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References
The Journal of the American Society of Nephrology

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References:

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

¹For 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.
**INDICATIONS AND USAGE**

Neoral is indicated for the prophylaxis of organ rejection in kidney, liver, and heart allograft recipients. Neoral has been used in combination with azathioprine and corticosteroids.

**CONTRAINDICATIONS**

Neoral is contraindicated in patients with a hypersensitivity to cyclosporine or to any of the ingredients of the formulation.

**WARNINGS**

(See boxed WARNING)

Cyclosporine, the active ingredient of Neoral, can cause nephrotoxicity and hypertension when used in high doses. It is not unusual for serum creatinine and BUN levels to be elevated during cyclosporine therapy. These elevations in some patients may not be dose related and may not necessarily indicate rejection, and each patient must be carefully evaluated before dosage adjustment is initiated.

Based on the historical Sandimmune experience with oral solution, nephrotoxicity associated with cyclosporine has been documented in rare instances in patients who were not on corticosteroids. It is possible that dose adjustments may be made in order to avoid toxicities due to high concentrations and possible organ rejection due to inadequate drug levels. In such cases, cyclosporine may need to be completely stopped, as compared to Sandimmune. If a patient who is receiving exceptionally high doses of Sandimmune is converted to Neoral, the cyclosporine concentration of the patient may be lower than with Sandimmune. If a patient who is receiving exceptionally high doses of Sandimmune is converted to Neoral, the cyclosporine concentration of the patient may be lower than with Sandimmune. These elevations were often responsive to cyclosporine dosage reduction.

Serum creatinine and BUN levels taken at any time prior to admission or taken after withdrawal of cyclosporine can be misleading. The serum creatinine and BUN levels of these patients will demonstrate one or several of the following alterations: tubular vacuolization, tubular micro- macronodular or extramicrosomal calcification, arteriopathy, and a striped form of interstitial fibrosis with tubular atrophy. Though none of these morphologic changes is entirely specific, a diagnosis of cyclosporine-associated arteriopathy should be entertained in renal biopsies from these patients.

When considering the development of cyclosporine-associated nephropathy, it is noteworthy that several authors have described a variety of renal parenchymal changes, particularly when compared to those seen in persons who are not on cyclosporine. These changes include frank interstitial fibrosis, tubular atrophy, and tubular casts. These changes may be observed on renal biopsies of patients who have been treated with cyclosporine and 1 administration of streptococcal and of the urea or analgesics, this appears to depend upon several factors. The severity of this complication is generally high circulating levels of cyclosporine. This is particularly true during the first 3 postpartum months when the dose levels tend to be highest, and in kidney recipients, the organ appears to be more susceptible to the toxic effects of cyclosporine. Among other contributing factors to the development of interstitial fibrosis in these patients are prolonged perfusion time, warm ischemia time, as well as episodes of acute toxicity, and acute and chronic rejection. The reversibility of interstitial fibrosis and its correlation to renal function have not yet been determined. Reversibility of arteriopathy has not been reported after stopping cyclosporine or lowering the dosage. In patients receiving other immunosuppressive therapies, those patients receiving cyclosporine are at increased risk for development of this arteriopathy, particularly in those patients with impaired renal function at the time of transplantation.

**WARNINGS**

(See boxed WARNING)

Occasionally patients have developed a syndrome of thrombocytopenia and microangiopathic hemolytic anemia which may result in graft failure. The vasoocclusion can occur in the absence of rejection and is accompanied by platelet consumption within the graft as demonstrated by flow techniques. Platelet counts should be performed if thrombocytopenia develops. The pathogenesis of this phenomenon is unknown. The thrombocytopenia is selflimiting and the platelet counts return to normal usually by week 4, without treatment. These patients should be treated with the same supportive measures as patients with other forms of platelet dysfunction.

**WARNINGS**

(See boxed WARNING)

Cyclosporine therapy in young children (≤16 years) with neutrophil counts <1,500/mm³ requires dose reduction. Serum cyclosporine levels below 200 ng/mL do not provide adequate immunosuppression. Serum trough levels should be kept between 100 and 200 ng/mL. Serum trough levels should be kept between 100 and 200 ng/mL. Neoral should not be used in patients with a creatinine clearance <30 mL/min.

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WARNING: Prolonged use is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where vitamin B12 is deficient. Keep out of reach of children. ADVERSE REACTION: Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

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

HOW SUPPLIED: Round, yellow tablet, film coated. NDC #04091-1009-1. Tablets in blue blister of 100. A child proof safety cap is standard on each 100 tablet bottle as a safeguard against accidental ingestion by children. Store at controlled room temperature 15-30°C (59-86°F). The most recent revision of this labeling is July, 1994.

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Angioedema may occur at any time during treatment. Discontinue LEXXEL at the first sign of angioedema and treat appropriately. It should be noted that black patients receiving ACE inhibitors have been reported to have a higher incidence of angioedema compared to non-blacks. (See WARNINGS, Angioedema.)

In clinical trials, the most common adverse events were headache, dizziness, and peripheral edema.

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INDICATIONS AND USAGE
LEXEL is indicated for the treatment of hypertension. It is not indicated for the initial therapy of patients with hypertension. If ACE inhibitors have already been used and discontinued, LEXEL may be used as an alternative treatment.

Contraindications
- ACE inhibitors are contraindicated in patients who are hypersensitive to any component of the product. Because of the component, LEXEL is contraindicated in patients with a history of angioneurotic edema related to treatment with ACE inhibitors.

Warnings
- Angiospasm: Angiospasm of the face, extremities, lips, tongue and/or glottis should be reported in patients treated with an ACE inhibitor. If angiospasm occurs, management should include immediate discontinuation of the ACE inhibitor and the use of potassium-sparing diuretics and/ or a vasodilator.

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- Renal Function: Increased serum creatinine and BUN levels have been observed in patients treated with ACE inhibitors. Therefore, treatment with ACE inhibitors should be used with caution in patients with renal insufficiency.

ADDITIONAL INFORMATION
- ACE inhibitors can cause fetal and neonatal morbidity and mortality when administered to pregnant women. Therefore, when used in pregnancy, LEXEL should be discontinued as soon as possible.

The use of ACE inhibitors during the second and third trimesters of pregnancy has been associated with fetal and neonatal morbidity and mortality, including hemolytic anemia, hyperkalemia, hypotension, and respiratory distress syndrome. These findings had been associated with fetal and neonatal morbidity and mortality, including hemolytic anemia, hyperkalemia, hypotension, and respiratory distress syndrome. These findings are consistent with fetal and neonatal thrombocytopenia. In infants who survived, transient thrombocytopenia and anemia were observed. ACE inhibitors should be discontinued as soon as possible if pregnancy is detected.

