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.

### Brief Summary

**NORVASC** (amlodipine besylate) Tablets

For Oral Use

**CONTRAINDICATIONS:** NORVASC is contraindicated in patients with known sensitivity to amlodipine. **WARNINGS:** Increased Angina and/or Myocardial Infarction: Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina with sublingual nitroglycerin or on standing when calcium channel blockers were added or increased. The mechanism of this effect has not been elucidated.

**PRECAUTIONS: General:** Since the volume of distribution of NORVASC is gradual in onset, acute hypertension has rarely been reported after oral administration of NORVASC. Nonetheless, caution should be exercised when administering NORVASC with other peripheral vasodilators particularly in patients with low cardiac output.

**Use in Patients with Congestive Heart Failure:** In general, calcium channel blockers should be used with caution in patients with heart failure. NORVASC (5-10 mg per day) has been studied in a placebo-controlled trial of 1153 patients with NYHA Class II or III heart failure, digoxin, and diuretics. Follow-up was at least 6 months, with a mean of about 14 months. There was no overall adverse effect on survival or cardiac morbidity (as defined by the composite of death, rehospitalization for heart failure, or urgent coronary revascularization) for women in heart failure, involving a total of 687 patients. In these studies, there was evidence of worsening heart failure based on measures of exercise tolerance, NYHA classification, symptoms, or URI.

**Beta-Blocker Withdrawal:** NORVASC is not a beta-blocker and therefore gives no protection against the dangers of abrupt withdrawal of a beta-blocker. Abrupt withdrawal should be avoided at all costs.

**Patients with Hepatic Failure:** Since NORVASC is extensively metabolized by the liver and the plasma elimination half-life (5-10 hours in patients with impaired hepatic function, caution should be exercised when administering NORVASC in 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 known to bind plasma proteins (e.g., warfarin, phenytoin, and indomethacin).

**Other Amlodipine Drugs, Antibiotics, and Oral Hypoglycemic Drugs:**

**Drug/Laboratory Test Interactions:** None known.

**Cardiovascular, Metabolic, Impairment of Fertility:** Rats and mice treated with amlodipine in the diet for two years, at an oral dose of 15 mg/kg (about 1.5 times the maximum recommended human daily dose on a mg/m2 basis) was toxic to the male and female rats and mice of both species. No evidence of carcinogenicity. The highest dose for mice, for rats, the maximum recommended clinical dose of 10 mg/m2 was toxic to the male and female rats and mice of both species. Mutagenic studies revealed no drug-related effects at either the gene or chromosome levels.

There was no evidence of the teratogenicity of amlodipine (mice and rats) for 5 days and females 14 days prior to mating and up to 10 mg/kg (about 1.5 times the maximum recommended human daily dose on a mg/m2 basis). The maximum dose of 10 mg/kg (about 1.5 times the maximum recommended human daily dose on a mg/m2 basis) was toxic to the male and female rats and mice of both species. No evidence of carcinogenicity. The highest dose for mice, for rats, the maximum recommended clinical dose of 10 mg/m2 was toxic to the male and female rats and mice of both species. Mutagenic studies revealed no drug-related effects at either the gene or chromosome levels.

### Once-Daily

**5 mg and 10 mg tablets**

**NORVASC** (amlodipine besylate)

### Efficacy and Safety

**THAT’S EASY TO LIVE WITH**

**Rx**

NORVASC 5mg #30

Sig: 1 tablet no daily

### References


### Labs • HMO • Pratt • Roerig

U.S. Pharmaceuticals Group

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PhOSLO (Calcium Acetate) tablets contain 667 mg of calcium acetate (anhydrous) and 10 mg of the inert carrier if an effective phosphate binder that reduces the absorption of phosphorus.

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THE AMERICAN HEART ASSOCIATION
AND
THE AMERICAN SOCIETY OF NEPHROLOGY

This annual award recognizes young investigators for excellence in nephrological research. The awardee will be judged primarily on the significance and originality of his or her published work. The candidate will have provided evidence of creativity and productivity for several years beyond the fellowship level and must be less than 41 years of age on the first day of the annual meeting of the American Society of Nephrology in which the award is presented.

The award will consist of a certificate of recognition, an unrestricted grant of $5,000 to the laboratory of the awardee, and paid travel expenses to the annual meeting.

HOW TO APPLY:

* Candidates must be proposed and seconded — in one letter — by two members of the American Society of Nephrology, or by one member of the American Society of Nephrology and one member of the Council on the Kidney of the American Heart Association. All pertinent materials must be received by March 1 of the year in which the annual meeting of the American Society of Nephrology is held.

* The letter of nomination — not exceeding two pages — should emphasize the originality and significance of the scientific accomplishments of the candidate, and identify and highlight the three or four most important publications of the candidate.

* No more than four additional letters of support should accompany the letter of nomination, and these should be from individuals well familiar with the candidate’s work. At the most, only two of these supporting letters should be from a candidate’s own institution, and ideally should be from individuals who can give a national perspective on the work being acclaimed in the letter of nomination.

* A complete curriculum vitae with a bibliography of the candidate should be submitted with the letter of nomination.

* Nominators of candidates who are not chosen may submit an updated application for a subsequent year providing the candidate still meets the age criterion. (Reconsideration is not automatic).

* Nine copies of the curriculum vitae, letter of nomination, and supporting letters should be sent in one packet, no later than March 2, 1998, to the American Society of Nephrology, Attention Young Investigator Award Committee, 1200 19th Street, N.W., Suite 300, Washington, DC 20036-2422.

QUESTIONS? CALL THE ASN AT 202/857-1190
Reduce the Pressure of Hypertension

- Effective as monotherapy\(^1\)
- Effective in combination with other antihypertensive agents\(^{1,2}\)

Well Tolerated

- Like other alpha\(_1\)-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.\(^1\)

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HYTRIN® TERTAZOSIN HCL CAPSULES

Reduce the Pressure

References:
1. HYTRIN package insert, Abbott Laboratories.

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WARNINGS: Syncope and 'first-dose' effect: HYTRIN capsules, like other alpha-adrenergic blocking agents, can cause postural hypotension and syncope. Postural hypotension may occur with the initial dose and in the event of an introduction of another antihyper- tension drug. Syncope is believed to be due to an excessive peripheral vasodilatation that may be initiated as a result of the first dose of HYTRIN. To prevent this, the patient should be told to rise slowly after sitting and, if necessary, to lie down slowly after supine to a sitting position.

To decrease the likelihood of syncope or excessive hypotension, treatment should always be initiated with a 2 mg dose (1 capsule) at bedtime.

