarate was found to be the least toxic of three popular oral iron salts, with an oral LD50 of 630 mg/kg. In the same report, the LD50 of ferrous gluconate was reported to be 320 mg/kg and ferrous sulfate 230 mg/kg.

INDICATIONS

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.

CONTRAINICATIONS

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

WARNING

Accidental overdose 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.

PRECAUTIONS

Folic acid should not be prescribed until 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


In combination therapy

**Roche brings the first humanized monoclonal antibody to renal transplantation.**
**Introducing precision**

**New ZENAPAX® (Daclizumab),**
the first humanized IL-2R-specific monoclonal antibody,
prevents acute renal allograft rejection as part of an immunosuppressive regimen.

- Binds with high affinity to the Tac subunit which is expressed on activated but not resting lymphocytes.
- A unique, bioengineered monoclonal antibody therapy, 90% human IgG sequences and 10% murine sequences, that mirrors human IgG.
- Inhibits IL-2-mediated activation and proliferation of T cells, a critical pathway in the cellular immune response involved in allograft rejection.

**WARNING:** Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should prescribe ZENAPAX® (Daclizumab). The physician responsible for ZENAPAX administration should have complete information requisite for the follow-up of the patient. Patients receiving the drug should be managed in facilities equipped and staffed with adequate laboratory and supportive medical resources.

Patients on immunosuppressive therapy are at increased risk for developing lymphoproliferative disorders and opportunistic infections and should be monitored accordingly. ZENAPAX is contraindicated in patients with known hypersensitivity to Daclizumab or to any components of this product. Anaphylactoid reactions have not been observed following ZENAPAX administration, but can occur following the administration of proteins. Please see brief summary of product information for ZENAPAX and for CellCept® (mycophenolate mofetil), which include contraindications, warnings, precautions and adverse events, on back pages of this advertisement.

*Data from two randomized, double-blind, multicenter trials that compared a dose of 1.0 mg/kg of ZENAPAX with placebo when each was administered as part of an immunosuppressive regimen with triple therapy (cyclosporine + corticosteroids + AZA) or double therapy (cyclosporine + corticosteroids).
New ZENAPAX
increases efficacy
without an
increase in serious
side effects.

- Significantly reduces acute renal allograft rejection episodes when added to triple and double immunosuppressive protocols.*
- Associated with significantly better patient survival at 1 year in the double-therapy regimen. No significant difference in patient survival when added to a triple-therapy regimen.
- A retrospective analysis of the combined endpoint of patient survival, graft survival and acute rejection in triple- and double-therapy regimens at 1 year suggests a better outcome for patients receiving ZENAPAX as part of their immunosuppressive regimen.
- No increases in lymphomas or overall incidence of infectious episodes were observed.
- The most frequently reported adverse events were GI disorders (e.g., constipation, nausea, diarrhea, vomiting), which were reported with equal frequency in the ZENAPAX group (67% [226/336]) and placebo group (68% [199/293]). The overall incidence of infectious episodes was not higher in patients treated with ZENAPAX compared with patients receiving placebo. However, cellulitis and wound infections occurred in 8.4% (24/286) of patients treated with ZENAPAX and 4.1% (11/268) receiving placebo.
- Well tolerated with CellCept® (mycophenolate mofetil), cyclosporine and corticosteroids.

New ZENAPAX®
Daclizumab
Immunosuppression with a human touch.
ZENAPAX® (Daclizumab)

Geriatric Use: Clinical studies of ZENAPAX did not include sufficient numbers of subjects age 65 and older to determine whether they respond differently from younger subjects. Caution must be used in giving immunosuppressive drugs to elderly patients.

ADVERSE REACTIONS: The safety of ZENAPAX was determined in four clinical studies, three of which were randomized controlled clinical trials, in 629 patients receiving renal allografts of whom 336 received ZENAPAX and 283 received placebo. All patients received concomitant cyclosporine and corticosteroids.

ZENAPAX did not appear to alter the pattern, frequency or severity of known major toxicities associated with the use of immunosuppressive drugs.

Adverse events were reported by 95% of the patients in the placebo-treated group and 98% of those in the ZENAPAX-treated group. The proportion of patients prematurely withdrawn from the combined studies because of adverse events was 8.5% in the placebo-treated group and 6.6% in the ZENAPAX-treated group.

ZENAPAX did not increase the number of serious adverse events observed compared with placebo. The most frequently reported adverse events were gastrointestinal disorders, which were reported with equal frequency in ZENAPAX- and placebo-treated (67%) patient groups.