Patients and physicians should be aware, however, that oligohydramnios may appear and may persist for days or weeks even after the uterus has sustained irreversible injury. Women with history of or in whom exposure to ACE inhibitors is likely to be followed by oligohydramnios, oliguria, or anuria and/or other signs and symptoms of renal failure may require dialysis. Women exposed to ACE inhibitors should be immediately referred for the evaluation of their renal function.

Actions on the Renin-Angiotensin-Aldosterone System
- ACE inhibitors inhibit the production of angiotensin II and aldosterone. Because of this, ACE inhibitors may be used in the management of hypertension and congestive heart failure.

Hypertension: Elevation in serum potassium (greater than 5.7 mg/dL) was observed in approximately one percent of patients treated with LEXEL. Treatment of hypertension with LEXEL should be accompanied by appropriate monitoring of the patient's potassium levels. Hypertension is a common side effect of ACE inhibitors. If hypertension occurs, it should be treated with appropriate antihypertensive therapy.

Adverse Reactions
- Drug Interactions: Drug interactions may occur with LEXEL. The concomitant use of ACE inhibitors with thiazide diuretics, NSAIDs, or renin-angiotensin inhibitors may increase the risk of hyperkalemia.
- Pregnancy: Pregnancy Category B (1st trimester) and B (2nd and 3rd trimesters). See WARNINGS, Fetal/Neonatal Morbidity and Mortality. LEXEL has not been evaluated in pregnant women. Adverse events related to the use of ACE inhibitors in pregnant women have not been reported.

Preparability
- Pregnancy: Pregnancy Category B (1st trimester) and B (2nd and 3rd trimesters). See WARNINGS, Fetal/Neonatal Morbidity and Mortality. LEXEL has not been evaluated in pregnant women. Adverse events related to the use of ACE inhibitors in pregnant women have not been reported.

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LEXEL* (Enalapril Maleate-Felodipine ER) Tablets

Other clinical adverse events observed related (possibly, probably or definitely) to treatment with enalapril-felodipine ER that occurred with an incidence of less than one percent in the placebo-controlled, double-blind trial are listed below. These events are listed in order of decreasing frequency within each category. Body as a Whole: Syncope, facial edema, orthostatic effects, chest pain, Cardiac/Myocardial: Hypertension, atrial fibrillation, premonitory ventricular contraction, increased blood pressure; Digestive: Dry mouth, constipation, dyspepsia, Rhinitis, and upper respiratory infection, vomiting, diarrhea, nausea, anorectal pain; Metabolic: Gout; Miscellaneous: Neck pain, joint swelling; Nervous/Psychiatric: Insomnia, nervousness, somnolence, paresthesia, agitation, paresthesia, larynx, Ramsay-Hunt syndrome, tremor, Somnolence; Respiratory: Nasal congestion. Other adverse events reported have been seen in clinical trials with enalapril-felodipine ER (causal relationship unknown). These included: Body as a Whole: Edema, fever, upper respiratory infection, fever, influenza; Dermatologic: Rash, dry skin; Gastrointestinal: Nausea, vomiting, diarrhea, anorectal pain; General: Fatigue, pyrexia; Hematologic: Anemia; Hepatic: Jaundice; Laboratory: Elevated transaminases, hemoglobin, hematocrit, and platelets; Metabolic: Hyperglycemia; Musculoskeletal: Myalgia, weakness; Nervous/Psychiatric: Nervousness, dizziness, headache, insomnia, somnolence; Sensory: Hyperacusis, syncope, taste disturbance; Special Senses: Vision disturbances; Urinary: Frequent urination, urinary urgency, dysuria, polyuria; Urogenital: Impotence, hot flashes.

Other commonly reported adverse events were seen in clinical trials with enalapril-felodipine ER (categorization related). These included: Body as a Whole: Headache, edema, infection, flu-like syndrome, fatigue, pyrexia; Dermatologic: Rash; Gastrointestinal: Nausea, vomiting, abdominal pain; Hematologic: Anemia; Hemodynamic: Hypotension; Laboratory: Elevated transaminases, hemoglobin, hematocrit, and platelets; Metabolic: Hyperglycemia; Nervous/Psychiatric: Nervousness, dizziness, headache, insomnia, somnolence; Sensory: Hyperacusis, syncope, taste disturbance; Special Senses: Vision disturbances; Urinary: Frequent urination, urinary urgency, dysuria, polyuria; Urogenital: Impotence, hot flashes.

Warnings:

Enalapril

Enalapril has been reported in patients receiving enalapril maleate, with an incidence higher in black than in non-black patients. Angioedema associated with leukocyte edema may be fatal. If angioedema of the face, extremities, lips, tongue, glottis and/or larynx occurs, treatment with LEXEL should be discontinued and appropriate therapy instituted immediately. (See WARNINGS.) Body as a Whole: Angioedema reactions (see WARNINGS, Anaphylactic and Possibly Related Reactions). Cardiac/Myocardial: Cardiac arrest, ventricular tachycardia, angina pectoris, arrhythmias, angina pectoris, premonitory ventricular contraction, increased blood pressure; Digestive: Nausea, anorexia, pyrosis, vomiting, diarrhea, anorectal pain; Gastrointestinal: Nausea, vomiting, diarrhea, anorectal pain; General: Fatigue, fever, pyrexia, edema; Hematologic: Anemia, neutropenia, thrombocytopenia; Laboratory: Elevated transaminases, hemoglobin, hematocrit, and platelets; Metabolic: Hyperglycemia; Nervous/Psychiatric: Nervousness, dizziness, headache, insomnia; Sensory: Hyperacusis, syncope, taste disturbance; Special Senses: Vision disturbances; Urinary: Frequent urination, urinary urgency, dysuria, polyuria; Urogenital: Impotence, hot flashes.

Felodipine

Felodipine as an Extended-Release Formulation: Other adverse events that have been reported with felodipine ER, without regard to causality, are listed (in decreasing severity) below. Body as a Whole: Flu-like illness; Dermatologic: Myocardial infarction, angina pectoris, rash, arthralgia, laryngitis, premonitory pain, fever; Digestive: Gastritis, hypersensitivity; Hematologic: Anemia, neutropenia, thrombocytopenia; Laboratory: Elevated transaminases, hemoglobin, hematocrit, and platelets; Metabolic: Hyperglycemia; Nervous/Psychiatric: Dizziness, headache, anorexia, pyrosis, vomiting, diarrhea, anorectal pain; Gastrointestinal: Nausea, vomiting, diarrhea, anorectal pain; General: Fatigue, fever, pyrexia, edema; Hematologic: Anemia, neutropenia, thrombocytopenia; Laboratory: Elevated transaminases, hemoglobin, hematocrit, and platelets; Metabolic: Hyperglycemia; Nervous/Psychiatric: Nervousness, dizziness, headache, insomnia, somnolence; Sensory: Hyperacusis, syncope, taste disturbance; Special Senses:Vision disturbances; Urinary: Frequent urination, urinary urgency, dysuria, polyuria; Urogenital: Impotence, hot flashes.