Drug Interactions: In controlled clinical trials, terazosin has been added to diuretics, and several beta-adrenergic blockers: no unex- pected interactions were observed. Terazosin has also been used in patients with chronic obstructive pulmonary disease, and while the trend was toward lower blood pressure, none of the patients had a fall in blood pressure. In at least 50 patients on the following drugs or drug classes: 1) anal- gesics/anti-inflammatory agents (e.g. acetaminophen, aspirin, codeine, ibuprofen, propacetamol, salicylates, ibuprofen, ketoprofen, trimethoprim and sulfamethoxazole); 2) antihistamines/sympa- thomimetics (e.g. phentolamine hydrochloride, phenylpropanolamine hydrochloride); 3) antidepressants (e.g. amitriptyline, imipramine); 4) antihypertensives (1.3% - 0.4%), tachycardia (1.9% - 2.6%), nausea (4.6% - 0.6%), abdominal pain (5.0% - 2.4%), weight gain (0.5% - 0.6%), headache (3.5% - 3.0%), depression (0.3% - 0.2%), dizziness (19.3% - 7.5%), bilateral nasal congestion (4.4% - 1.4%), constipation (1.5% - 0.6%), sinusitis (4.1% - 0.6%), sinusitis (1.5% - 0.6%), pharyngitis (1.0% - 0.6%), headache (3.5% - 1.4%). Asthenia includes weakness, tiredness, lassitude, and fatigue. Other effects: blurred vision, dry mouth, somnolence, rhinitis, rash, pruritus, extrapyramidal reactions, pruritus, rash, sweating; Special: abnormal vision, delirium tremens, whole body tremor: urinary frequency, urination incontinence primarily reported in elderly patients.

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 pruritus during post-marketing surveillance. The reaction almost always occurred within hours of drug administra- tion but sometimes were serious enough to interrupt treatment. The adverse reactions that were most bothersome, as judged by their frequency as reported as 'serious', have involved patients by at least 0.5% of the terazosin group and being reported more often than placebo.

Adverse reaction rates were generally comparable in both groups. Placebo [n=506]: are: asthma (1.6% - 0.9%), headache (1.3% - 1.0%), palpatations (1.4% - 0.2%), postural hypotension (0.5% - 0.2%), rash (0.5% - 0.2%), dry mouth (0.5% - 0.2%), nausea (0.8% - 0.0%), peripheral edema (0.6% - 0.0%), dizziness (3.1% - 0.4%), paraesthesia (0.8% - 0.2%), somnolence (0.6% - 0.2%), pruritus (0.5% - 0.8%), dry mouth (0.6% - 0.0%), and blurred vision (0.6% - 0.0%).

OVERDOSAGE: Should overdose of HYTRIN lead to hypotension, support of the cardiovascular system is of first importance. Restoration of blood pressure and normalization of heart rate may be achieved by use of i.v. fluids administered as needed. Laboratory data indicate that terazosin is 90-94% protein-bound; therefore, dialysis is unlikely to be useful. Dosage and administration: If HYTRIN administration is discontinued for several days, therapy should be restarted using the lowest dose. Dosage: terazosin is not recommended for use in children. Hydrochloride: 2 mg (1 capsule) at bedtime. 4 mg (2 capsules) at bedtime. In general, the dose should not exceed 4 mg daily. 2 mg at bedtime. Increased dosages, retardation of growth, or side effects (e.g. headache) noted in clinical trials. Laboratory Tests: Small but statistically significant decreases in hemoglobin, hematocrit, white blood cells, total protein and albumin were observed in controlled clinical trials. Laboratory tests suggested the possibility of hemodilution. Treatment with terazosin for up to 24 months had no significant effect on prostatic specific antigen (PSA) levels.

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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.

References:

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CONTRADICTIONS: CYTOVENE-IV and CYTOVENE are contraindicated in patients with hypersensitivity to ganciclovir or any component of the formulation.

WARNINGS: Hemorrhagic: CYTOVENE-IV and CYTOVENE should not be administered if the absolute neutrophil count is less than 1500 cells/mm³ or if platelet counts are less than 40,000 cells/mm³. CKD: Due to the renal clearance of ganciclovir and its metabolite, anemia and thrombocytopenia in patients receiving CYTOVENE-IV and CYTOVENE may occur at any time during treatment. Close monitoring of blood counts should be performed during treatment.

ADMINISTRATION: CYTOVENE-IV is administered as an infusion over at least 1 hour. The infusion is administered through a central venous catheter or a peripheral vein in patients treated for CMV retinitis. It is recommended that the infusion be monitored during the infusion or for at least 30 minutes after completion.

ADJUSTMENTS: CYTOVENE-IV and CYTOVENE are contraindicated in patients with concomitant use of cyclosporine, azathioprine, or mercaptopurine due to the potential for increased toxicity. In patients receiving concomitant treatment with cyclosporine, azathioprine, or mercaptopurine, the dose of CYTOVENE-IV or CYTOVENE should be decreased by 25%. In patients receiving concomitant treatment with cyclosporine, azathioprine, or mercaptopurine, the dose of CYTOVENE-IV or CYTOVENE should be decreased by 25%.

DOSAGE: The maximum single dose of CYTOVENE-IV should not exceed 5 g/kg/day. The total daily dose of CYTOVENE-IV should be administered over at least 1 hour. CYTOVENE-IV should be administered to patients with a creatinine clearance of 50 to 100 ml/min. A dose of 1 g/kg/day administered over 1 hour for 15 days is recommended for the treatment of CMV retinitis. The dose of CYTOVENE-IV should be reduced by 25% in patients with a creatinine clearance of 25 to 50 ml/min.

ADVERSE EVENTS: The most common adverse events reported in patients receiving CYTOVENE-IV are neutropenia, infections, and myelosuppression. These events are generally reversible and may occur at any time during treatment. Close monitoring of blood counts is recommended during treatment.

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DOSAGE: The maximum single dose of CYTOVENE-IV should not exceed 5 g/kg/day. The total daily dose of CYTOVENE-IV should be administered over at least 1 hour. CYTOVENE-IV should be administered to patients with a creatinine clearance of 50 to 100 ml/min. A dose of 1 g/kg/day administered over 1 hour for 15 days is recommended for the treatment of CMV retinitis. The dose of CYTOVENE-IV should be reduced by 25% in patients with a creatinine clearance of 25 to 50 ml/min.

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Cytovene®-IV (ganciclovir sodium for injection) and Cytovene® (ganciclovir capsules)

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

**Subjects with AIDS:** Three controlled, randomized, phase 3 trials comparing CYTOVENE-IV and CYTOVENE capsules for maintenance treatment of CMV retinitis have been completed. During these trials, CYTOVENE-IV 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 because of adverse events, new or worsening intercurrent illness, or laboratory abnormalities in 59% of subjects treated with CYTOVENE capsules and 75% 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>Neutrophils</td>
<td>CYTOVENE-IV: 3000 mg/day</td>
<td>Placebo: 4790 mg/day</td>
</tr>
<tr>
<td>Arteries</td>
<td>CYTOVENE-IV: 500 mg/day</td>
<td>Placebo: 7900 mg/day</td>
</tr>
<tr>
<td>Areneol:</td>
<td>CYTOVENE-IV: 3000 mg/day</td>
<td>Placebo: 11%</td>
</tr>
<tr>
<td>Minimum Serum Creatinine:</td>
<td>≤2.5 mg/dL</td>
<td>Placebo: 3%</td>
</tr>
</tbody>
</table>

* Data from treatment Studies, ICM 150, ICM 1570 and ICM 1699. ** Study ICM 150 and ICM 1570.
---

