ANNOUNCEMENTS

NHLB-FUNDED STUDY OF CHRONIC THROMBOCYTOPENIA CALL FOR PATIENTS

Patients will be evaluated and treated locally. To be eligible, they must have a platelet count \( \leq 30,000 \); failed corticosteroids and splenectomy; or splenectomy contraindicated.

For more information, please contact: Craig S. Kitchens, MD, Professor of Hematology, Chief of Medicine, Gainesville Veterans Administration Medical Center. Telephone: (904) 374-6016. Or contact Mary S. Aplin, MD. Telephone: (904) 392-4630.

Stohlman Foundation and the Leukemia Society of America present the
FIFTEENTH ANNUAL FREDERICK STOHLMAN, JR, MD MEMORIAL SYMPOSIUM: AN INTERNATIONAL SYMPOSIUM ON THE BIOLOGY OF HEMATOPOIESIS

Topics: Tissue culture systems for purified stem cell; surface molecules and cellular differentiation; matrix components and cell surface glycoconjugates; hematopoietic growth factor receptors; second messenger signalling symptoms; recombinant growth factors; gene transfer and expression in hematopoietic cells; transcriptional and translational control of hematopoiesis; ethical considerations of human gene therapy; megakaryocytepoiesis; radiation injury and bone marrow function; and clinical trials of hematopoietic growth factors.

Location: Royal Sonesta Hotel, Cambridge, MA
Dates: October 15-20, 1989

Deadlines: Deadline for abstracts for Poster Session is June 1, 1989. ASH format on 8½ \( \times \) 11 white paper and less than 350 words. Include title of poster; all authors; and name, address, and phone number of contact person. Deadline for Registration is September 1, 1989. Registration is limited to 250.

CME credits-30 hours--Category I for Physician’s Recognition Award of AMA.
For more information about registration and abstracts please contact: Bernadette Stohlman-Trenholm, 736 Cambridge St, Boston, MA 02135. Telephone (617) 789-2494.

FIFTH ANNUAL SYMPOSIUM
MOLECULAR BIOLOGY OF HEMATOPOIESIS

July 10-12, 1989
University of Innsbruck, Austria

Abstract Deadline: April 28, 1989
For program details and registration form, please apply to: G. Konwalinka, Department of Internal Medicine, University of Innsbruck, 6020 Innsbruck, Austria. Telephone: 5222-504-3255. Or contact N. Abraham, New York Medical College, Valhalla, NY 10595. Telephone: (914) 993-4426.
NATIONAL PEDIATRIC BLOOD CLUB
AMERICAN PEDIATRIC SOCIETY/SOCIETY PEDIATRIC RESEARCH
Clinical Spectrum Of Iron Overload, Novel Uses Of Iron Chelators, And Potential Treatment
Of Pediatric Anemias With Erythropoietin

May 1, 1989
8:00 to 10:00 PM
Sheraton Washington Hotel
Washington DC

Chairman: Mitchell S. Cairo MD, Childrens Hospital of Orange County, University of California, Irvine.
Program: Clinical Spectrum and Management of Iron Overload: Alan Cohen MD, Childrens Hospital of Philadelphia, University of Pennsylvania; Novel Uses of Iron Chelators: Immunosuppressant and Antiproliferative: Ken Weinberg MD, Childrens Hospital of Los Angeles, University of Southern California; Erythropoietin and Anemia of Prematurity: Kevin Shannon MD, University of California, San Francisco; and Erythropoietin and Hemoglobin F Regulation: George Stamatoyannopoulos MD, University of Washington.
Sponsored by Sandoz Pharmaceuticals.

1989 BLOOD COAGULATION CONFERENCE
May 1-5, 1989

Seventh Annual Techniques Workshop (May 1-2)
Course Director: Dr Houria I. Hassouna

Twenty-third Annual Blood Coagulation Course (May 3-5)
Course Director: Dr John A. Penner

Sponsored by Michigan State University, College of Human Medicine.
For additional information please contact: Martha J. Muth, Conference Coordinator, PO Box 6370, East Lansing, MI 48826. Telephone: (517) 353-9092.