References:

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
Pharmaceutical Division

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 anaphylactoid-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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For documented iron-deficiency anemia not amenable to oral therapy

**INFeD®**

Iron Dextran Injection, USP 50 mg/mL

Replaces Iron Rapidly
**Fetal Iron Transfer**

Intrauterine transfer of iron is a critical process for developing fetal hemoglobin. It involves a complex and regulated system of iron transport across the placenta. The transfer of iron from the maternal to the fetal circulation is essential for the development of the fetal liver and bone marrow, leading to the synthesis of fetal hemoglobin.

**Iron Levels**
- **Intrauterine**: Iron stores increase rapidly in the third trimester, with the highest levels noted in term infants.
- **Postnatal**: Iron stores decrease rapidly after birth, especially in premature infants, necessitating iron supplementation.

**Iron Deficiency**
- **Risk Factors**: Premature birth, low birth weight, and rapid growth are significant risk factors for iron deficiency in infants.
- **Clinical Manifestations**: Pallor, fatigue, and hypoglycemia are common symptoms associated with iron deficiency.

**Iron Administration**
- **Route of Administration**: Intravenous iron is preferred for infants with severe or life-threatening iron deficiency anemia.
- **Dosage Calculation**: The dose of intravenous iron is calculated based on the infant's weight.

**Iron Overload**
- **Clinical Implications**: Iron overload can lead to organ damage, particularly the liver, heart, and pancreas.
- **Management**: Chelation therapy with desferrioxamine is used to remove excess iron from the body.

**Safety Considerations**
- **Monitoring**: Regular monitoring of iron levels and liver function tests is essential to prevent iron overload.

**Conclusion**
- Effective management of iron deficiency in infants involves a combination of iron supplementation, careful monitoring, and consideration of iron overload risks.

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**References**
Why Try Your Patience In a Traffic Jam.

At Marshfield Clinic, there are only a few traffic lights between your practice and your patients.

While we can't guarantee you'll never have to wait at a red light on your way to work, wouldn't it be comforting to know you can leisurely prepare for your day ahead without having to calculate rush hour into your drive time.

Marshfield Clinic, one of the nation's most respected and recognized health care systems, is seeking a BC/BE NEPHROLOGIST to join our expanding practice in Rice Lake, Wisconsin.

At Marshfield Clinic/Indianhead Center, in Rice Lake, you will enjoy the autonomy of a private practice with the professional, financial and administrative resources of the main campus in Marshfield, Wisconsin. Fiber optic connection to Marshfield is available to consult with Nephrology colleagues, and on-site back up is provided for vacations and other sabbaticals.

Enjoy a lifestyle rich with recreational diversity, excellent schools and a family focus. For more information, or to send your curriculum vitae, contact Cindy M. Schuster, Physician Recruitment Manager, Marshfield Clinic, 1000 N. Oak Avenue, Marshfield, WI 54449, phone 1-800-782-8581, extension 93725. E-Mail: schustec@mlldclin.edu.

Journal of the American Society of Nephrology

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Editorial Profile: Journal of the American Society of Nephrology publishes original articles of high quality and relevant to the broad field of nephrology. Nephrology is an alliance of scientists and physicians who seek to understand the function of the kidneys and the means to improve the medical care of individuals with renal disease. Subjects appropriate for the journal include: clinical nephrology, renal and epithelial physiology, renal pathophysiology, body fluid, electrolyte and acid-base metabolism, hypertension, dialysis, and renal transplantation.

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Contacts: Journal of the American Society of Nephrology, Classified Advertising, 351 W. Camden Street, Baltimore, MD 21201-2436. Michael Faulkner - (800) 528-1843, Jason Pointe - (800) 528-5660 or Taron Butler - (800) 645-3658. Fax (410) 528-4452; E-mail: mfaulkner@wwilkins.com jpointe@wwilkins.com
DEXFERRUM®
(IRON DEXTRAN INJECTION, USP)

For effective intravenous treatment of iron deficiency anemia, it positively delivers.

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

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

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<th>Pre-study</th>
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<th>Day 30</th>
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<td>Serum TIBC (µg/dL)</td>
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<td>201.3 ± 51.6</td>
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<tr>
<td>Transferrin saturation (%)</td>
<td>14.3 ± 2.8</td>
<td>32.3 ± 13.0</td>
<td>22.9 ± 3.3</td>
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<tr>
<td>Effect of Iron Dextran (probability value)</td>
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Study was conducted to determine the rate and extent of iron utilization after administration of intravenous iron dextran and to compare the efficacy of iron dextran of different molecular weights. Twenty patients were randomized to receive either a 500 mg dose of DEXFERRUM (267,000 daltons) or INFeD (96,000 daltons) administered in five sequential 100 mg doses. Indices of iron status were examined before treatment and at weekly intervals up to four weeks later.

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

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

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

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

DEXFERRUM®
(IRON DEXTRAN INJECTION, USP)

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

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

(IRON DEXTRAN INJECTION, USP)

**WARNING**

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

**DESCRIPTION**

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

**Therapeutic Class:** Hematolytic.

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

**CONTRAINDICATIONS:** Hypersensitivity to the product. Anemia not associated with iron deficiency.

**WARNING:** SEE BOXED WARNING.

A risk of anaphylactic reactions may attend the intravenous injection of iron-carbohydrate complexes. Such complexes have been found under experimental conditions to produce serum sickness when large doses or small doses injected repeatedly at the same site were given in rats, mice, and rabbits, and possibly in humans.

The long latent period between the injection of a potential antigen and the appearance of a tumor makes it impossible to measure accurately the risk in man. There have, however, been several reports in the literature describing tumors at the injection site in animals who have previously received intravenous injections of iron-carbohydrate complexes. Large intravenous doses, such as used with total dose infusions (TDI), have been associated with an increased incidence of adverse effects. The adverse effects are usually manifested as one or more of the following symptoms: arthralgia, backache, cutaneous, diarrhea, myalgia, nausea, and vomiting. The onset is usually 36-48 hours after administration and symptoms generally subside within 3-4 days. The etiology of these reactions is not known. The potential for a delayed reaction must be considered when estimating the need for transfusion treatment.