<table>
<thead>
<tr>
<th>Event</th>
<th>Subjects, number</th>
<th>Mean time on therapy (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>10%</td>
<td>7 days</td>
</tr>
<tr>
<td>Injection</td>
<td>9%</td>
<td>7 days</td>
</tr>
<tr>
<td>Rash</td>
<td>7%</td>
<td>7 days</td>
</tr>
<tr>
<td>Sepsis</td>
<td>4%</td>
<td>3 days</td>
</tr>
<tr>
<td>Nervous System</td>
<td>2%</td>
<td>2 days</td>
</tr>
<tr>
<td>Nervous System</td>
<td>1%</td>
<td>1 day</td>
</tr>
</tbody>
</table>

**Adverse Events**

The following table shows selected adverse events reported in 5% or more of the subjects in placebo-controlled clinical trials conducted under the following schedules: CYTOVENE capsules (5 mg/gelatin) or CYTOVENE capsules (3000 mg/day), and in one controlled clinical trial in which CYTOVENE capsules (3000 mg/day) were compared to placebo for the prevention of CMV disease.

**Adverse Events in Clinical Trials**

<table>
<thead>
<tr>
<th>Body System</th>
<th>Body as a Whole</th>
<th>Digestive System</th>
<th>Hematologic System</th>
<th>Nervous System</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>36%</td>
<td>8%</td>
<td>8%</td>
<td>9%</td>
<td>13%</td>
</tr>
<tr>
<td>Injection</td>
<td>9%</td>
<td>15%</td>
<td>15%</td>
<td>17%</td>
<td>13%</td>
</tr>
<tr>
<td>Rash</td>
<td>7%</td>
<td>14%</td>
<td>14%</td>
<td>6%</td>
<td>6%</td>
</tr>
<tr>
<td>Sepsis</td>
<td>4%</td>
<td>8%</td>
<td>8%</td>
<td>3%</td>
<td>5%</td>
</tr>
<tr>
<td>Nervous</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
<td>2%</td>
</tr>
<tr>
<td>Other</td>
<td>1%</td>
<td>1%</td>
<td>1%</td>
<td>2%</td>
<td>2%</td>
</tr>
</tbody>
</table>

**Catheter Related**

<table>
<thead>
<tr>
<th>Event</th>
<th>Subjects, number</th>
<th>Mean time on therapy (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catheter infection</td>
<td>4%</td>
<td>3 days</td>
</tr>
<tr>
<td>Catheter Sepsis</td>
<td>5%</td>
<td>2 days</td>
</tr>
</tbody>
</table>

**Adverse Events in Selected Subjects of Three Randomized Placebo Controlled Clinical Trials Comparing CYTOVENE Capsules to CYTOVENE-IV Solution for Maintenance Treatment of CMV Retinitis and in One Placebo Controlled Clinical Comparing Capsules to Placebo for Prevention of CMV Disease**

<table>
<thead>
<tr>
<th>Serum Creatinine</th>
<th>Subjects, number</th>
<th>Mean time on therapy (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤2.5 mg/dL</td>
<td>10%</td>
<td>2 days</td>
</tr>
<tr>
<td>&gt;2.5 mg/dL</td>
<td>5%</td>
<td>3 days</td>
</tr>
</tbody>
</table>

**Adverse Events Reported During Postmarketing Experience with CYTOVENE-IV and CYTOVENE Capsules**

The following events have been identified during the postmarketing experience with CYTOVENE and CYTOVENE capsules. The presence of these events do not necessarily mean that the products caused them. They are reported voluntarily from a population of unknown size, frequencies of estimates cannot be made. These events have been chosen for inclusion due to either the potential or importance of the causal relationship to the products or because of an unusual frequency with which they have been noted.

**Cytovene®-IV (ganciclovir sodium for injection)**

- **Heart Attack:** 10%
- **Bone Marrow Ablation:** 10%
- **Liver Ablation:** 10%

**Cytovene® (ganciclovir capsules)**

- **Heart Attack:** 10%
- **Bone Marrow Ablation:** 10%
- **Liver Ablation:** 10%

---

**Pharmaceuticals**

Roche Laboratories Inc.

340 Kingland Street
Nutley, New Jersey 07110-1199

---

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 Trials - Transplant Recipients</th>
<th>Cytovene®-IV</th>
<th>Cytovene® Capsules</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart Ablation</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Bone Marrow Ablation</td>
<td>10%</td>
<td>10%</td>
</tr>
<tr>
<td>Liver Ablation</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>

**Transplant Recipients**

<table>
<thead>
<tr>
<th>Serum Creatinine</th>
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<td>3 days</td>
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---

Cytovene®-IV (ganciclovir sodium for injection) and Cytovene® (ganciclovir capsules)

- **Heart Attack:** 10%
- **Bone Marrow Ablation:** 10%
- **Liver Ablation:** 10%

---

Cytovene®-IV (ganciclovir sodium for injection) is supplied in 10 ml sterile vials, each containing ganciclovir sodium equivalent to 500 mg of ganciclovir, in cartons of 5 (NDC 0004-0940-00).

Cytovene® (ganciclovir capsules) 500 mg are two-piece, size No. 10, opaque green hard gelatin capsules. Cytovene capsules are supplied as follows: Bottles of 180 capsules (NDC 0004-0056-40).

Cytovene®-IV (ganciclovir sodium for injection) is supplied in 5 ml sterile vials, each containing ganciclovir sodium equivalent to 250 mg of ganciclovir, in cartons of 25 (NDC 0004-0946-40).

---

**Revised:** December 1997

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Cytovene®-IV (ganciclovir sodium for injection) and Cytovene® (ganciclovir capsules)

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<td>3 days</td>
</tr>
</tbody>
</table>
The American Society of Nephrology Board Review Course & Update continues to expand—this year offering 24 new workshops to supplement the main review. These workshops have been scheduled during breakfast and lunch so as not to conflict with the general session. Choose the workshops that best suit your needs!

Again this year, 10 advanced workshops will be presented concurrently with the main review allowing certified nephrologists to plan their own customized course—obtaining the information they need from the main review and attending some or all of the advanced workshops.

In addition to 24 supplementary workshops and 10 advanced workshops, the 1998 Board Review Course & Update will offer:

- Lectures
- Panel Discussions
- Case Discussions
- UpToDate (projected onto a viewing screen)
- Electrolyte Quiz
- Audience Response Pads
- Final Exam
- Up to 50 Hours of Continuing Medical Education (CME) Credits

For more information or to request a brochure, please contact:
The American Society of Nephrology
Telephone: (202) 857-1190
Fax: (202) 223-4579
E-Mail: christine_fiorini@dc.sba.com
Web Site: www.asn-online.com
In combination therapy

**Roche brings the first humanized monoclonal antibody to renal transplantation.**
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 (eg, 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.
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.

OVERDOSAGE: 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.)

Printed in U.S.A.