FIRST INTERNATIONAL SYMPOSIUM ON HIRUDIN

June 23-24, 1989
Frankfurt, West Germany

Topics: Pharmacologic and biochemical profile; mode of action of hirudin; platelet interactions with hirudin; assay methods for hirudin; practical considerations in the development of hirudin; preclinical studies; status of clinical trials; hirudin as a reagent; comparative studies with other anticoagulants; future of hirudin; standardization of hirudin.

The First International Symposium on Hirudin is organized in conjunction with the German Society of Angiology and all interested individuals are cordially invited to attend. The symposium will take place at the Old Opera House in the center of Frankfurt. The official language of this symposium is English and abstracts for poster presentation are being accepted at this time.

For further information on the meeting and registration, please contact: Professor H.K. Breddin, J.W. Goethe University Center for Internal Medicine, Section of Angiology, Theodore Stern KA1 6000, Frankfurt, West Germany; or Dr J. Fareed, Hemostasis Research Laboratories, Department of Pathology, Loyola University Medical Center, 2160 S First Ave, Maywood, IL 60153.
DEVELOPMENT OF NON-HEPARIN GLYCOSAMINOGLYCANS AS THERAPEUTIC AGENTS

May 12-13, 1989
Hyatt Oak Brook Hotel
Oak Brook, Illinois

SPEAKERS

T. Ban, Nashville, TN
S. Beguin, Maastricht, Netherlands
P. Bianchini, Corlo, Italy
B. Boneu, Toulouse, France
K. Breddin, Frankfurt, West Germany
B. Casu, Milan, Italy
G. Celesia, Maywood, IL
J. Choay, Paris, France
U. Cornelli, Abano Terme, Italy
E. Coyne, Maywood, IL
C. Dietrich, Sao Paulo, Brazil
H. Engelberg, Beverly Hills, CA
J. Fareed, Maywood, IL
S. Fredd, Washington, DC
C. Hemker, Maastricht, Netherlands
D. Hoppensteadt, Maywood, IL
L. Jaques, Saskatoon, Saskatchewan, Canada
R. Klauser, Munich, West Germany
R. Linhardt, Iowa City, Iowa
S. Lorens, Maywood, IL
P. Lucchelli, Milan, Italy
J. Maffrand, Toulouse, France
J. Mardigian, Paris, France
H. Messmore, Maywood, IL
D. Meuleman, Oss, Netherlands
H. Moelker, Oss, Netherlands
F. Ofosu, Hamilton, Ontario, Canada
W. Raake, Munich, West Germany
M. Samama, Paris, France
E. Sache, Paris, France
E. Stemberger, Munich, West Germany
D. Tollefsen, St. Louis, MO
G. Torri, Milan, Italy
J. Walenga, Maywood, IL
T. Yin, St. Louis, MO

Topics: Dermatans, heparans and related agents, chondroitin sulfates and derivatives, synthetic hypersulfated compounds, sulfomucopolysaccharide mixtures, basis of the antithrombotic actions of GAGS, Alzheimer's disease and vascular deficit, clinical trials with GAGS.

All interested individuals are welcome to participate in this open meeting. The attendance is limited to the first 200 registrants. Final program and detailed instructions will be available in mid-February.

For registration and further information, please contact: Dr. J. Fareed, Loyola University Medical Center, 2160 S First Ave, Maywood, IL 60153. Telephone: (312) 531-3256, Facsimile: (312) 531-2115.

REGISTRATION FORM

Name: __________________________________________

Address: _______________________________________

Affiliation and Title: ______________________________

Phone: ___________________ FAX: __________________

Areas of Interest: __________________________________
STANDARDIZATION OF ANTITHROMBOTIC DRUGS: ARE CURRENT PRACTICES RELEVANT?