The maximum daily dose should not exceed 5 ml, undiluted iron dextran.

This preparation should be used with extreme care in patients with serious impairment of liver function.

It should not be used during the acute phase of infectious or inflammatory disease.

Adverse reactions experienced following administration of DexFerrum may exacerbate cardiovascular complications in patients with pre-existing cardiovascular disease.

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

Anaphylactic and other hypersensitivity reactions have been reported after uneventful test doses as well as therapeutic doses of iron dextran injection. Therefore, administration of subsequent test doses during therapy should be considered. (See DOSAGE AND ADMINISTRATION Administration.)

Administration of DEXFERRUM is contraindicated in patients with a history of acute hypersensitivity reactions. (Usual adult dose: 0.5 ml of a 1:1000 solution, by subcutaneous or intravenous injection.) Note: Patients using beta-blocking agents may not respond to epinephrine and should be treated with other vasoactive agents. Patients with myocardial artery thrombosis may have an acute exacerbation of pain and swelling following the administration of DexFerrum.

**INTERACTIONS:**

**For Patients:** Patients should be advised of the potential adverse reactions associated with the use of DexFerrum.

**Drug/Laboratory Test Interactions:** Large doses of iron dextran (5 ml or more) have been reported to give a brown color to serum from a patient 4 hours after administration.

The drug may cause falsely elevated values of serum bilirubin and falsely decreased values of serum calcium.

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

Serum ferritin peaks approximately 7 to 9 days after an intravenous dose of DexFerrum and slowly returns to baseline after about 3 weeks.

Examination of the bone marrow for iron stores may not be meaningful for prolonged periods following iron dextran therapy because residual iron dextran may remain in the reticuloendothelial cells.

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

**Carboxyhemoglobin, Metabolism, Impairment Of Fertility:** See WARNINGS.

**Pregnancy:** Teratogenic Effects. Pregnancy Category D. Iron dextran has been shown to be teratogenic and embryotoxic in mice, rats, rabbits, dogs, and monkeys when given in doses of about 3 times the maximum human dose. No consistent adverse fetal effects were observed in mice, rats, rabbits, dogs, and monkeys at doses of 50 mg iron/kg or less. Field and maternal toxicity has been reported in monkeys at a total intravenous dose of 80 mg iron/kg over a 14 day period. Similar effects were observed in mice and rats on administration of a single dose of 125 mg iron/kg. Fetal abnormalities in rats and dogs were observed at doses of 500 mg iron/kg and higher. The animals used in these tests were not iron deficient. There are no adequate and well-controlled studies in pregnant women. DEXFERRUM should not be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Pregnant Use:** Not recommended for use in infants under 4 months of age. (See DOSAGE AND ADMINISTRATION ADVERSE REACTIONS: SevereReactions: Anaphylactic reactions have been reported with the use of iron dextran injection; on occasion these reactions have been fatal. Such reactions, which occur most often within the first few minutes of administration, have been generally characterized by sudden onset of respiratory difficulty and/or cardiovascular collapse. (See boxed WARNING and PRECAUTIONS: General, pertaining to immediate availability of epinephrine.)

**Chest pain, chest tightness, shock, hypotension, hypertension, tachycardia, flushing, arthralgias.** (Flushing and hypotension may occur from too rapid injection by the intravenous route.)

**Dermatologic:** Urticaria, pruritus, purpura, rash.

**Gastrointestinal:** Abdominal pain, nausea, vomiting, diarrhea.

**Hematologic:** Leukopenia, lymphopenopatHy.

**Musculoskeletal:** Arthralgia, arthritis, myalgia, muscle stiffness, joint stiffness, joint pain, joint swelling. (See PRECAUTIONS: General myalgia, backache, safer strains, lower back pain and underlying tissue dissection (including), cellulitis, swelling, inflammation, local phlebitis or at the needle injection site)

**Neurologic:** Convulsions, seizures, syncope, headache, weakness, depression, anxiety, dizziness, disorientation, numbness.

**Respiratory:** Respiratory distress, dyspnea, bronchospasm.

**Urogenital:** Hematuria.

**Delayed reactions:** Arthralgia, backache, chest, dizziness, fever, headache, malaise, myalgia, nausea, vomiting (See Warnings).

**Other:** Fabrics episodes, sweating, shivering, chills, malaise, altered taste.

**DOSAGE AND ADMINISTRATION:** Oral iron should be discontinued prior to administration of dose.

**Iron Dextran Injection, USP:** PRIOR TO RECEIVING THEIR FIRST DEXFERRUM THERAPEUTIC DOSE, ALL PATIENTS SHOULD BE GIVEN AN INTRAVENOUS TEST DOSE OF 0.5 ml. (See PRECAUTIONS: General) THE TEST DOSE SHOULD BE ADMINISTERED AT A GRADUAL RATE OVER AT LEAST 5 MINUTES. Although anaphylactic reactions have not been reported following DEXFERRUM administration, patients with a history of significant allergy should be monitored. The trial dose should be repeated if no reaction occurs 30 minutes after the first dose is given. Several cases of iron toxicity exceeding 0.2 mg/kg, or less, may be given in a single dose, and the calculated total amount required has been reached. DEXFERRUM is given undiluted at a stated number per day not to exceed 50 mg (2 ml) per minute. DEXFERRUM, if administered at a rate exceeding 50 mg (2 ml) per minute, may be given in a single dose not to exceed 50 mg (2 ml) per minute. DEXFERRUM, if administered at a rate exceeding 50 mg (2 ml) per minute, may be given in a single dose, and the calculated total amount required has been reached. Each daily dose should not exceed. 505.65 mg (26 mg of iron) for infants weighing less than 10 kg (22 lbs). In children under 10 kg (22 lbs), and 2 ml (100 mg of iron) for other patients.

Do not mix DexFerrum with other medications or add to parenteral nutrition solutions for intravenous infusion. Parenteral drug products that should be inspected visually for particulate matter and discoloration prior to administration, whenever the solution and container permit.

**HOW SUPPLIED:** DEXFERRUM Iron Dextran Injection, USP containing 50 mg of elemental iron per ml, is available in 2 ml, 5 ml, and 10 ml vials for intravenous use in 10 pack cartons (26-2024-10) and individually packaged (IND-26-2024-01). Store at controlled room temperature 15° - 30°C (59° - 86°F).