17-090-072-002-028

Lot 0000009072

Issued: December 1997

Pharmaceuticals

Roche Laboratories Inc.
340 Kingsland Street
Nutley New Jersey 07110-1199
Belbie malignancies. graft Patients been susceptibility 10 year. enrollment delayed (absolute of 5).sdimmune#{174}, the development of immunosuppression rather than to the use of any specific agent. Overexpression of the immune system can also increase susceptibility to infections. Patients have been investigated in clinical trials: antithymocyte globulin (ATGAM), OKT3 (Orthoclone OKT3), 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 developing in patients receiving CellCept with other immunosuppressive agents should be considered a potentially life-threatening event. If any of these conditions is suspected, the use of CellCept should be terminated immediately.

ADVERSE REACTIONS: The most common side effects observed with CellCept are nausea, vomiting, diarrhea, and headache. Other possible adverse effects include fatigue, anorexia, fever, and rash. In some cases, these side effects may be severe and require medical intervention.

Indications and Usage: CellCept® (mycophenolate mofetil capsules) is indicated for the prophylaxis of organ rejection in patients receiving allogenic renal 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 history of mycophenolate mofetil, mycophenolic acid or any component of the drug product.

WARNING: Prolonged immunosuppressive regimens involving combinations of drugs, including CellCept, as part of an immunosuppressive approach are associated with an increased risk of developing lymphomas and other malignancies, particularly of the skin. The risk of skin cancers is increased in patients who receive prolonged immunosuppression. The risk of lymphomas was increased in patients who received concomitant immunosuppressive therapy with CellCept, 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 developing in patients receiving CellCept with other immunosuppressive agents should be considered a potentially life-threatening event. If any of these conditions is suspected, the use of CellCept should be terminated immediately.

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<table>
<thead>
<tr>
<th>Common Side Effects of CellCept and Azathioprine</th>
<th>Common Side Effects of CellCept and Azathioprine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Body as a Whole</strong></td>
<td><strong>Body as a Whole</strong></td>
</tr>
<tr>
<td>Body as a Whole</td>
<td>Body as a Whole</td>
</tr>
<tr>
<td>Pain</td>
<td>Pain</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>Abdominal pain</td>
</tr>
<tr>
<td>Fever</td>
<td>Fever</td>
</tr>
<tr>
<td>Headache</td>
<td>Headache</td>
</tr>
<tr>
<td>Infection</td>
<td>Infection</td>
</tr>
<tr>
<td>Sepsis</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>Arthralgia</td>
</tr>
<tr>
<td>Chest pain</td>
<td>Chest pain</td>
</tr>
<tr>
<td>Back pain</td>
<td>Back pain</td>
</tr>
<tr>
<td><strong>Hemic and Lymphatic</strong></td>
<td><strong>Hemic and Lymphatic</strong></td>
</tr>
<tr>
<td>Anemia</td>
<td>Anemia</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>Leukopenia</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>Thrombocytopenia</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>Hematocrit</td>
</tr>
<tr>
<td>Leukocytosis</td>
<td>Leukocytosis</td>
</tr>
<tr>
<td><strong>Urogenital</strong></td>
<td><strong>Urogenital</strong></td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>Urinary tract infection</td>
</tr>
<tr>
<td>Kidney tubular necrosis</td>
<td>Kidney tubular necrosis</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td><strong>Cardiovascular</strong></td>
</tr>
<tr>
<td>Hypertension</td>
<td>Hypertension</td>
</tr>
<tr>
<td><strong>Metabolic and Nutritional</strong></td>
<td><strong>Metabolic and Nutritional</strong></td>
</tr>
<tr>
<td>Peripheral edema</td>
<td>Peripheral edema</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>Hypercholesterolemia</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>Hyperlipidemia</td>
</tr>
<tr>
<td>Edema</td>
<td>Edema</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>Hypokalemia</td>
</tr>
<tr>
<td>Hyperglycemia</td>
<td>Hyperglycemia</td>
</tr>
<tr>
<td><strong>Dietary</strong></td>
<td><strong>Dietary</strong></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Diarrhea</td>
</tr>
<tr>
<td>Constipation</td>
<td>Constipation</td>
</tr>
<tr>
<td>Nausea</td>
<td>Nausea</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>Dyspepsia</td>
</tr>
<tr>
<td>Vomiting</td>
<td>Vomiting</td>
</tr>
<tr>
<td>Anaemia and vomiting</td>
<td>Anaemia and vomiting</td>
</tr>
<tr>
<td>Oral nausia</td>
<td>Oral nausia</td>
</tr>
<tr>
<td><strong>Respiratory</strong></td>
<td><strong>Respiratory</strong></td>
</tr>
<tr>
<td>Infection</td>
<td>Infection</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>Dyspnea</td>
</tr>
<tr>
<td>Cough increased</td>
<td>Cough increased</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>Pharyngitis</td>
</tr>
<tr>
<td><strong>Skin and Appendages</strong></td>
<td><strong>Skin and Appendages</strong></td>
</tr>
<tr>
<td>Acne</td>
<td>Acne</td>
</tr>
<tr>
<td>Rash</td>
<td>Rash</td>
</tr>
<tr>
<td><strong>Nervous System</strong></td>
<td><strong>Nervous System</strong></td>
</tr>
<tr>
<td>Tremor</td>
<td>Tremor</td>
</tr>
<tr>
<td>Inomnia</td>
<td>Inomnia</td>
</tr>
<tr>
<td>Dizziness</td>
<td>Dizziness</td>
</tr>
<tr>
<td><strong>Europe Study</strong></td>
<td><strong>Europe Study</strong></td>
</tr>
<tr>
<td>CellCept</td>
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</tr>
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<td>Urinary tract infection</td>
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<tr>
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<tr>
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<tr>
<td>Diarrhea</td>
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<tr>
<td><strong>Respiratory</strong></td>
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</tr>
<tr>
<td>Infection</td>
<td>Infection</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>Bronchitis</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>Pneumonia</td>
</tr>
</tbody>
</table>

The above data demonstrate that in three controlled trials for prevention of rejection, patients receiving 3.0 g per day of CellCept had an overall better safety profile than did patients receiving 3.0 g per day of CellCept. Sepsis, which was generally CMV viremia, was slightly more common in patients treated with CellCept, with an incidence of 18-22%, compared to 16% in patients receiving azathioprine and 5% in patients receiving placebo. The incidence of diarrhea was most clearly increased in patients receiving CellCept, with an incidence of 42%, compared to 21% in patients receiving azathioprine and 6% in patients receiving placebo. The incidence of malignancies among the 1,483 patients enrolled in controlled trials for the prevention of rejection who were followed for 24 months was similar to the incidence reported in the literature for 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.
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>
<tr>
<th>Measure</th>
<th>1 Year</th>
<th>2 Years</th>
<th>3 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secondary Patency (Graft Survival)</td>
<td>89%</td>
<td>89%</td>
<td>87%</td>
</tr>
<tr>
<td>Primary Patency (Clot-free Survival)</td>
<td>76%</td>
<td>72%</td>
<td>71%</td>
</tr>
</tbody>
</table>


GORE-TEX is a registered trademark of W.L. Gore & Associates, Inc.

W. L. Gore & Associates, Inc. • Flagstaff, Arizona 86007-3200 • 800-528-8763

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.