The incidence and types of adverse events were similar in both placebo-treated and ZENAPAX-treated patients. The following adverse events occurred in 5% of ZENAPAX-treated patients. These events included: Gastrointestinal System: constipation, nausea, diarrhea, vomiting, abdominal pain, pyrosis, dyspepsia, abdominal distention, epigastric pain not food-related; Metabolic and Nutritional: edema, extremities, edema; Central and Peripheral Nervous System: tremor, headache, dizziness; Urinary System: oliguria, dysuria, renal tubular necrosis; Body as a Whole — General: post-traumatic pain, chest pain, fever, pain, fatigue; Autonomic Nervous System: hypertension, hypotension, aggravated hypertension; Respiratory System: dysnea, pulmonary edema, coughing; Skin and Appendages: impaired wound healing without infection, acne; Psychiatric: insomnia; Musculoskeletal System: musculoskeletal pain, back pain; Heart Rate and Rhythm: tachycardia; Vascular Extracardiac: thrombosis; Platelet, Bleeding and Clotting Disorders: bleeding; Hemic and Lymphatic: lymphoedema.

The following adverse events occurred in <5% and 2% of ZENAPAX-treated patients. These events included: Gastrointestinal System: nausea, vomiting; Metabolic and Nutritional: fluid overload, diabetes mellitus, dehydration; Urinary System: renal damage, hypoglycemia, urinary tract bleeding, urinary tract disorder, renal insufficiency; Body as a Whole — General: shivering, generalized weakness; Central and Peripheral Nervous System: urinary retention, leg cramps, pricky sensation; Respiratory System: atelectasis, congestion, pharyngitis, rhinitis, hoarseness, abnormal breath sounds, pleural effusion; Skin and Appendages: pruritus, hirsutism, rash, night sweats, increased sweating; Psychiatric: depression, anxiety; Musculoskeletal System: arthralgia, myalgia; Vision: vitreous hemorrhage; Application Site: pain.

Incidence of Malignancies: One year after treatment, the incidence of malignancies was 2.7% in the placebo group compared with 1.5% in the ZENAPAX group. Addition of ZENAPAX did not increase the number of post-transplant lymphomas, which occurred with a frequency of <1% in both placebo-treated and ZENAPAX-treated groups.

Hyperglycemia: No differences in abnormal hematologic or chemical laboratory test results were seen between placebo-treated and ZENAPAX-treated patients with the exception of fasting blood glucose. Fasting blood glucose was measured in a small number of placebo- and ZENAPAX-treated patients. A total of 16% (10 of 64) patients of placebo-treated and 22% (28 of 128) patients of ZENAPAX-treated patients had fasting blood glucose values. Most of these high values occurred either on the first day post-transplant when patients received high doses of corticosteroids or in patients with diabetes.

Infections: Of Infectious Episodes The overall incidence of infections, which included viral infections, fungal infections, bacteremia and septicaemia, and pneumonia, was not higher in ZENAPAX-treated patients than in placebo-treated patients. The types of infections reported were similar in both the ZENAPAX-treated and the placebo-treated groups.

Cytomegalovirus infection was reported in 16% of the patients in the placebo group and 15% of the patients in the ZENAPAX group. One exception was cellulitis and wound infections, which occurred in 4.1% of placebo-treated and 5.4% of ZENAPAX-treated patients. At 1 year post-transplant, 7 placebo patients and only 1 ZENAPAX-treated patient had died of an infection.

Thrombosis: There have not been any reports of overdoses with ZENAPAX. A maximum tolerated dose has not been determined in patients. A dose of 1.5 mg/kg has been administered to bone marrow transplant recipients without any associated adverse events.

CAUTION: Federal (USA) law prohibits dispensing without a prescription.

Pharmaceuticals

Roche Laboratories Inc.
340 Kingland Street
Nutley New Jersey 07110-1199

Issued: December 1997

Lot 000008072
17-000-072-002-028
Printed in U.S.A.
**WARNING** — Increased susceptibility to infection and the possible development of lymphoproliferative disorders. Patients who have been experiencing immunosuppressive therapy and management of renal transplant patients should use CellCept. Patients have been observed to have an increased risk of developing grade 2 or greater CMV viremia, as well as pneumonia, bacteremia, and cerebral toxoplasmosis. CellCept therapy should be started at the time of renal transplantation when there is an increased risk of CMV reactivation, and then maintained post-transplantation in order to reduce the risk of CMV infection in the recipient.