May 11, 1989
1:30 to 4:30 PM
Loyola University Medical Center
Stritch School of Medicine
Lower Level Amphitheater
Maywood, Illinois

Chairman: J. Fareed and H.C. Hemker.
Moderator: S. Fredd.

Topics: Low molecular weight heparins; Dermatan and related heparinoids; synthetic antithrombotic agents; recombinant hirudin; Defibrotide.

The basic purpose of this workshop is to discuss the current difficulties in the standardization of newer antithrombotic drugs. The question of the current methods utilized by various agencies such as WHO, NIBSC, Pharmacopeial, and other organizations will be discussed. This meeting is open and sponsored solely by the Hemostasis Research Laboratory of Loyola University Medical Center.

For further information, please call: E. Grzeda at (312) 531-3256.

EIGHTEENTH ANNUAL MEETING OF THE INTERNATIONAL SOCIETY FOR EXPERIMENTAL HEMATOLOGY (ISEH)

July 16-20, 1989
Paris, France

For further information, please contact: Convergences, ISEH 89, 16, rue Jean Jacques Rousseau, 75001 Paris, France. Telex: 216911F, Telefax: (1) 40 13 02 31. Or contact Dr N.C. Gorin (Meeting Chairman) or Dr L. Douay (Meeting Secretary), Department of Hematology, Hopital St Antoine, 184, Rue du Fg St Antoine, 75571 Paris, Cedex 12, France.

UPDATE IN HEMATOLOGY/ONCOLOGY
FIRST AMERICAN/AUSTRIAN SYMPOSIUM

June 21-23, 1989
Vienna, Austria

Organizing Committee: Josef D. Schwarzmeier, MD, First Medical Clinic, University of Vienna; John E. Ultmann, MD, Section Hematology/Oncology, Cancer Research Center, University of Chicago; Heinz Weber, MD, Fortbildungsreferat, Ärztekammer für Wien.

For more information, please contact: Congress Secretariat, Irene Semlak, c/o Interconvention, A-1450 Vienna, Austria. Telephone: + 43/1/23 69/2641; Telex: 11 18 03; Telefax: + 43/1/23 69/648.
NATIONAL MARROW DONOR PROGRAM

The National Marrow Donor Program is a centrally organized, federally funded, computerized network of 53 donor centers and 25 transplant centers.

Only 25% of patients who are otherwise eligible for bone marrow transplantation will have an HLA-identical or partially matched family donor. This program links volunteer marrow donors from various centers throughout the US with patients in need of marrow transplants.

Searches for HLA-matched unrelated donors can be requested through any of the 25 affiliated transplant centers. The initial (preliminary) search is run free of charge.

For information about locating a donor for your patient, becoming a participating transplant center, or becoming a participating donor center, please contact: The National Marrow Donor Program, 100 S Robert St, St Paul, MN 55107. Telephone: 1-800-654-1247.

AMERICAN SOCIETY OF HEMATOLOGY
THIRD ANNUAL SPRING SYMPOSIUM
CHROMOSOMAL ABNORMALITIES: ORIGINS AND CONSEQUENCES

June 23-24, 1989
Hotel del Coronado
La Jolla, California

Abstracts will be accepted for poster presentation. The abstract submission deadline is May 19, 1989. Attendance will be limited to 250.