**CAUTION:** Federal law prohibits dispensing without prescription.

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

**SI2334**

Rev: 2/97

**AMERICAN REGENT LABORATORIES, INC.**

**SHIRLEY, NY 11967**
“I never liked taking shots. But now, this is so easy, I do it myself.”

It’s Already Ready.

Nutropin AQ™
[somatropin (rDNA origin) injection]
The only growth hormone that doesn’t require reconstitution.
"There's no reconstitution so it's easier to use. We like that. And so do our patients."

Fewer steps to greater convenience
Nutropin AQ eliminates all of the steps necessary for a patient or parent to reconstitute lyophilized growth hormone.

Reduces time to train patients and parents
Nutropin AQ significantly reduces training time compared to lyophilized growth hormone products.

Ideal for families who are new to growth hormone therapy
Nutropin AQ is ideal for new starts and for families challenged by reconstitution of lyophilized growth hormone products.

"It's easier to train families to use AQ. And that saves me time!"

It's Already Ready.™

Nutropin AQ™
[somatropin (rDNA origin) injection]

For more information, contact your Genentech representative or call Genentech Customer Service at 1-800-551-2231.

Please see accompanying full prescribing information for Nutropin AQ.
Nutropin AQ® (somatropin (rDNA origin) injection) is also indicated for the long-term treatment of short stature associated with Turner syndrome.

CONTRAINDICATIONS
Nutropin AQ should not be used in subjects with closed epiphyses.

Nutropin AQ® (somatropin (rDNA origin) injection) should not be used in patients with active neoplasia. Growth hormone therapy should be discontinued if evidence of neoplasia develops.

WARNINGS
None.

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

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

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

Patients with growth failure secondary to chronic renal insufficiency should be examined periodically for evidence of progression of renal osteodystrophy. Slipped capital femoral epiphysis or avascular necrosis of the femoral head may be seen in children treated with growth hormone. X-rays of the hips should be obtained prior to initiating therapy for CRI patients. Physicians and parents should be alerted to the development of a limp or complaints of hip or knee pain in patients treated with Nutropin AQ.

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

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

Patients with Turner syndrome should be evaluated carefully for uterine media and other ear disorders since these patients have an increased risk of ear or hearing disorders. In a randomized-controlled trial, there was a statistically significant increase in hearing thresholds in untreated controls, in uterine media (47% vs. 25%) and in ear disorders (18% vs. 7%) in patients receiving growth hormone. In addition, patients with Turner syndrome should be monitored closely for cardiovascular disorders (e.g., stroke, aortic aneurysm, hyperlipidemia) as these patients are also at risk for these conditions.

Intracranial hypertension (IH) with papilledema, visual changes, headache, nausea and vomiting has been reported in a small number of patients treated with growth hormone products. Symptoms usually occurred within the first eight (8) weeks of the initiation of growth hormone therapy. In all reported cases, HI-associated signs and symptoms resolved after termination of therapy, generally within a period of one year. While the recommendation of patients is recommended at the initiation and periodically during the course of growth hormone therapy. Patients with CRI and Turner syndrome may be at increased risk for development of IH.

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

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

Unlimited hypothyroidism presents optimal response to Nutropin AQ Therapy. Patient with Turner syndrome have an inherently increased risk of developing autoimmune thyroid disease. Changes in thyroid hormone laboratory measurements may develop during Nutropin AQ treatment. Therefore, patients should have periodic thyroid function tests and should be treated with thyroid hormone replacement if indicated.

Drug Interaction: The use of Nutropin AQ® (somatropin (rDNA origin) injection) in patients with CRI undergoing glucocorticoid therapy has not been evaluated. Concomitant glucocorticoid therapy may inhibit the growth-promoting effect of Nutropin AQ. If glucocorticoid replacement is required, the glucocorticoid dose should be carefully adjusted.

There was no evidence in the controlled studies of somatropin's interaction with drugs commonly used in CRI patients. Limited published data indicate that growth hormone treatment increases cytochrome P450 (CYP450) mediated antiparasite clearance with a potential for drug interactions. Nutropin AQ administration may alter the clearance of some drugs known to be metabolized by CYP450 liver enzymes (e.g., corticosteroids, amiodarone, anticoagulants, cyclosporine). Careful monitoring is advisable when GH is administered in combination with other drugs known to be metabolized by CYP450 liver enzymes.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenicity, mutagenicity and reproduction studies have not been completed with Nutropin AQ.

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

Nursing Mothers: It is not known whether Nutropin AQ is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Nutropin AQ is administered to a nursing mother.

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

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

ADVERSE REACTIONS
As with all protein pharmacologicals, a small percentage of patients may develop antibodies to the protein. Growth hormone antibody binding capacities below 2 mU/L have not been associated with growth attenuation. In some cases when binding capacity decreases and growth rate has been observed, in clinical studies of patients that were treated with Nutropin AQ® (somatropin (rDNA origin) injection) for the first time, GHD/17 growth hormone deficient (GHD) patients, GHD CRI patients and GHD Turner syndrome patients screened for antibody production developed antibodies with binding capacities below 2 mU/L, at the end of study in patients that were treated with Nutropin AQ® (somatropin (rDNA origin) injection) for the first time, GHD patients screened for antibody production, for up to 15 months, developed antibodies to the biopharmaceutical product.

Additional short-term immunogenic and renal function studies were carried out in a group of patients with CRI after approximately one year of treatment to detect other potential adverse effects of antibodies to growth hormone. Testing included measurements of C1q, C3, C4, rheumatoid factor, creatinine, creatinine clearance, and BUN. No adverse effects of growth hormone antibodies were noted.

In addition to an evaluation of compliance with the prescribed treatment program and thyroid status, testing for antibodies to human growth hormone should be carried out in any patient who fails to respond to therapy.

Injection site discomfort has been reported. This is more commonly observed in children switched from another growth hormone product to Nutropin AQ.

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

Other adverse drug reactions that have been reported in growth hormone-treated patients include the following:
1. Metabolic: hypoglycemia, mild and transient peripheral edema. 2. Musculoskeletal: Arthralgia, rare carpal tunnel syndrome. 3. Skin: Rare increased growth of pre-existing nevus, patients should be monitored carefully for malignant transformation. 4. Endocrine: Rare gynecomastia, rare pancreatitis.

OVERDOSAGE
The recommended dosage for growth hormone deficiency is up to 0.30 mg/kg (approximately 90 mU/kg) of body weight weekly. The recommended dosage for chronic renal insufficiency is up to 0.35 mg/kg (approximately 1.05 mU/kg) of body weight weekly. The recommended dosage for Turner syndrome is up to 0.375 mg/kg (approximately 1.25 U/kg) of body weight weekly. Long-term overdosage could result in signs and symptoms of gigantism and/or acromegaly consistent with the known effects of excess human growth hormone.