**INDICATIONS AND USAGE:** CellCept is indicated for the prophylaxis of organ rejection in patients undergoing renal, hepatic, or cardiac transplants. CellCept should be used concomitantly with cyclosporine and corticosteroids.

**CONTRAINDICATIONS:** Allergic reactions to CellCept have been observed; therefore, CellCept is contraindicated in patients with a hypersensitivity to mycophenolate mofetil, mycophenolic acid, or other ingredients in the formulation. CellCept is not for intravenous use and must be administered orally.

**WARNINGS:** (See boxed WARNING.) Patients receiving immunosuppressive regimens involving combinations of drugs, including CellCept, as part of an immunosuppressive regimen are at increased risk for developing lymphoproliferative disorders. The risk appears to be related to the intensity and duration of immunosuppression rather than to any single drug or drug combination. Overimmunosuppression in transplantation can cause not only rejection but also the development of malignancies. Women of childbearing potential should have a negative serum or urine pregnancy test with a sensitivity of at least 50 mIU/mL within 1 week prior to beginning therapy. It is recommended that women of childbearing potential use an effective contraceptive to prevent pregnancy during therapy, and that the physician discuss the desirability of continuing the pregnancy.

**ADVERSE REACTIONS:** In the controlled studies for prevention of rejection, rates of serious infections were generally similar in patients treated with Mycophenolate Mofetil and patients treated with CellCept. Treatment with immunosuppressive agents can cause or exacerbate infections in transplant patients who have been recently exposed to the risk of infection. The use of immunosuppressive agents may increase the risk of certain infections. Some patients may experience a reactivation of a previously inactive latent infection. Such reactivations may be due to changes in the immune system caused by the use of immunosuppressive agents. The possibility of other infections cannot be ruled out. When infections do occur, they may be more severe and may be potentially fatal. The severity and type of infections may be different from those occurring in the general population and may be more difficult to treat. The severity and type of infections may be different from those occurring in the general population and may be more difficult to treat. It is recommended that patients have a complete medical history and physical examination at the time of initiation and during therapy with immunosuppressive agents.

**PREGNANCY:** CellCept is not recommended for use in pregnant women. CellCept is embryotoxic and teratogenic in animals and has the potential to cause harm in the human fetus. A similar risk may also be present in the offspring of patients taking CellCept. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, birth defects may occur. CellCept is not recommended for use in women who are or plan to become pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, birth defects may occur. CellCept is not recommended for use in women who are or plan to become pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, birth defects may occur. CellCept is not recommended for use in women who are or plan to become pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, birth defects may occur. CellCept is not recommended for use in women who are or plan to become pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, birth defects may occur. CellCept is not recommended for use in women who are or plan to become pregnant. If this drug is used during pregnancy or if the patient becomes pregnant while taking this drug, birth defects may occur.

**NURSING MOTHERS:** It is not known whether CellCept is excreted in human milk. However, because of the potential for serious adverse reactions in nursing infants from mycophenolate mofetil, a decision should be made to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

**Pediatric Patients:** Safety and effectiveness in pediatric patients have not been established. The pediatric pharmacokinetic data are not available.