For further information, please contact: ASH Registration Supervisor, 6900 Grove Rd, Thorofare, NJ 08086-9447. Telephone: (609) 848-1000.
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<tr>
<td>AMERICAN JOURNAL OF CARDIAC IMAGING</td>
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<td>*AMERICAN JOURNAL OF EMERGENCY MEDICINE</td>
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<td>AMERICAN JOURNAL OF KIDNEY DISEASES</td>
<td>Monthly</td>
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<td>*AMERICAN JOURNAL OF OTOLARYNGOLOGY</td>
<td>Bimonthly</td>
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<td>APPLIED NURSING RESEARCH</td>
<td>Quarterly</td>
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<td>ARCHIVES OF PSYCHIATRIC NURSING</td>
<td>Bimonthly</td>
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<tr>
<td>BLOOD</td>
<td>16 Issues</td>
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<tr>
<td>COMPREHENSIVE PSYCHIATRY</td>
<td>Bimonthly</td>
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<td>HUMAN PATHOLOGY</td>
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<td>JOURNAL OF CARDIOTHORACIC ANESTHESIA</td>
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<td>*JOURNAL OF DIGITAL IMAGING</td>
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<td>Monthly</td>
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<td>JOURNAL OF PEDIATRIC NURSING</td>
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<td>*JOURNAL OF PHARMACY PRACTICE</td>
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<td>JOURNAL OF POST ANESTHESIA NURSING</td>
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<td>*JOURNAL OF PROFESSIONAL NURSING</td>
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<td>METABOLISM—CLINICAL AND EXPERIMENTAL</td>
<td>Monthly</td>
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<tr>
<td>PROGRESS IN CARDIOVASCULAR DISEASES</td>
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<td>SEMINARS IN ANESTHIA</td>
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<td>SEMINARS IN ARTHRITIS AND RHEUMATISM</td>
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<td>SEMINARS IN RESPIRATORY INFECTIONS</td>
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<td>SEMINARS IN ROENTGENOLOGY</td>
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<td>*SEMINARS IN SPINE SURGERY</td>
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<td>SEMINARS IN ULTRASOUND, CT, AND MR</td>
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<td>SEMINARS IN UROLOGY</td>
<td>Quarterly</td>
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<td>*SEMINARS IN VASCULAR SURGERY</td>
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<tr>
<td>SEMINARS IN VETERINARY MEDICINE AND SURGERY</td>
<td>Quarterly</td>
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<td>(SMALL ANIMAL)</td>
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<td>TRANSFUSION MEDICINE REVIEWS</td>
<td>Quarterly</td>
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* To order subscriptions, write to Subscription Services, W.B. Saunders Company, The Curtis Center, Independence Square West, Philadelphia, PA 19106-3399.
HEMATOPATHOLOGIST
DEPARTMENT OF PATHOLOGY
AND LABORATORY MEDICINE

The Department of Pathology and Laboratory Medicine of the University of Florida is seeking an academic hematopathologist at the rank of Assistant/Associate Professor. The successful candidate will be expected to engage in original research activities and to assume service responsibilities of a diagnostic hematopathology laboratory which consist mainly of surgical pathology, immunohistology and flow cytometry of bone marrow, blood and lymphoid tissues. The candidate will also have teaching commitments to residents, fellows in pathology and medical students, and colleagues in hematology, oncology and radiation therapy. The applicant should have training and experience commensurate with a career in an academic department associated with a major tertiary care medical center and a very active referral laboratory. Initial inquiries and Curriculum Vitae are being accepted until May 1, 1989. The employment starting date is July 1, 1989 or thereafter. This is a tenure accruing position. Salary will depend on experience. Contact R.C. Braylan, M.D., Department of Pathology, Box J-275; JHMHC, University of Florida, Gainesville, Florida 32610

EQUAL OPPORTUNITY/AFFIRMATIVE ACTION EMPLOYER

THE CLEVELAND CLINIC FOUNDATION

STAFF POSITION
BLOOD COAGULATION

A staff position is available in the Department of Laboratory Hematology at The Cleveland Clinic Foundation for a hematologist with a special interest and experience in blood coagulation including hemostasis and thrombosis. Responsibilities will include supervision of the coagulation section of the laboratory, consultation on clinical coagulation problems, participation in clinical and laboratory research projects and participation in the residency training program. Experience in molecular biology techniques is desirable. Qualified individuals may also hold a secondary appointment within the Research Institute of the Cleveland Clinic Foundation. The Foundation, a National Referral Center, has over 1,000 beds and is committed to excellence in clinical care, research and education. The Department of Laboratory Hematology has a professional staff of six and offers a complete test repertoire for the investigation of hematologic disease. Interested persons should write, enclosing a current CV, to
Dr. Ralph Green, Chairman
Department of Laboratory Hematology
Cleveland Clinic Foundation
One Clinic Center, Cleveland, Ohio 44195-5139