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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.

1 Patients should be monitored for neutropenia. If neutropenia develops (ANC <1.3 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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ONCE-DAILY 80 mg • 160 mg

Diovan
valsartan capsules
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.

No significant differences between adverse events (AEs), DIOVAN vs placebo, AE more frequent than placebo: cold skin (3% vs. 2%), headache (4% vs. 1%), abdominal pain (2% vs. 1%); the most common AE were headache and dizziness.

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  - lisinopril 10 mg\(^3,4\)

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\(^4,5\)
Diovan™
valsartan
Capsules

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

USE IN PREGNANCY

Valsartan, being a non-selective direct-acting renin-angiotensin 2 (AT1) receptor antagonist, is a drug in the same class as losartan and irbesartan. In laboratory animals, treatment with angiotensin II receptor antagonists, including valsartan, results in dose-dependent decreases in fetal body weight and decreases in fetal renal weight, with decreases in renal parenchymal thickness, cortical volume, and medullary weight. In rats, valsartan resulted in a dose-related decrease in fetal kidney weight and a decrease in renal cortical thickness. These effects were reversible upon withdrawal of treatment. In rabbits, valsartan produced a dose-related decrease in embryonic weight and decrease in body weight that were reversible upon withdrawal of treatment. These effects in laboratory animals are consistent with the known actions of renin-angiotensin system on kidney development, and are expected to be associated with a reduction in the renal perfusion pressure. In clinical trials, a slight decrease in birth weight has been observed in infants whose mothers received valsartan during the second and third trimesters of pregnancy. This decrease occurred in infants weighing less than the 10th percentile for gestational age and sex. The clinical significance of these findings is unknown. Valsartan is not expected to cause significant fetal or neonatal risk when administered to pregnant women, but it is not known whether the drug will affect the developing human fetus. Because animal reproduction studies are not always predictive of human response, Diovan should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus.

RATIOS AND INDICATIONS

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 Mortality and Morbidity

Drugs that act directly on the renin-angiotensin system can cause fetal and neonatal morbidity and death when administered to pregnant women. Several cases of fetal death or adverse neonatal outcomes following treatment with angiotensin II receptor antagonists 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. The use of a drug that acts directly on the renin-angiotensin system during the second and third trimesters of pregnancy is likely to result in fetal death. Angiotensin II is essential for normal intrauterine growth and development. Prematurity, intrauterine growth retardation, and patent ductus arteriosus have also been reported, although it is not clear whether these occurrences were due to exposure to drug. These adverse effects do not appear to have resulted from intraneonatal drug exposure that has been limited to the second and third trimesters and thus are exposed to an angiotensin II receptor antagonist only during the first trimester should be so informed. Nonetheless, when patients become pregnant while taking Diovan, they should be apprised of the embryofetal risks and should be closely monitored for the development of oligohydramnios, if Diovan is still being used.

The occurrence of oligohydramnios, if Diovan is still being used, can result in fetal lung hypoplasia and respiratory distress at or near the time of delivery. Infants so affected may exhibit respiratory distress as soon as the first few minutes of life and, in addition, low birth weight, prolonged decelerations on fetal heart rate monitoring, tachypnea and labored breathing, and decreased or absent cry. If oligohydramnios occurs, Diovan should be discontinued as soon as possible unless clearly indicated to maintain maternal hypertension. However, if Diovan must be used in a pregnant woman despite the presence of oligohydramnios, it is essential that close monitoring of maternal and fetal conditions be conducted throughout the next several weeks, at which time, if oligohydramnios persists, the drug should be discontinued as soon as possible, regardless of the management of the pregnancy.

The administration of a drug to the mother can be associated with adverse reactions in the newborn. If angiotensin II is blocked, the sympathetic system, which is normally stimulated to compensate for the decreased renin-angiotensin system activity, is not stimulated, so that hypotension may occur, and unless the newborn is adequately supported, symptoms may occur. The potential for these effects is the reason for advising women of the importance of not discontinuing Diovan or changing its dose if pregnancy is suspected. However, if Diovan is still being used when pregnancy is detected, it should be discontinued as soon as possible. The patient should be apprised of the potential effects of Diovan on the fetus and should be referred to a perinatologist for consultation.

Controlled clinical trials of Diovan have not provided adequate evidence of fetal risk associated with using Diovan during pregnancy. Diovan should be administered to pregnant women only if the potential benefit justifies the potential risk to the fetus.

Morbidity

Fetal-Neonatal

In controlled clinical trials of Diovan, 124.6% (58.6%) of patients treated with Diovan were 65 years and 265.7% (7.3%) were 75 years. There were no differences in the efficacy or safety of Diovan was observed in this patient population, but the safety of some older individuals cannot be ruled out.

ADVERSE REACTIONS

Diovan has been evaluated for safety in more than 4000 patients, including over 1000 who were treated for over 6 months, and more than 150 for over 1 year. Adverse experiences have generally been mild and transient in nature and have only infrequently required discontinuation of therapy. The overall incidence of adverse experiences with Diovan was similar to placebo.

The overall frequency of adverse experiences was very similar to placebo-controlled clinical trials in all at 1% of patients treated with Diovan and at a higher incidence in patients (7.6%) than placebo (1%).

Diabetes mellitus, upper respiratory infection, cough, dizziness, sinusitis, nausea, pharyngitis, rhinitis, and rash occurred at a rate that was 1% or more. The most common reasons for discontinuation of therapy were death and adverse experiences with Diovan were similar to placebo.

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Comparable control to high-dose CCBs with significantly less edema

- LOTREL reduces blood pressure as effectively as high-dose Norvasc® 10 mg and Procardia XL® 60 mg*¹
- Significantly less edema than Norvasc 5 and 10 mg and high-dose Procardia XL 60 mg*¹

JNC VI recommends low-dose combination therapy

“... (C)ombinations... have been shown to provide additional antihypertensive efficacy, thereby minimizing the likelihood of dose-dependent adverse effects.”²

LOTREL®
amlodipine/benazepril HCl
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* In patients who did not adequately respond to 5 mg Norvasc or 30 mg Procardia XL, respectively. LOTREL is not indicated for the initial treatment of hypertension.

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 brief summary of Prescribing Information on the adjacent page.

Norvasc (amlodipine) is a registered trademark of Pfizer Labs. Procardia XL (nilnidipine) is a registered trademark of Pratt Pharmaceuticals, a division of Pfizer, Inc.

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IMPORTANT NEW INFORMATION

LOTREL as effective as high-dose Norvasc 10 mg and Procardia XL 60 mg... with significantly less edema*¹

JNC VI endorses low-dose combination therapy²

SUPERIOR BP CONTROL AT LOW DOSES vs its components³

³ In patients who did not adequately respond to 5 mg Norvasc or 30 mg Procardia XL, respectively. LOTREL is not indicated for the initial treatment of hypertension.

* In African-American patients, virtually all of the antihypertensive effect of LOTREL 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 brief summary of Prescribing Information on last page.