**ADVERSE REACTIONS:** The principal adverse reactions associated with the administration of CellCept include dyspepsia, diarrhea, vomiting, nausea, and epigastric pain, and there is evidence of a higher frequency of certain types of infections. The incidence of adverse events for CellCept was determined in three randomized controlled trials involving 266 patients, all of whom had both prophylactic and therapeutic indications for immunosuppressive therapy. The lower overall reporting of events in the European placebo-controlled trials of prevention of rejection is not due to the other active treatment, since these trials were not compared with the other two active-controlled prevention trials, but are instead presented separately. Safety data are summarized below for all patients in the double-blind prevention studies while using CellCept, for patients enrolled in the maintenance study, and for patients in the open-label prevention study. Adverse events that were reported in 210% of patients in either CellCept treatment group are presented below for the two active-controlled studies combined (USA and Europe) and for the one European placebo-controlled study. Opportunistic infections are summarized separately.
<table>
<thead>
<tr>
<th>Adverse Events in Prevention of Renal Allograft Rejection</th>
<th>Malignancies Observed in Prevention of Renal Rejection Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>USA Study Combined with Europe/Canada/Australia Study</strong></td>
<td><strong>USA Study Combined with Europe/Canada/Australia Study</strong></td>
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<tr>
<td><strong>CellCept</strong> (mycophenolate mofetil capsules)</td>
<td><strong>CellCept</strong> (mycophenolate mofetil capsules)</td>
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<tr>
<td><strong>Azathioprine</strong></td>
<td><strong>Azathioprine</strong></td>
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<td><strong>100-150 mg/day</strong></td>
<td><strong>100-150 mg/day</strong></td>
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<td><strong>(n=330)</strong></td>
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<td><strong>Body as a Whole</strong></td>
<td><strong>Body as a Whole</strong></td>
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<tr>
<td>Pain</td>
<td>Lympoma/lymphoproliferative disease</td>
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<tr>
<td>33.0%</td>
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<tr>
<td>Abdominal pain</td>
<td>Non-melanoma skin cancer</td>
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<tr>
<td>24.7</td>
<td>4.0</td>
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<tr>
<td>Fever</td>
<td>Other malignancy</td>
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<td>21.4</td>
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<td>Headache</td>
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<td>21.1</td>
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<td>Infection</td>
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<td>19.2</td>
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<td>Sepsis</td>
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<td>17.6</td>
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<tr>
<td>Asthenia</td>
<td>Leukopenia</td>
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<td>13.7</td>
<td>2.8</td>
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<td>Cough</td>
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<td>13.4</td>
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<td>Black</td>
<td>Peptic ulceration</td>
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<td>11.6</td>
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<td>Hematologic and Lymphatic</td>
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<td>Anemia</td>
<td>Leukocytosis</td>
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<td>25.6</td>
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<td>Leukopenia</td>
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<td>23.2</td>
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<td>Neutropenia</td>
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<td>Urogenital</td>
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<td>Urinary tract infection</td>
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<td>37.2</td>
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<td>Hematuria</td>
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<td>Kidney tubular necrosis</td>
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<td>Metabolic and Nutritional</td>
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<td>Pancreatic edema</td>
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<td>28.8</td>
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<tr>
<td>Hypercholesterolemia</td>
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<td>Hyperglycemia</td>
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<td>12.5</td>
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<td>Asthenia</td>
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<td>Skin and Appendages</td>
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<td><strong>CellCept</strong> (mycophenolate mofetil capsules)</td>
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<td><strong>Placebo</strong></td>
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<td><strong>(n=160)</strong></td>
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<td><strong>Body as a Whole</strong></td>
<td><strong>Body as a Whole</strong></td>
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<tr>
<td>Pain</td>
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<td>21.5%</td>
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<td>Abdominal pain</td>
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<td>45.5</td>
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<td>Urinary tract disorder</td>
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<td>16.4</td>
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<td>The above data demonstrate that in three controlled trials for prevention of rejection, patients receiving 2 g per day of CellCept had an overall better safety profile than did patients receiving 3 g per day of CellCept. Sepsis, which was generally CMV viremia, was slightly more common in patients treated with CellCept, with an incidence of 16-22%, compared to 10% in patients receiving azathioprine and in patients receiving placebo. In the digestive system, diarrhea was most clearly increased in patients receiving CellCept, with an incidence of up to 36%, compared to 21% for patients receiving azathioprine. The incidence of malignancies among the 1,483 patients enrolled in controlled trials for the prevention of rejection 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 and azathioprine groups. (See WARNINGS.) The following table summarizes the incidence of malignancies observed in the prevention of rejection trials.</td>
<td>The following table shows the incidence of opportunistic infections that occurred in the transplant population in the prevention of rejection trials:</td>
</tr>
</tbody>
</table>
A few years ago, nephrologists were confronted with a major void in managing dialysis patients with iron-deficiency anemia: the lack of an injectable iron product—an important component in optimizing erythropoiesis.1 Schein Pharmaceutical fulfilled this critical need with an injectable iron therapy for documented iron-deficiency anemia not amenable to oral therapy: INFeD® (Iron Dextran Injection, USP), which has a documented safety profile.2

Recognizing that appropriate use of drug therapies can help optimize patient outcomes, we actively support educational activities and clinical programs for the nephrology community. Today, Schein Pharmaceutical is gratified that the medical community recognizes the crucial role of iron in anemia management and supports its use in the NKF-DOQI™ guidelines. Looking toward the future, we promise to continue our commitment to the nephrology community by researching and bringing to market new products for iron-deficiency anemia. By working together, we can enhance the quality of care for dialysis patients.

For more information call the iron experts at 1-888-EXP-IRON or contact our web site: www.infed.com

Iron products for today...Research for tomorrow
Schein Pharmaceutical, Inc., 100 Campus Drive, Florham Park, NJ 07932

Please see adjacent full prescribing information including the boxed WARNING.