PEDiatric
HEMATOLOGY

Oncology Division—Research position available for a Pediatric Oncologist or Medical Oncologist with strong background and demonstrated research ability in molecular genetics of childhood cancer. Tenure-track position offers greater than 60% research time, start-up funding, faculty rank, salary commensurate with experience. Please contact: Joseph Gootenberg, M.D., Director, Division of Pediatric Hematology-Oncology, Department of Pediatrics, Georgetown University School of Medicine, 3800 Reservoir Road, N.W., Washington, D.C. 20007, (202) 687-2224. Georgetown University is an equal opportunity employer.

ROYAL POSTGRADUATE MEDICAL SCHOOL

MRC/LRF LEUKAEMIA UNIT

One or two Research Fellowships to work in the above unit have been made available through the generosity of the Hunting Gate organisation. The Unit has research programmes in the molecular and cell biology of leukaemia, and its primary objective to improve the management of patients with leukaemia. Applications are invited from young investigators either medically qualified or with a Ph.D. who are interested in work on the molecular basis of leukaemia, and who have relevant research experience. Additional details can be obtained and an informal meeting can be arranged with the Director, Professor L. Luzzatto, and members of the Unit by phoning 01-740 3234.

The appointment is for three years with salary on the University scale.

Applications, including C.V., bibliography, statement of research interests and intentions and names of three scientific referees to the Personnel Office, Royal Postgraduate Medical School, 150 Ducane Road, London W12 ONN quoting ref: HG/LRF.
FACULTY POSITION(S) IN MARROW TRANSPLANTATION HEMATOLOGY

The Medical College of Wisconsin is seeking candidates with interests in clinical and laboratory research for faculty positions in an expanding multidisciplinary transplant program. Opportunities exist for one or more individuals for appointment at the Assistant Professor level. Minimum requirements include credentials for Wisconsin M.D. licensure, with six years of postgraduate medical training and board certification in Internal Medicine or Pediatrics, eligibility for (or certification by) Hematology or Hematology/Oncology boards, and demonstrated expertise in teaching (position requires lecturing in transplant care and basic biology), clinical care, and research. Our faculty are engaged in allogeneic and autologous transplantation serving adult and pediatric patients, with expertise in alternative donor transplants, transfusion medicine, immunohematology, and viral infectious diseases. Interactions with the scientific team of the International Bone Marrow Transplant Registry provide an opportunity for advanced biostatistical training in outcome analyses. Laboratory interests of team members include: clonal regulation of GVH, GVL and HVG responses in animals and man; biology of immunoreconstitution; immunogenetic analysis by advanced cellular, serologic, and molecular technology; in vitro hematopoieses, cellular proliferation and receptor biology; monoclonal antibody and photochemical treatments for marrow T-depletion and tumor cell purging; and photobiology. Programs in adoptive cellular immunotherapy and in hemopoietin and lymphokine augmentation of marrow recovery are in development. Interested individuals should reply by letter with CV and references to:

Robert C. Ash, M.D., Director, Bone Marrow Transplant Program, Medical College of Wisconsin, 8700 West Wisconsin Avenue, Milwaukee, WI 53225, 414-257-7142.

The Medical College of Wisconsin is an equal opportunity employer.

UNIVERSITY OF FLORIDA

Seeks an Assistant/Associate Professor in Medicine with M.D. or M.D./Ph.D. Individual should be experienced academic hematologist with active research program to join Hematology/Oncology conducting research projects. Recruiting deadline: 05/15/89.
Starting date: July 1, 1989. Contact: Ward Noyes, M.D., University of Florida, Department of Medicine, Box J277 JHMHC, Gainesville, Florida 32610.