DOSAGE AND ADMINISTRATION
The Nutropin AQ® (somatropin (rDNA origin) injection) dosage and administration schedule should be individualized for each patient. Therapy should not be continued if epiphyseal fusion has occurred. Response to growth hormone therapy tends to decrease with time. However, failure to increase growth rate, particularly during the first year of therapy, suggests the need for close assessment of compliance and evaluation of other causes of growth failure, such as hypothyroidism, endocrine function, and advanced bone age.

 Agents
Growth Hormone Deficiency (GHD)
A weekly dosage of up to 0.30 mg/kg (approximately 90 mU/kg) of body weight divided into daily subcutaneous injections is recommended.

Chronic Renal Insufficiency (CRI)
A weekly dosage of up to 0.35 mg/kg (approximately 1.05 mU/kg) of body weight divided into daily subcutaneous injections is recommended.

Nutropin AQ therapy may be continued up to the time of renal transplantation.

In order to optimize therapy for patients who require dialysis, the following guidelines for injection schedule are recommended:
1. Hemodialysis patients should receive their injection at night just prior to going to sleep or at least 3-4 hours after hemodialysis to prevent hematuria formation due to the heparin.
2. Chronic Cycling Peritoneal Dialysis (CCPD) patients should receive their injection in the morning after they have completed dialysis.
3. Chronic Ambulatory Peritoneal Dialysis (CAPD) patients should receive their injection in the evening at the time of the overnight exchange.

Turner Syndrome
A weekly dosage of up to 0.375 mg/kg (approximately 1.25 U/kg) of body weight divided into equal doses 3 to 7 times per week by subcutaneous injection is recommended.

Adulthood
The solution should be clear immediately after removal from the refrigerator. Occasionally, after refrigeration, you may notice that small colorless particles of protein are present in the solution. This is not unusual for solution containing proteins. Allow the vial to come to room temperature and gently swirl. If the solution is cloudy, the contents MUST NOT be injected.

Before needle insertion, wipe the septum of the Nutropin AQ® (somatropin (rDNA origin) injection) vial with rubbing alcohol or an antiseptic solution to prevent contamination of the contents by microorganisms that may be introduced by repeated needle insertions. It is recommended that Nutropin AQ be administered using sterile, disposable syringes and needles. The syringes should be of small enough volume that the prescribed dose can be drawn from the vial with reasonable accuracy.

STABILITY AND STORAGE
Vial contents are stable for 28 days after initial use when stored at 2-8°C/36-46°F (under refrigeration). Avoid freezing the vial of Nutropin AQ.

HOW SUPPLIED
Nutropin AQ is supplied as 10 mg (approximately 30 IU) of sterile liquid somatropin per vial.

Each carton contains six single vial cartons containing one 2 mL vial of Nutropin AQ® (somatropin (rDNA origin) injection) (5 mg/mL). NDC 50342.114-11

Nutropin AQ® (somatropin (rDNA origin) injection) manufactured by:

460 Post Street San Bruno Boulevard
South San Francisco, CA 94080-4990

OBIKA

G71146-R1

G60342-101

LP1129

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Revised March, 1997
**DESCRIPTION**

Nutropin AQ® (somatropin [DNA origin] injection), is a human growth hormone (hGH) produced by recombinant DNA technology. Nutropin AQ has 19 amino acid residues and a molecular weight of 22,125 daltons. The amino acid sequence of the product is identical to human growth hormone. The protein is produced using a baculovirus expression system with an E. coli cell line as a producer consisting of the hGH molecule preceded by the signal sequence from an E. coli cell. This precursor is cleaved and the signal removed and the mature protein is isolated from the periplasmic space so that the protein is folded appropriately as it is synthesized.

**PHARMACOLOGY**

Nutropin AQ is a highly purified preparation. Biological potency is determined by measuring the increase in body weight observed in hypophysectomized rats. Nutropin AQ may contain not more than fifteen percent undissociated growth hormone as determined by the deamidated form of growth hormone has been extensively characterized and has been shown to be safe and fully active.

**CLINICAL PHARMACOLOGY**

**General**

In vivo and in vitro, preclinical, and clinical testing have demonstrated that Nutropin AQ is therapeutically equivalent to pituitary-derived human growth hormone. Treatment of patients who lack adequate endogenous growth hormone secretion, patients with Turner Syndrome, or those with growth hormone deficiency due to hypopituitarism, is associated with chronic, severe, and potentially life-threatening conditions. Treatment of adolescent patients with growth hormone deficiency is associated with chronic, severe, and potentially life-threatening conditions.

**Actions that have been demonstrated for Nutropin AQ, somatropin, somatotropin and/or pituitary-derived human growth hormone include:**

1. **Tissue Growth (1)-** Skeletal Growth: Nutropin AQ stimulates skeletal growth in patients with growth hormone deficiency as a result of a lack of adequate secretion of endogenous growth hormone or secondary to chronic renal insufficiency and in patients with Turner Syndrome. Skeletal growth is the major effect of growth hormone at the end of the first year of therapy. Increase in length and improvement in clinical status of patients with Turner Syndrome are also apparent. Growth hormone and metabolism of epiphyseal plate cartilage are directly stimulated by growth hormone and one of its mediators, insulin-like growth factor-I (IGF-I). Serum levels of insulin-like growth factor-I, insulin-like growth factors, and insulin-like growth factor-binding proteins are increased during treatment with growth hormone.

2. **Cardiovascular Homeostasis:** Nutropin AQ is a modulator of carbohydrate metabolism. For example, patients with inadequately controlled growth hormone deficiency have improved glucose tolerance. The protein is synthesized and released in the circulation in response to growth hormone. This results in linear growth until these growth plates fuse at the end of puberty. 2) Cell Growth: Treatment with pituitary-derived human growth hormone results in an increase in both the size and the number of skeletal muscle cells. 3) Organ Growth: Growth hormone of human pituitary origin influences the size of internal organs, including bone mass, muscle mass, and organ mass.

3. **Hypophyseal Hormone:** Nutropin AQ does not contain a hypophyseal hormone.

4. **Neuroendocrine:** Nutropin AQ stimulates the synthesis of corticosteroids and collagen in addition to effects on the normal range.

5. **Lipid Metabolism:** Acute administration of pituitary-derived human growth hormone is recognized as an acute metabolic effect and is associated with increased glucose metabolism and utilization.