LOTREL®
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2.5/10 • 5/10 • 5/20-mg capsules

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It is important to note that Loteri® is not a cure for depression or anxiety disorders. It is typically used in combination with other treatments, such as psychotherapy, lifestyle changes, and adherence to a healthy diet and exercise regimen.

Please consult with your healthcare provider for more information on the appropriate use of Loteri® and to discuss any concerns or questions you may have.

References:


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- low levels of activity
- developmental delay
- slow growth

Carnitor® is the only treatment for carnitine deficiency.

For Carnitor® Medicare reimbursement 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.
L-carnitine is not bound to plasma protein or albumin when tested at any concentration or with any species including humans. 17

Adverse reactions

Various mild gastrointestinal complaints have been reported during the long-term administration of L- or DL-carnitine. These include transient nausea and vomiting, abdominal cramps, and diarrhea. Less frequent gastrointestinal complaints include body odor, nausea, and gas. An incidence of these reactions is difficult to estimate due to the confounding effects of the many underlying pathologies (especially malnutrition) that may have been described only in uric acid patients receiving DL-carnitine.

Decreasing the dosage often diminishes or eliminates drug-related patient odor or gastrointestinal symptoms when present. Tolerance should be monitored very closely during the first week of administration, and after any dosage changes. Fecal methylmalonic acid excretion with CARNI’TOR® Oral Solution decreased in liquid might be avoided by a slow decrease in the solution or by a greater dilution.

Overdosage

There have been no reports of toxicity from carnitine overdoses. The potential toxic dose of carnitine in mice is 12.4 g/kg. Carnitine may cause diarrhea. Overdosage should be treated with supportive cares.

Doseage and administration

CARNI’TOR® Tablets.

Adults: Recommended dose for adults is 900 mg two or three times a day using the 330 mg tablets, depending on clinical responses.

Children: The recommended dose of carnitine for infants and children is between 50 and 100 mg/kg/day in divided doses, with a maximum of 3 g/day. Dosage should be reduced to 1 mg/kg/day. The exact dosage will depend on clinical responses.

Monitoring should include periodic blood chemistries, vital signs, plasma carnitine concentrations and overall clinical condition.

CARNI’TOR® Oral Solution.

For use only not for parenteral use.

Adults: The recommended dosage of carnitine is 1 to 3 g/kg a day, equivalent to 10 to 30 mL/day of CARNI’TOR® Oral Solution. Higher doses should be administered only with caution and only when and where clinical and biochemical considerations make it seem likely that higher doses will be of benefit. Dosage should start at 1 g/day (10 mL/day), and be increased slowly while assessing potential therapeutic responses. Dosage should include periodic blood chemistries, vital signs, plasma carnitine concentrations, and overall clinical condition.

Children: The recommended dosage of carnitine is 0.5 to 100 mg/kg/day, which is equivalent to 0.5 mL/kg/day CARNI’TOR® Oral Solution. Higher doses should be administered only with caution and only where clinical and biochemical considerations make it seem likely that higher doses will be of benefit. Dosage should start at 0.5 g/kg/day and be increased slowly while assessing potential therapeutic responses.

Monitoring should include periodic blood chemistries, vital signs, plasma carnitine concentrations, and overall clinical condition.

CARNI’TOR® Oral Solution may be consumed alone or dissolved in or other liquid food. Dose should be spaced every three hours (every day for three hours) preferentially during or after meals and should be consumed slowly in order to minimize tolerance.

CARNI’TOR® (L-carnitine) injection.

Pediatric uses: CARNI’TOR® (L-carnitine) injection is administered intravenously. The recommended dose is 50 mg/kg given as a slow 2-3 minute bolus injection or by infusion. Often a loading dose is given in patients with severe metabolic deficiencies known to benefit from intravenous therapy. Following 24 hours of therapy, it should be administered q3h or q4h, and never less than q4h either by intravenous or by intramuscular injection. All subsequent doses should be given in the range of 0.5 to 1 mg/kg or as therapy may require. The highest dose administered has been 300 mg/kg.

It is recommended that a plasma carnitine level be obtained prior to beginning the parenteral therapy Weekly and monthly monitoring is recommended as well. The monitoring should include: total plasma, urine, and plasma carnitine concentrations (the plasma free carnitine level should be between 30 and 60 µmol/l), and overall clinical condition.

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

Compatibility and Stability

CARNI’TOR® Injection is compatible and stable when mixed in normal saline, D5W, Ringer’s 1/5 Lactated and Ringer’s 0.9% or Lactated Ringer’s solution in concentrations ranging from 250 mg/mL to 0.5 mg/mL to 4200 mg/mL to 80 (µg/mL) and stored at room temperature (25°C) for up to 24 hours in PVC plastic bags.

How supplied

CARNI’TOR® Tablets are supplied as 330 mg unit dose tablets embossed with CARNI’TOR® S-14, 330 mg unit dose tablets embossed with CARNI’TOR® T-7, and individual blisters packaged in boxes of 90 (NDC 54442-144-09). Store at room temperature (25°C/77°F).

CARNI’TOR® Oral Solution is supplied in 16 mL (4 fl. oz.) multi-unit plastic containers. The multi-unit plastic containers are packaged 24 per case. NDC 54442-145-08. Store at room temperature (25°C/77°F).


CARNI’TOR® Injection, 200 mg per mL, is available in 5 mL single-dose ampoules packaged 5 ampoules per cartridge (NDC 54442-146-09) and 2.5 mL single-dose ampoules packaged 5 ampoules per cartridge (NDC 54442-147-09). Store in air-tight containers at room temperature (25°C/77°F) in carton until their use to protect from light. Discard unused portion of an opened ampule, as they contain no preservative.

Caution

In the U.S.A. law prohibits dispensing without prescription.

References


NEPHROLOGIST
Growing multi-specialty group seeks to add second Nephrologist. Group currently includes two-internists, a nephrologist, two pulmonologists, gastroenterologist and endocrinologist. Practice includes hemodialysis, CAPD, CAVHD and transplant follow-up, and covers 3 hospitals and two hemodialysis units. Some internal medicine is expected. Location is 90 miles north of NYC in beautiful Catskill/Hudson Valley Region close to ski resorts and other recreational activities. Excellent Financial Package leading to full partnership. Reply to: JASN Box #1-12, 351 W. Camden Street-5N, Baltimore, MD 21201-2436.

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ASSISTANT/ASSOCIATE PROFESSOR
The University of Florida seeks an Assistant/Associate Professor for a tenure track position in the Department of Medicine, Division of Nephrology. M.D., M.D./Ph.D degree with a minimum of two years of clinical experience or equivalent. Duties will include participation in the clinical, teaching and research activities of the division. The major clinical responsibility will be directed toward the renal transplant program to provide care in both the inpatient and outpatient setting. Individual will also participate in care of patients with hypertension, chronic renal failure and ESRD. An interest in clinical research would be desirable. Salary and benefits commensurate with experience. Recruiting deadline date: March 31, 1998. Anticipated starting date: July 01, 1998. Please reply with CV to Dr. R. Tyler Miller, Associate Professor, Box 100224, Division of Nephrology, JHMHC, Gainesville, FL 32610. An Affirmative Action/Equal Opportunity Employer.