AN EQUAL OPPORTUNITY/AFFIRMATIVE ACTION EMPLOYER.

NATIONAL BLOOD CLUB
SATURDAY, APRIL 29, 1989
8:00 PM–10:00 PM
Washington Ballroom
Sheraton Washington Hotel

The Hematopoietic Stem Cell
“Correction of Genetic Defects by Retrovirus Mediated Gene Transfer into Hematopoietic Stem Cells”
Richard C. Mulligan
Massachusetts Institute of Technology

“Isolation of the Hematopoietic Stem Cell”
Irving L. Weissman
Stanford University

“CSF-1 and its Receptor”
Charles J. Sherr
St. Jude Children's Research Hospital

Everyone is welcome to attend!

Coagulation Factor Deficient Human Plasma

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- Kininogen (HMW)
- Passovoy Trait
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HEMATOLOGY PRODUCTS AVAILABLE:

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INCREASED SURVIVAL IN SELECT PATIENTS WITH AIDS-RELATED KAPOSI'S SARCOMA

RESPONSE RATE BY $T_4 (CD_4)$ CELL COUNT

- Percent of patients with complete response
- Percent of patients with partial response

Roche Laboratories

28.0%
$T_4 = > 200-300$
$n = 7/25$

13.5%
$T_4 = > 100-200$
$n = 5/37$

5.4%
8.1%

2.2%
$T_4 = 0-100$
$n = 1/46$

12.0%
16.0%
Response rate of 45.4% in select patients

The highest response was seen in patients with a baseline T4 (CD4) cell count of greater than 400. All patients were treated with Roferon-A daily using either 36 million IU or an escalating dose regimen for an induction period of 10-12 weeks. A maintenance dose of 36 million IU, three times per week, followed. The median time to response was 2.7 months. At study entry, no patient had prior opportunistic infections or B symptoms.

Greater than 2.7 years median survival in patients with a better baseline immune status

Median survival for responding patients with T4 (CD4) lymphocyte counts of greater than 200 to 400 cells/mm³ had not been reached but was greater than 32.7 months from the initiation of therapy. For responding patients with T4 (CD4) lymphocyte counts of greater than 400 cells/mm³, the median survival had not been reached but was greater than 29.5 months.

Side effects are generally manageable and may subside over time

- Flu-like symptoms of fatigue, fever, chills, myalgias, headache, anorexia, and nausea occur in the majority of patients at the start of therapy and may be ameliorated by evening administration. Please see product information for full list of adverse reactions.
- Dose reduction may be necessary if severe reactions occur.
- Myelosuppression can occur, particularly early in treatment, and warrants careful monitoring.
- Caution should be exercised when administering Roferon-A in combination with other agents known to cause myelosuppression, including zidovudine (AZT).

New 36 million IU/mL single dose, ready-to-use injectable solution ideal for outpatient use

First-line systemic therapy that can increase survival

Roche Laboratories / Leading the way in biotherapy

Please see complete product information on following pages.


* Symptoms include night sweats, weight loss greater than 10% of body weight or
18 pounds, or fever greater than 100°F without an identifiable source of infection.

This dosage form should not be used for the treatment of hairy cell leukemia.

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**DESCRIPTION:**
Recombinant interferon-α2a (Roferon-A) is a sterile protein product for use by injection. Roferon-A is manufactured by recombinant DNA technology that employs a genetically engineered strain of E. coli containing a plasmid carrying the human interferon-α2a gene. Recombinant interferon-α2a is highly purified protein containing 165 amino acids, and has a molecular weight of 19,000 Daltons. The purification process includes affinity chromatography using a monovalent monoclonal antibody. Fermentation is carried out in a defined nutrient medium containing the antibiotic tetracycline hydrochloride. 5 mg/L. However, the presence of antibiotics in the final product. Roferon-A is supplied as an injectable solution or as a sterile powder for injection with its accompanying diluent.