6. **Insulin Resistance:** Insulin resistance is the most pronounced of all the metabolic effects; however, insulin sensitivity is not significantly altered in these patients. Saline repletion also occurs. (See PRECAUTIONS: Laboratory tests.)

**Tissue Growth (1)**

Nutropin AQ® stimulates the synthesis of chondroitin sulfate and collagen along with the normal range of hyaluronic acid.

**Pharmacokinetics**

**Subcutaneous Absorption:** The absolute bioavailability of recombinant human growth hormone (rGH) after subcutaneous administration in healthy adult males has been determined to be 81% ± 20%. The mean terminal t1/2 after subcutaneous administration is significantly longer than that seen after intravenous administration (2.3 ± 0.4 hrs vs. 19.5 ± 3.1 hrs) indicating that the subcutaneous absorption of the component is slow and rate-limiting.

**Distribution:** In normal adults, growth hormone levels are low in the portal vein but high in the systemic circulation.

**Elimination:** The mean terminal t1/2 after intravenous administration of rGH in healthy adult males is estimated to be 19.5 ± 3.1 minutes. Clearance of rGH after intravenous administration in healthy adults and children is reported to be in the range of 116–174 mL/hr/kg.

**Benevolence of Formulations:** Nutropin AQ® (somatropin [DNA origin] injection) has been determined to be bioequivalent to Genotropin® (somatropin [DNA origin] injection) based on the statistical evaluation of AUC and Cmax of N=30.

**Special Populations**

**Pediatric:** Available literature data suggest that rGH clearance is similar in adults and children.

**Gender:** No data are available for comparison of the rGH in adults and children. Growth hormone is a peptide hormone and is subject to the normal variability of the population and, therefore, cannot be used as a reference value.

**Race:** Reported values for height of adult males are not different from normal values for black males. The data are comparable to those observed in white adults and children.

**Growth Hormone Deficiency (GHD):** Reported values for clearance of rGH in adults and children with GHD range from 135–743 mL/hr/kg and are similar to those observed in healthy adults and children. Mean terminal t1/2 values following

**Ninhydrase and subcutaneous administration in adult and pediatric GHD patients are also similar to those observed in healthy adult males.

**Residual Insensitivity:** Children and adults with chronic renal failure (CRF) and end-stage renal disease (ESRD) tend to have decreased growth hormone secretion. Endogenous growth hormone levels also increase in some individuals with CRF. However, no rGH accumulation has been reported in children with CRF or ESRD treated with current regimens.

**Turner Syndrome:** Nutropin AQ® is pharmacodynamic available for use in children with Turner Syndrome (CRF) who may be deficient in growth hormone. The data are comparable to those observed in healthy adults and children. Mean terminal t1/2 values following

**Ninhydrase and subcutaneous administration in adult and pediatric GHD patients are also similar to those observed in healthy adult males.

**Efficiency Studies**

**Effects of Nutropin AQ® (somatropin [DNA origin] injection) on Growth Parameters**

**In adult growth hormone deficient (IGH) patients:**

- **Two multicenter, randomized, controlled clinical trials were conducted to determine whether treatment with Nutropin prior to renal transplantation in children with chronic renal insufficiency could improve their growth rates and height deficit.**

- **One study developed patient cohorts at the time of transplantation and the second was a randomized, controlled trial.**

- **In both controlled studies, patients were randomized to either receive Nutropin (n=27) or placebo (n=15).**

- **The second peak growth rate was 8.7 cm/year for the Nutropin-treated group compared with 5.5 cm/year for the control group (p<0.005).**

- **There was a significant increase in mean height standard deviation (SD) at 2 years in the Nutropin group (-0.9 cm vs. +3.6 cm, p<0.0005).**

- **The mean third year growth rate of 7.6 cm/year in the Nutropin-treated patients (n=27) suggests that Nutropin stimulates growth hormone secretion after two years of participation.**

**The height gain was accompanied by appropriate advancement of pubertal age.**

**These studies demonstrate that NADH (somatropin [DNA origin] injection) for injection had no effect on weight gain.**

- **These results were consistent with the finding that renal failure patients continue to grow without transplantation.**

**Pre-Transplant Growth**

The North American Pediatric Transplant Cooperative Study (NAPTS) has reported data for growth post-transplant in children who did not receive growth hormone. The average change in height 50 score during the first two years post-transplant was 0.18 ± 0.30 m/year. (Felmley. 1992:957-965).**

- **Controlled studies of growth hormone treatment for the short stature associated with CRF were not designed to compare the growth effects of recombinant rGH in children with other growth hormone scaffolds.**

- **Data from other studies have shown that rGH treatment in children with CRF leads to an increase in mean height (SD) at 2 years of 0.9 cm/year (p<0.005).**

**In the studies of BS-022 and BS-044, the effect of long-term growth hormone treatment (0.375 mg/kg/week given every 3 times per week or daily) on adult height was determined by comparing adult height in the treated patients with those of age-matched historical controls with Turner syndrome who never received any growth-promoting therapy.**

- **In both studies, BS-022 and BS-044, the greatest improvement in adult height was observed in patients who received early growth hormone treatment and estradiol treatment after adolescence.**

- **In a randomized blinded dose-response study, GHD patients were treated from a mean age of 11.2 years for a mean duration of 5.9 years.**

- **The mean final height for those treated for 5 years was 147.1 cm (±2.1 cm). By analysis of variance, the effect of four groups of treatment after 5 years was 147.1 cm (±2.1 cm).**

- **In the studies of BS-022, BS-023 and BS-044, the greatest improvement in adult height was observed in patients who received early growth hormone treatment and estradiol treatment after adolescence.**

**INDICATIONS AND USAGE**

Nutropin AQ® (somatropin [DNA origin] injection) is indicated for the long-term treatment of growth failure due to a lack of adequate endogenous growth hormone secretion.

Nutropin AQ® (somatropin [DNA origin] injection) is also indicated for the treatment of growth hormone deficiency associated with chronic renal insufficiency.
The 1996 ASN Board Review Course has Expanded to...

The 1997 ASN Board Review and Update
August 23-29, 1997
Palace Hotel
San Francisco

Since board certification exams are given annually, the ASN will now offer its board review each year. The enormously successful 1996 course program has been expanded for 1997 to include an update for more senior nephrologists. Advanced workshops will be presented concurrently with the main review. This new format will allow you to shape your own course. Certified nephrologists may now obtain what information they need from the board review and choose to attend some or all of the advanced workshops. Highlights of the 1997 program include:

**Board Review:**
- 48 hours of teaching and 48 continuing medical education (CME) credits
- Three full days, three half days (more time to see San Francisco)
- New topics: Pregnancy, Resistant Hypertension
- Audience Response Pads
- Two exams

**Advanced Workshops:**
- 15 additional hours of teaching
- Ten 1½-hour workshops with ten new topics
- Cutting-edge updates

Course Director:
Robert G. Narins, M.D.