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

Schein Pharmaceutical, Inc.
100 Campus Drive, Florham Park, NJ 07932

Please see references and prescribing information including the boxed WARNING on following page.
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INFeD® and EPO for target HCT range of 30% to 36%

- Treatment is currently targeted to a hematocrit range of 30% to 36%\(^5\)

INFeD® for effective erythropoiesis

- Erythropoiesis can rapidly mobilize iron reserves and deplete even ample iron stores\(^1\)

INFeD® for rapid iron repletion

- IV iron should be considered for all patients with low iron stores requiring a rapid EPO response\(^4\)
- 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…”\(^7\)

INFeD® evaluated for safety in hemodialysis patients

- After reviewing the charts of 573 patients treated with INFeD® from four hemodialysis centers, Fischbene et al concluded: “We found serious adverse reactions with IVFe in hemodialysis patients to be uncommon.”\(^8\)

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
PRECAUTIONS: General. Unwarmed therapy with parenteral iron will cause excessive storage of iron with the consequent possibility of toxic reactions. Hepatic iron overload may occur, particularly in patients who have been previously transfused or who have gastrointestinal blood loss. The patients taking iron should be monitored for the development of elevations in serum transaminase levels. Iron overload may cause biliary cirrhosis.

Anaphylactic reactions may occur in patients who have been treated with iron. These reactions are characterized by dizziness, weakness, dyspnea, hypotension, cardiovascular collapse, and even sudden death. Iron overload may cause biliary cirrhosis.

Hematology. The hematological effects of iron therapy include anemia, anemia, and anemia. Hemoglobin levels are elevated in patients who have been treated with iron. Iron overload may cause biliary cirrhosis.

Drug Interactions: Iron may interfere with the absorption of several drugs. Iron may interfere with the absorption of several drugs. Iron overload may cause biliary cirrhosis.

ADVERSE REACTIONS: The major adverse reactions to parenteral iron therapy are allergic reactions, anaphylactic reactions, and iron overload. The patients taking iron should be monitored for the development of elevations in serum transaminase levels. Iron overload may cause biliary cirrhosis.

Overdose: Iron overload is the most common adverse reaction to iron therapy. The patients taking iron should be monitored for the development of elevations in serum transaminase levels. Iron overload may cause biliary cirrhosis.

Iron overload is the most common adverse reaction to iron therapy. The patients taking iron should be monitored for the development of elevations in serum transaminase levels. Iron overload may cause biliary cirrhosis.
In renal failure patients, renal specific vitamin replacement is essential. The Nephro-Vite® family of renal vitamins is formulated to meet the special micronutrient replacement needs of renal failure patients.

Nephro-Vite® provides complete B and C vitamin replacement therapy, with increased amounts of folic acid and B6. It also includes B1, B2, B12, biotin, pantothenic acid and niacin.
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A high priority at Williams & Wilkins.

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351 West Camden Street
Baltimore, MD 21201-2436

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A WAVERLY COMPANY

SUB 58854
For consistent exposure in kidney, liver, and heart transplant recipients

Look for the Sign
Vanessa Underwood
Kidney transplant recipient
January 16, 1979
The Sign of Precision

Specify Neoral®—because tight control is critical

• To maintain each patient within his or her own narrow therapeutic range of a critical drug

• To provide consistent cyclosporine exposure

• To avoid the clinical consequences associated with inadvertent switching between formulations that are not bioequivalent

Specify Neoral cyclosporine capsules and oral solution for microemulsion

There really is a difference

*Neoral and Sandimmune® (cyclosporine, USP) are not bioequivalent and cannot be used interchangeably without physician supervision.

Please see brief summary of prescribing information and boxed warning for Neoral on the page following this advertisement.
• Precision:
  Consistent cyclosporine exposure to keep each patient within his or her narrow therapeutic range

• Performance:
  Clinically proven efficacy and safety*

• Experience:
  The most widely used immunosuppressant in transplant recipients, both in the United States and worldwide³

Specify NEORAL®
cyclosporine capsules and oral solution for microemulsion

There really is a difference

Neoral® and Sandimmune® (cyclosporine, USP) are not bioequivalent and cannot be used interchangeably without physician supervision. Any change of cyclosporine formulation should be made cautiously and under physician supervision because it may result in the need for a change in dosage for optimal performance.

*Neoral provides increased bioavailability with adverse events comparable to those of Sandimmune® when the dosage of the two drugs is adjusted to achieve the same cyclosporine blood trough concentrations. The principal adverse reactions of cyclosporine therapy in transplantation are renal dysfunction, tremor, hirsutism, hypertension, and gum hyperplasia.