**Injection Site Solution:**
3 million IU Roferon-A per vial — The solution is colorless and each mL contains 3 million IU of interferon-α2a, recombinant/Roche. 9 mg sodium chloride. 5 mg Albumin (Human) and 3 mg phenol as a preservative.

18 million IU Roferon-A per vial — The solution is colorless and each mL contains 6 million IU of interferon-α2a, recombinant/Roche. 9 mg sodium chloride. 5 mg Albumin (Human) and 3 mg phenol as a preservative.

**Diluent for Sterile Powder for Injection:**
3 million IU Roferon-A per vial — The solution is white to beige and when reconstituted with Diluent for Sterile Powder for Injection each mL of reconstituted solution contains 6 million IU of interferon-α2a, recombinant/Roche and 3 mg phenol as a preservative.

**INDICATIONS AND USAGE:**
Roferon-A is indicated for use in the treatment of hairy cell leukemia and the management of Kaposi's sarcoma in patients with HIV infection.

**DOSAGE AND ADMINISTRATION:**
Roferon-A should be used only by persons who have been adequately trained in the use and storage of injectable therapeutic products. For precise routes of administration, see the package insert for Roferon-A.

**RATE OF ADMINISTRATION:**
Roferon-A should be administered at a dose of 3 to 36 million IU daily as a single injection or divided into two or three injections per week, or divided into two or three divided injections per week. Although the recommended duration of therapy may be 12 to 20 months, the duration of therapy can be extended if the patient achieves a clinical benefit from the treatment.

**SIDE EFFECTS:**
Infections: The mechanism by which interferon-α2a, recombinant/Roche, or any other interferon, exerts antitumor activity is not clearly understood. However, it is believed that direct antiproliferative action against tumor cells and modulation of the host immune response play a role in the antitumor activity of interferons.

The biological activities of interferon-α2a, recombinant/Roche are species restricted, i.e., they are not active in a variety of mammalian cells. As a consequence, the clinical evaluation of interferon-α2a, recombinant/Roche has involved in vitro experiments with human cells as test systems. In the course of clinical studies, interferon-α2a, recombinant/Roche has shown to have antiproliferative and immunomodulatory activities that are very similar to those of the mixture of interferon-α2a subtypes produced by human leukocytes. Therefore, interferon-α2a, recombinant/Roche has shown to inhibit the growth of several human tumors growing in immunocompromised (nude) mice. Because of its species-restricted nature, interferon-α2a, recombinant/Roche is unlikely to have antitumor activity in intact syngeneic murine tumor models. Effects on the host immune system must be observed. However, with the exception of cases resembling the above-mentioned animal experiments, patients with interferon-α2a, recombinant/Roche observed no meaningful antitumor activity in patients with hairy cell leukemia or transplanted mouse tumor systems. The clinical significance of these findings is unknown.

The mechanism of interferon-α2a, recombinant/Roche is consistent with that of all interferons in general. Interferons are totally filtered through the glomeruli and undergo rapid proteolysis in circulation. They are not detectable in plasma beyond 2 to 4 hours after intravenous injection. The half-life of intravenous administration of 36 million IU, peak serum concentrations ranged from 1500 to 2500 pg/mL (mean 200 pg/mL) at a mean peak of 3 to 5 hours and from 1250 to 2250 pg/mL (mean 1750 pg/mL) at a mean peak of 3 to 5 hours. These concentrations were observed at all the times after administration. No significant absorption after intravenous injection was greater than 80%.

The mechanism of interferon-α2a, recombinant/Roche after single intramuscular doses to patients with disseminated cancer were similar to those found in healthy volunteers. Dose proportional increase in serum concentrations were observed after single doses up to 198 million IU (5 to 6 mg/m2). Dose proportional increase in serum concentrations was observed after each injection and the apparent half-life of absorption after intramuscular injection was greater than 80%.