Faculty:
*T. Andreoli, Little Rock, Ark.
A. Arieff, San Francisco, Calif.
G. Appel, New York, N.Y.
P. August, New York, N.Y.
H. Black, Chicago, Ill.
J. Breyer, Nashville, Tenn.
F. Coe, Chicago, Ill.

M. R. First, Cincinnati, Ohio
*R. Glassock, Lexington, Ky.
T. Golper, Little Rock, Ark.
M. Halperin, Toronto, Ont.
K. Hruska, St. Louis, Mo.
R. Johnson, Seattle, Wash.
B. Kahan, Houston, Texas
N. Kaplan, Dallas, Texas
S. Moe, Indianapolis, Ind.
B. Myers, Stanford, Calif.
B. Peraino, Pittsburgh, Pa.

M. Pohl, Cleveland, Ohio
H. Remke, Boston, Mass.
B. Rose, Boston, Mass.
R. Rubin, Boston, Mass.
J. Verbalis, Washington, D.C.
D. Wannock, Birmingham, Ala.
C. Wilcox, Washington, D.C.
R. Zager, Seattle, Wash.

* Denotes ASN past president.

Enrollment is limited!
For information or to request a brochure, contact:

American Society of Nephrology
Telephone: 202/857-1190 • Fax: 202/429-5112 • E-mail: asn@sba.com
Stretch Grafts:

A six-year experience with 310 GORE-TEX* Vascular Grafts showed a statistically significant improvement in primary patency and cumulative graft survival with the GORE-TEX Stretch Vascular Graft over the non-stretch grafts. In fact...“this graft may be comparable to the Brescia-Cimino fistula in long-term survival.”

DIASTAT Grafts:

Typical time to hemostasis post-dialysis for ePTFE grafts is between 10-15 minutes and sometimes longer. It is reported that with the DIASTAT Vascular Access Graft, time to hemostasis was less than 15 minutes in all patients and usually ranged between 2-4 minutes. The DIASTAT graft may be cannulated within one week of implantation using appropriate techniques.
A Future Of Choices.

Ringed Grafts:
Many surgeons use FEP-Ringed GORE-TEX Vascular Grafts to cross the knee in peripheral arterial reconstruction. This illustration depicts a method for using these grafts to prolong the life of forearm access grafts.⁴

Tapered Grafts:
The 4-7mm Tapered GORE-ThX Vascular Graft...“appears to be the most successful available prophylaxis against steal phenomenon.”⁵

³. W.L. Gore & Associates, Inc. Technical Supplement #985A.
Nephrologist

Growing multi-specialty group seeks to add second Nephrologist. Group currently includes two-internists, a nephrologist, pulmonologist, 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, 351 W. Camden Street-5N, Baltimore, MD 21201-2436.

New York State (Upstate)

100% nephrology practice with 5 other nephrologists. Over 300 patients on dialysis; very busy practice; all aspects of nephrology including transplantation; teaching option. Superb group with unique compensation plan rewards all physicians for group’s success. Live in one of the most beautiful, culturally exciting areas of New York State. Richard Glehan, EG Todd Physician Search, 914-273-5666, Fax: 914-273-5895, e-mail: egtodd@w-w-w.com, Web: w-w-w.com/egtodd.

Fellow-Trained Associate

Excellent Opportunity for a fellowship-trained associate to join a well established private Nephrology practice located in Richmond, Virginia. Salary plus bonus (2 year contract) with complete benefits. Call 1:6. For more information, call on Columbia at 1-888-COL-DOCS (1-888-265-3627), send your CV to Columbia Physician Recruitment, One Park Plaza, Nashville, TN 37203, Attn: KM0797ASN, fax your CV to 1-615-344-2754 or visit our web site at http://www.columbia.net.

Gundersen Lutheran is seeking a Board Certified/Board Eligible General Nephrologist. Gundersen Lutheran is a multi-specialty group practice with over 300 physicians. We are a modern, state of the art facility adjacent to a 402-bed hospital with Level II Trauma Center. In addition, the Gundersen system includes 36 regional community clinics based throughout western Wisconsin, eastern Minnesota and northeast Iowa.

La Crosse, Wisconsin nestled between towering bluffs is located where the Mississippi, La Crosse and Black Rivers merge. The area was untouched by the glaciers, leaving many hills and valleys as an outstanding scenic area. The metropolitan area of La Crosse, with its 100,000 people, offers exceptional year round opportunities for recreational activities.

Gundersen Clinic offers excellent working conditions and fringe benefits. Salaries are competitive. Interested candidates should send a letter of application and curriculum vitae to Frank Perez-Guerra, Manager, Recruitment, Retention and Resource Planning, Gundersen Lutheran, 1836 South Avenue, La Crosse, WI 54601; or call Frank Perez-Guerra at 1-800-362-9567.

Nephrology Private Practice Opportunities

Seeking BC/BE Nephrologist for private practice opportunities nationwide. Positions range from hospital sponsored solo practices to group practices. To discuss your personal and professional needs contact:

Carolyn Strasbaugh or Treg Fuller
Nephrology Recruitment Specialists

Medical Staffing Associates, Inc.
8614 Westwood Center Drive, Suite 320, Vienna, VA 22182
Phone (800) 235-5105 * Fax (703) 893-7358

Nephrologist

BC/BE to join two Nephrologists in well-established practice in dynamic West Central Georgia. Excellent income and benefits and early partnership opportunity in our 30-physician multi-specialty group.

Fax CV to (706) 321-0470.
Application for Active and Corresponding Membership

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**Business Telephone**

**Business Fax**

**E-mail Address**

**Date of Birth**

**Sex**

**Country of Citizenship**

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

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

**Academic Appointment:**

- Full Time
- Part Time
- None

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

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

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

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

<table>
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<tr>
<th>Clinical</th>
<th>Research</th>
<th>Teaching</th>
<th>Administration</th>
<th>Other</th>
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</table>

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

**Institutional Name/Address**

**Degree**

**Dates**

**For office use only:**

ID#

Date entered:

Check#

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

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<thead>
<tr>
<th>Institution Name and Address</th>
<th>Position</th>
<th>Preceptor(s)</th>
<th>Inclusive Dates</th>
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List your five most significant publications.

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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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List other societies to which you belong.

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

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

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

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

- ✔ Visa
- ❏ MasterCard

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<th>Signature</th>
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