References:
Cyclosponine

When the cardiac function is impaired, the susceptibility to infection and the development of nephropathy may increase. The risk of infection and the development of nephropathy may increase in the presence of cyclosporine in transplant patients.

Neoral Soft Gelatin Capsules (cyclosporine capsules for microemulsion) and Neoral® Oral Solution (cyclosporine oral solution for microemulsion) have been used in combination to treat hematological malignancies, autoimmune diseases, and transplant recipients. Cyclosporine blood concentrations should be monitored for the following:

- Neoral Soft Gelatin Capsules and Neoral® Oral Solution: Serum cyclosporine concentrations should be monitored throughout the duration of therapy for the following:
  - Neoral Soft Gelatin Capsules and Neoral® Oral Solution: Serum cyclosporine concentrations should be monitored throughout the duration of therapy for the following:

Cyclosporine A immunosuppressant should be used in transplant patients to cyclosporine or to any of the ingredients of the formulation.

Based on the mechanism of action (see ADVERSE REACTIONS), Neoral is indicated for the prophylaxis of organ rejection in kidney, heart, and lung allografts.

Patients receiving Neoral require frequent monitoring of serum creatinine. Elderly patients should be monitored with particular attention to changes in renal function, which may occur. Serum creatinine concentrations may not be properly adjusted. Neoral or cyclosporine can be used in conjunction with the incidence of structural kidney damage and pre-existing risk factors. An increase in serum creatinine and BUN may occur during Neoral therapy and reflect a reduction in the glomerular filtration rate. Neoral is known to be a more potent immunosuppressant than cyclosporine and more frequent serum creatinine and BUN levels should be obtained during therapy. Changes should be noted in patients taking Neoral to avoid systemic drug interactions. Dosage adjustments should be made in patients to minimize possible organ rejection due to low concentrations. Comparison of blood concentrations in the published literature and the doses required to achieve concentrations obtained using current assays must be done with detailed knowledge of the assay methods employed.

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THE MEETING WILL:

♦ Discuss new technologies and their applications
♦ Showcase major controversies in clinical theory and practice through debates and panel sessions
♦ Completely review the latest epidemiological findings, including a wide variety of intermediate outcomes.

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♦ 6 Swimming Pools ♦ Short Shuttle To Gulf of Mexico Beach
♦ 20 Minutes To Clearwater Beach And 45 Minutes to Tampa

MEETING REGISTRATION:
Renal Research Institute
Sylvia Cevallos — 212-360-4900

TRAVEL REGISTRATION:
Fresenius Medical Care
Mary Carruth — 781-402-9729 (Fax Only)

PROGRAM TO FOLLOW
♦ Including a Special Session and Job Fair for Nephrology Fellows
♦ Lineup of Internationally Known Speakers Will Be Invited

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HOSTED BY:
Nathan Levin, M.D.
J. Michael Lazarus, M.D.

Fresenius Medical Care
The only oral prophylaxis for CMV disease in solid organ transplantation.

**TWO CYTOVENE 500 MG CAPSULES** have been shown to be bioequivalent to four 250 mg capsules in subjects who are seropositive for CMV and human immunodeficiency virus.1

**MANAGEABLE SAFETY PROFILE.** The most common adverse events reported in a study (GAN 040) of liver transplant recipients included immune system disorders (graft rejection), infection, fever, abdominal pain, headache and diarrhea. There was also a trend toward increased creatinine levels (≥2.5 mg/dL) in 16% of the 150 patients treated with CYTOVENE capsules compared with 10% of the 154 patients receiving placebo; however, this was not statistically significant.2

Monitoring of renal function during therapy is essential, especially for patients receiving medications that may cause nephrotoxicity. Please refer to the complete product information for dose modifications for patients with renal impairment.

**CONVENIENT ORAL DOSAGE.**
1000 mg (two 500 mg capsules) tid with food.

The clinical toxicity of CYTOVENE includes granulocytopenia, anemia and thrombocytopenia. In animal studies ganciclovir was carcinogenic and teratogenic and caused aspermatogenesis.

CYTOVENE should not be administered if the absolute neutrophil count is less than 500 cells/μL or the platelet count is less than 25,000 cells/μL.

Please see summary of product information on the following pages.

**References:**

Copyright © 1998 by Roche Laboratories Inc. All rights reserved.
Cytovene-IV (ganciclovir sodium for injection) FOR INTRAVENOUS INJECTION ONLY
Cytovene-IV (ganciclovir capsules) FOR ORAL ADMINISTRATION

Before prescribing, please see complete product information, a summary of which follows:

WARNING: THE CLINICAL TOXICITY OF CYTOVENE-IV INCLUDES GRANULOCYTIC-LEUKOCYTIC NEUTROPHIL DHL AND HEPATOCYTE DILI. IN STUDIES BANDWOB was CARCINOGENIC, TERATOGENIC AND CAUSED ASPHRESIS.