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- 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.

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*The principal adverse reactions of cyclosporine therapy are renal dysfunction, tremor, hirsutism, hypertension, and gum hyperplasia.

1 For de novo patients, start with the same Neoral dosage used with Sandimmune. For maintenance patients, conversion to Neoral is generally safe and well tolerated: Start with a simple 1:1 dosage conversion to Neoral (see boxed warning). Adjust the Neoral dosage to attain preconversion blood trough concentrations. The daily dosage of Neoral should always be given in two divided doses (b.i.d.).

Please see brief summary of prescribing information, boxed warning, and reference for Neoral on the next page.
NEORAL® Soft Gelatin Capsules (cyclosporine capsules for microemulsion)

NEORAL® Oral Solution (cyclosporine oral solution for microemulsion)

Microemulsion technology

Dosing and administration

Dosing

BRIEF SUMMARY: Please see package insert for full prescribing information.

WARNING: Only physicians experienced in immunosuppressive therapy and management of organ transplant patients should administer this product. Because anaphylactic reactions can occur, adequate laboratory and support personnel should be present at the time of administration. The physician responsible for maintenance therapy should have complete information regarding side effects and appropriate emergency treatment of possible complications. Please read the package insert before dispensing this product.

INDICATIONS AND USAGE: Neoral® is indicated in patients with a hypersensitivity to cyclosporine or to any of the ingredients of the formulation.

(See Usage WARNINGS) Cyclosporine, the active ingredient of Neoral®, can cause nephrotoxicity and hypotension when used in high doses. It is not useful for serum creatinine and BUN levels to be elevated during cyclosporine therapy. These elevations in mean trough levels may not necessarily indicate rejection, and each patient must be fully evaluated before dosage adjustment is initiated.

Based on the historical Sandimmun® experience with oral solution, nephrotoxicity associated with cyclosporine has been observed in 33% of transplant 30%, 53% of cases of heart transplantation, and 53% of cases of bone marrow transplantation. Mild nephrotoxicity was generally noted 3-5 mo after renal transplant and consisted of an arrest in the rise of serum creatinine. Neoral® and Sandimmun® are not bioequivalent and cannot be used interchangeably without physician supervision. In transplant patients taking Neoral® and that dose adjustments be made in order to avoid toxicity due to high concentrations and possible organ rejection due to low concentrations. Neoral® concentrations should be used to monitor Neoral® plasma concentrations which are associated with an increased risk of fungal infections. Neoral® should be given cautiously to patients with a history of severe hypersensitivity reactions to Neoral®, oral solution, or to cyclosporine, and one that is not associated with a dose increase, the control of the trough concentration of Neoral® is critical, particularly when the trough concentration is high and/or the patient is at a high risk for rejection.

Other Immunosuppressants

Increased susceptibility to infection and the possible development of lymphoma and other neoplasms may result from the degree of immunosuppression.

Neoral® Soft Gelatin Capsules (cyclosporine capsules for microemulsion) and Neoral® Oral Solution (cyclosporine oral solution for microemulsion) are not bioequivalent. The direct conversion of Sandimmun® (cyclosporine capsules, USP) and Sandimmun® Oral Solution (cyclosporine oral solution, USP) cannot be used interchangeably without physician supervision. Neoral® and Sandimmun® are not bioequivalent and cannot be used interchangeably without physician supervision.

Drug Interactions: All of the individual drugs cited below are well substantiated to interact with cyclosporine.

Differential Doctarity

Certain Cautions: Neoral® should be used cautiously in patients with creatinine clearances less than 30 ml/min. Healthcare workers are advised to take precautions to minimize exposure to cyclosporine, in particular when opening packages or preparing the solution, because cyclosporine is highly vasoactive and can cause bronchoconstriction. Neoral® solution should not be used in infants under 2 mo of age. Neoral® solution should be kept refrigerated. The solution, once opened, should be used within 24 hours. Neoral® solution should not be used in patients with active fungal infection, as it may mask signs and symptoms of fungal infection. The drug may be used in patients with proven fungal infections after adequate therapy is given to treat the fungal infection. Neoral® solution should be prepared and the solution must be administered within 24 hours after preparation.

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Increased susceptibility to infection and the possible development of lymphoma and other neoplasms may result from the degree of immunosuppression.
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**Nephro-Vite® Rx**

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

**PRECAUTIONS:** Palic acid may partially correct the hematochemical damage due to vitamins B12 deficiency of pernicious anemia, while the associated neurological damage progresses.

**WARNING:** Palic 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 REACTIONS:** Allergic sensitization has been reported following both oral and parenteral administration of palic acid.

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

**HOW SUPPLIED:** Round, yellow tablet, film-coated. NDC 54391-1008-0. Tablets in plastic bottles of 100. A child proof safety cap is standard on each 100 tablet bottles as a safeguard against accidental ingestion by children. Store at controlled room temperature 18-30°C (68-86°F). The most recent revision of this labeling is July 1994.

**Nephro-Vite®+Fe**

**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.

**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 syphilis or iron deficiency anemia.

**PRECAUTIONS:** Palic acid may partially correct the hematochemical damage due to vitamins B12 deficiency of pernicious anemia while the associated neurological damage progresses. Palic acid is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where vitamin B12 is deficient.

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

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

**HOW SUPPLIED:** Film-coated, oval tablets marked KED. NDC 54391-1018-0. Tablets in blister packaging, sealed in foil. Two 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.


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The New York Academy of Medicine announces the 1998 Edward N. Gibbs Memorial Lectureship & Award

The New York Academy of Medicine seeks nominations for the 1998 Edward N. Gibbs Memorial Lectureship & Award in Nephrology. The Awardee will have dedicated a career to advances in Nephrology and will have made cutting-edge contributions to the field. The distinguished recipient of this honor will present a lecture describing original research at the Academy in the Fall of 1998 and will receive a medal and a monetary award of $7,500.

The Selection Committee will accept nominations through April 1, 1998. Deserving individuals must be nominated by a detailed letter outlining the importance of the work and explaining why it has been a seminal discovery in the field of Nephrology (not to exceed 3 pages). In addition, the nominee’s curriculum vitae, and the names of three persons from whom we may solicit references, must be submitted.

For further details contact: Ms. Candice Mathew (212-822-7204 or cmathew@nyam.org) at: The New York Academy of Medicine
1216 Fifth Avenue, Room 612
New York, New York 10029
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.
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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%.

**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.

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(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%.

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Training in Nephrology (Give inclusive dates for residences, fellowships, other relevant postgraduate education.)

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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.

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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.

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International Congress of Nephrology and XIth Latin American Congress of Nephrology

The International Congress of Nephrology and XIth Latin American Congress of Nephrology will be held May 2 to 6, 1999, in Buenos Aires, Argentina, with the Argentine Society of Nephrology as host society. The deadline for abstracts is September 22, 1998. For more information, contact the XVth International Congress of Nephrology, Secretariat of the Congress, Ayacucho 937, 18 G, 1111 Buenos Aires, Argentina. Telephone/fax: 54-1-812-1021; e-mail: bayfem@ibm.net.