CYTOVENE-IV IS INDICATED FOR USE ONLY IN THE TREATMENT OF CYTOMEGALOVIRUS (CMV) RETINITIS IN IMMUNOCOMPROMISED PATIENTS, AND FOR PREVENTION OF CMV DISEASE IN BONE MARROW TRANSPLANT RECIPIENTS. (SEE DOSAGE AND ADMINISTRATION FOR COMPLETE INFORMATION).

SIDE EFFECTS:

The following side effects were associated with a risk of more rapid rate of CMV RETINOPATHY PROGRESSION, THEY SHOULD BE USED AS MAINTENANCE TREATMENT ONLY IN THOSE PATIENTS FOR WHOM THIS RISK IS BALANCED BY THE BENEFIT ASSOCIATED WITH CONTINUATION THERAPY:

CONTINUATION THERAPY: CYTOVENE-IV AND CYTOVENE-IV are contraindicated in patients with hypersensitivity to ganciclovir or acyclovir.

WARNING: Hypersensitivity: CYTOVENE-IV and CYTOVENE-IV should not be administered if the absolute neutrophil count (ANC) is less than 1,000 cells/mm3 or if the hemoglobin is less than 9 g/dL in adult human populations (see ADVERSE EVENTS), CYTOVENE-IV and CYTOVENE-IV should, therefore, be used with caution in patients with pre-existing cytopenia or with a history of cytotoxic reactions to other drugs, chemicals or irradiation. Granulocytopenia usually occurs during the first or second week of treatment but may occur at any time during treatment. Cell counts usually begin to recover within 3 to 7 days discontinuing drug. Cytopenias may progress to agranulocytosis in rare cases which require administration of CYTOVENE-IV solution for treatment of CMV retinitis. Impairment of fertility: Animal data indicate that all forms of teratogenicity and carcinogenicity were seen in rats and mice. Studies in rabbits were not done. Effects on fertility in humans have not been adequately studied regarding this effect. It is considered probable that ganciclovir at the recommended doses causes temporary or permanent impairment of spermatozoa. Animal data also indicate that suppression of fertility in female rats was seen as early as 1 week after treatment. Teratogenicity: Teratogenicity of the mutagenic and teratogenic potentials of ganciclovir in 4 to 6-week-old mice and/or rats who received ganciclovir at dose levels which are >100 times (>1000 times at some dose levels) those of the human recommended dosages. Women of childbearing potential should be advised to use effective contraception during treatment. Tumors: Tumors have been observed in rats and mice following administration at doses which were greater than or equal to 10 times the human recommended dose. All tumors are not seen at the same sites compared to humans. Children should be monitored closely for signs of response to treatment.
### CYTOVENE-IV (ganciclovir sodium for injection) and CYTOVENE (ganciclovir capsules)  

**ADVERSE EVENTS:** Adverse events that occurred during clinical trials of CYTOVENE-IV and CYTOVENE capsules are summarized below, according to the participating study subpopulation.

#### Subjects with AIDS: Three controlled, randomized, phase 3 trials comparing CYTOVENE-IV and CYTOVENE capsules for maintenance therapy of CMV retinitis have been completed. During the trials, CMV retinitis or CYTOVENE capsules were prematurely discontinued in 9% of subjects because of adverse events. In a placebo-controlled, randomized, phase 3 trial of CYTOVENE capsules for prevention of CMV disease in AIDS, treatment was prematurely discontinued between treatment events, new or worsened illness, or laboratory abnormalities in 15.5% of subjects treated with CYTOVENE capsules and 16% of subjects receiving placebo. Laboratory data and adverse events reported during the conduct of these controlled trials are summarized below.