Strategies for Influencing Outcomes In Pre-ESRD and ESRD Patients

The American Society of Nephrology (ASN), National Institutes of Health, the National Kidney Foundation, and the Renal Physicians Association will present “Strategies for Influencing Outcomes in pre-ESRD and ESRD Patients,” June 12-14, 1998, at the Sheraton hotel in Washington, D.C. This conference is a first in the history of these organizations, and a follow-up to the landmark 1989 Dallas meeting, which focused on high morbidity and mortality associated with suboptimal delivered dialysis dose and malnutrition. The objectives of this conference are to demonstrate the trends in practice that have occurred since the 1989 Dallas meeting, determine whether these trends have favorably affected outcomes, and determine areas for further improvement. Conference sessions will include “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 Anemia Control, Practices, and Outcomes;” “Pre-ESRD Care, Risk Factors and Initiation of Renal Replacement Therapy;” and “Quality Improvement.” To register, contact Charlene Murphy. Telephone: (214) 358-2300; fax: (214) 358-0486; e-mail: murphyc@dneph.com. Registration is $225.

Third European Peritoneal Dialysis Meeting

The Third European Peritoneal Dialysis Meeting will be held in Edinburgh, Scotland, on April 5–7, 1998. The meeting will focus on maintaining longevity in peritoneal dialysis. The scientific programme will include state-of-the-art lectures and symposia, free communications and poster sessions. There will also be a workshop on animal models in peritoneal dialysis and continuing medical education sessions. The second announcement, call for abstracts, and registration will be sent out in August. Dr. R. I. Winney is the local organizer and can be contacted at the Department of Renal Medicine, Edinburgh Royal Infirmary NHS Trust, Lauriston Place, Edinburgh EH3 9YW Scotland. Telephone: +44-131-536-2305/6; fax +44-131-536-1541; e-mail: R. J. Winney@ed.ac.uk. For further information, please contact Ms. Margaret Sherry, In-Conference Ltd, The Stables, 10B Broughton Street Lane, Edinburgh EH1 2LY Scotland. Telephone: +44-131-556-9245; fax +44-131-556-9638; e-mail: 100256.1750@compuserve.com.

16th Annual Meeting of the International Society of Blood Purification

The 16th Annual Meeting of the International Society of Blood Purification (ISBP) will be held October 4–6, 1998, in Newport, Rhode Island. Sir Roy Calne will deliver the annual award lecture. The annual symposia include: new directions in pre-ESRD therapies; current thinking about diabetes in renal failure; and the influence of a changing health care infrastructure on the management of kidney failure patients. There will also be free communications and poster presentations. More information, visit our website at http://www.ISBP.org or contact Michael J. Lysaght, P.O. Box 2480, Providence, RI 02906; Telephone: (401) 863-7512; fax: (401) 863-1753; e-mail: ISBP98@Brown.edu.

First International Course on Critical Care Nephrology, Vicenza, Italy

The “First International Course on Critical Care Nephrology” will be held May 20–23, 1998, in Vicenza, Italy. Experts in the field of intensive care medicine and nephrology will conduct the course, and the first Vicenza Critical Care Nephrology Award will be given to an eminent scientist in the field. For more information, contact Dr. Claudio Ronco, Department of Nephrology, St. Bartolome Hospital, via Rodolfi, 36100 Vicenza, Italy. Telephone: 39-(0)44-993652; fax: 39-(0)44-920693; e-mail: cronco@golden.it.

XVII World Congress of The Transplantation Society

The XVII World Congress of The Transplantation Society will be held July 12–17, 1998, in Montréal, Canada. The deadline for abstracts is January 19, 1998. For information, contact Lucy Felicissimo & Associates, Inc., 12,449 rue Cousineau, Montréal, Quebec, Canada H4K 1P9. Fax: 514-334-5200.

CME Credit Available for Practicing Nephrologists

Credit hours in Category I of the Physician's Recognition Award of the American Medical Association are available in a course scheduled for May 3 to 8, 1998, Copley Plaza Hotel, Boston, MA. The course, designed for the practicing nephrologist, will review pathophysiologic and clinical advances in the major areas of nephrology, including glomerular disease, fluid, and electrolyte disorders, hypertension, dialysis, and renal transplantation. It is sponsored by the Department of Continuing Education, Harvard Medical School, and the Department of Medicine, Beth Israel Deaconess Medical Center. For more information, contact Professional Meeting Planners, 5 Central Square, Suite 201, Stoneham, MA 02180. Telephone: (781) 279-9887 or 800-378-6857; fax: (781) 279-9875; e-mail: PMPMeeting@aol.com.
Second Meeting of the International Society for Apheresis (ISFA)
The second meeting of the International Society for Apheresis (ISFA) will be held April 15 to 18, 1999, in Saarbrücken, Germany. The ISFA was founded in April 1996 in Kyoto, Japan. The program will include more than 15 main topics. Plenary sessions, symposia, workshops, and oral and poster sessions are planned. Main topics include clinical results, new aspects, immunomodulation in plasmapheresis, selective separation methods, and bioreactors. Costs and benefits of plasmapheresis will also be discussed. For more information, contact Dr. Rolf Bambauer, Congress President, Talstrasse 49, 66424 Hombrug/Saar, Germany, Telephone: 06841/2081; fax: 06841/61183.

17th Annual Meeting of the North American Society for Dialysis and Transplantation
The 17th annual meeting of the North American Society for Dialysis and Transplantation will be held July 26–30, 1998, at the Ritz-Carlton, Kapalua, Maui, Hawaii. This program is designed to enhance the participant’s knowledge in nephrology, dialysis, and transplantation. For more information regarding registration and submission of abstracts, contact Wadi N. Suki or Laura Brazil, 6550 Fannin, Suite 1273, Houston, TX 77030. Telephone: (713) 790-3275; fax: (713) 790-5053.

Psychonephrology 1998, Eleventh International Conference on Psychonephrology
Psychonephrology 1998, the eleventh international conference on psychonephrology, will be held in New York City October 9–11, 1998. This meeting will cover the psychosocial and ethical issues confronting patients with renal failure and offer information for the professional people caring for these individuals. Internationally recognized experts in this area will present in plenary sessions, concurrent large sessions, small group discussions, and a debate. The keynote speaker will be Dr. Eli A. Friedman. Sixteen and a half hours of AMA Category I CMA credit are offered. Continuing education credits will also be available for social workers and nurses. Tuition is $200. For more information, including submission of abstracts for Free Communication, contact Dr. Norman B. Levy, Coney Island Hospital, 2601 Ocean Parkway, Brooklyn, NY 11235. Fax: (718) 616-5314.

Erratum
Due to an editing error, an incorrect value was given in Table 1 in the article “D-Aspartate Content of Erythrocyte Membrane Proteins Is Decreased in Uremia: Implications for the Repair of Damaged Proteins,” J Am Soc Nephrol 8: 95-104, 1997. In part B, the mean for the D-Asx/D-Asx + L-Asx (%) under Uremics should have been 0.25 ± 0.18.