#### Laboratory Data:

<table>
<thead>
<tr>
<th>Treatment</th>
<th>CMV Retinitis Treatment</th>
<th>CMV Disease Prevention</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYTOVENE Capsules</td>
<td>3000 mg/day</td>
<td>Placebo</td>
</tr>
<tr>
<td>CYTOVENE-IV Capsules</td>
<td>5 mg/kg/day</td>
<td>Placebo</td>
</tr>
</tbody>
</table>

#### Laboratory Data:

- **Subjects:** 1408
- **Neutrophils:**
  - **<500 ANC:** 18% 25% 10% 5%
  - **500-1000:** 17% 16% 17% 16%
  - **50-300:** 19% 20% 22% 16%
- **Anemia:**
  - **<5 g/dL:** 2% 5% 1% <1%
  - **6-9 g/dL:** 10% 16% 10% 3%
  - **9-12 g/dL:** 25% 29% 15% 16%
- **Maximum Serum Creatinine:**
  - **<25 mg/dL:** 1% 2% 1% 2%
  - **25-<50 mg/dL:** 12% 14% 19% 11%
- **Platelet count:**
  - **<50,000:** 3% 1% 28% 0%
  - **50,000-200,000:** 3% 25% 37% 5%
  - **>200,000:** 8% 4% 57% 6%

- **Study GI-468:** Mean duration of treatment = 28 days
- **Study GI-1570 and IM 1569:** Mean duration of treatment = 45 days
- **Study GI-494:** Mean duration of treatment = 62 days

### CYTOVENE-IV (ganciclovir sodium for injection) and CYTOVENE (ganciclovir capsules)

The following table shows the frequency of elevated serum creatinine values in these controlled clinical trials:

<table>
<thead>
<tr>
<th>Controlled Trial</th>
<th>Capsules</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Allograft</td>
<td>CYTOVENE-IV (n=76)</td>
<td>CYTOVENE-IV (n=73)</td>
</tr>
<tr>
<td>Bone Marrow Allograft</td>
<td>CYTOVENE-IV (n=153)</td>
<td>CYTOVENE-IV (n=150)</td>
</tr>
<tr>
<td>Liver Allograft</td>
<td>CYTOVENE-IV (n=154)</td>
<td>CYTOVENE-IV (n=154)</td>
</tr>
</tbody>
</table>

### CYTOVENE-IV for Intraocular Retinal Detachment

In two recent, controlled, multicenter, randomized, clinical trials comparing CYTOVENE-IV capsules for the prevention of CMV disease in transplant recipients, laboratory data and adverse events reported during the conduct of these trials are summarized below.

#### Laboratory Data:

- **Neutropenia:** 4% 3% 12% 6% 3% 1%
- **TOTAL ANC:** 3% 8% 29% 17% 3% 2%
- **Thrombocytopenia:** 7% 11% 41% 23% 6% 3%
- **Platelet count:**
  - **<50,000:** 3% 1% 32% 28% 0% 3%
  - **50,000-200,000:** 3% 5% 25% 37% 5% 3%
  - **>200,000:** 8% 4% 57% 65% 5% 6%

- **Study GI-468:** Mean duration of treatment = 28 days
- **Study GI-1570 and IM 1569:** Mean duration of treatment = 45 days
- **Study GI-494:** Mean duration of treatment = 62 days

(Discussion of clinical trials under INDICATIONS AND USAGE in complete product information.)

**Pharmaceuticals**

Roche Laboratories Inc.

340 Kingsland Street
Nutley, New Jersey 07110-1199


Cytovene-IV (ganciclovir capsules) 500 mg are a two-piece, size No. 0, opaque green hard gelatin capsules. CYTOVENE Capsules are supplied as follows: Bottles of 180 capsules (NDC 0004-0278-40).

Bottles of 180 capsules (NDC 0004-6946-09). Store between 5°C and 25°C (41°F and 77°F).
American Society of Nephrology

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### Application for Active and Corresponding Membership

<table>
<thead>
<tr>
<th>LAST NAME</th>
<th>FIRST NAME</th>
<th>MIDDLE INITIAL(S)</th>
</tr>
</thead>
</table>

**Preferred Mailing Address**

<table>
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<tr>
<th>CITY</th>
<th>STATE/PROVINCE</th>
<th>ZIP/POSTAL CODE</th>
<th>COUNTRY</th>
</tr>
</thead>
</table>

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

<table>
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<tr>
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<th>COUNTRY</th>
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**Business Telephone**

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<tr>
<th>BUSINESS TELEPHONE</th>
<th>BUSINESS FAX</th>
<th>E-MAIL ADDRESS</th>
</tr>
</thead>
</table>

**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

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(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**

<table>
<thead>
<tr>
<th>Degree</th>
<th>Dates</th>
</tr>
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For office use only:

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

Institution Name and Address | Position | Preceptor(s) | Inclusive Dates
--- | --- | --- | ---

List your five most significant publications.

List other societies to which you belong.

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

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

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- [ ] MasterCard

Cardholder’s Name (Please print or type) | Signature
--- | ---

Card Number | Expiration Date