The clinical evaluation of interferon-α2a, recombinant/Roche observed no meaningful antitumor activity in patients with hairy cell leukemia. Sarcoma-related symptoms, such as fever, night sweats, weight gain, and weight loss, were observed in about 10% of patients. The clinical evaluation of interferon-α2a, recombinant/Roche has shown to inhibit the growth of several human tumors growing in immunocompromised (nude) mice. Because of its species-restricted nature, interferon-α2a, recombinant/Roche is unlikely to have antitumor activity in intact syngeneic murine tumor models. Effects on the host immune system must be observed. However, with the exception of cases resembling the above-mentioned animal experiments, patients with interferon-α2a, recombinant/Roche observed no meaningful antitumor activity in patients with hairy cell leukemia or transplanted mouse tumor systems. The clinical significance of these findings is unknown.

**CONTRAINDICATIONS:**
Roferon-A is contraindicated in patients with known hypersensitivity to any component, including tetracycline, mouse immunoglobulin G or any component of the product.

**WARNINGS:**
Roferon-A should be administered under the guidance of a qualified physician. Use during pregnancy and breastfeeding is not recommended. Used in combination with other drugs used in the treatment of AIDS-related Kaposi’s sarcoma is associated with rapid and severe toxicity in patients treated with alpha-interferon.

**PRECAUTIONS:**
General: In all instances where the use of Roferon-A is considered for chemotherapy, the physician must evaluate the patient's history and use appropriate precautions for the risk of severe adverse reactions. Most adverse reactions are reversible if detected early. If severe reactions occur, the drug should be discontinued immediately. Any potential adverse reactions should be taken into consideration when interpreting the clinical significance of the results. Roferon-A therapy should be continued only if the benefit of therapy outweighs the risk of adverse reactions.

**CLINICAL PHARMACOLOGY:**
**Pharmacokinetics:**
Dose-related increase in serum concentrations were observed after single doses up to 198 million IU (5 to 6 mg/m2). No effect on serum concentrations was observed after each injection and the apparent half-life of absorption after intramuscular injection was greater than 80%.

**ADVERSE REACTIONS:**
**Local Reactions:**
The most common adverse reactions reported in patients treated with Roferon-A were injection site reactions. These reactions were primarily injection site pain, redness, and swelling. In general, these reactions were not severe and were usually transient.

**Systemic Reactions:**
The systemic reactions reported in patients treated with Roferon-A were injection site reactions, injection site pain, systemic flu-like symptoms (fever, chills, myalgia, and headache), fatigue, malaise, myalgia, asthenia, nausea, vomiting, diarrhea, loss of appetite, anorexia, weight loss, headache, insomnia, neuropathy, paresthesia, and peripheral neuritis. In general, these reactions were not severe and were usually transient.

**Hematological Reactions:**
The hematological reactions reported in patients treated with Roferon-A were injection site reactions, injection site pain, systemic flu-like symptoms (fever, chills, myalgia, and headache), fatigue, malaise, myalgia, asthenia, nausea, vomiting, diarrhea, loss of appetite, anorexia, weight loss, headache, insomnia, neuropathy, paresthesia, and peripheral neuritis. In general, these reactions were not severe and were usually transient.

**Immunological Reactions:**
The immunological reactions reported in patients treated with Roferon-A were injection site reactions, injection site pain, systemic flu-like symptoms (fever, chills, myalgia, and headache), fatigue, malaise, myalgia, asthenia, nausea, vomiting, diarrhea, loss of appetite, anorexia, weight loss, headache, insomnia, neuropathy, paresthesia, and peripheral neuritis. In general, these reactions were not severe and were usually transient.

**Clinical Laboratory Abnormalities:**
The clinical laboratory abnormalities reported in patients treated with Roferon-A were injection site reactions, injection site pain, systemic flu-like symptoms (fever, chills, myalgia, and headache), fatigue, malaise, myalgia, asthenia, nausea, vomiting, diarrhea, loss of appetite, anorexia, weight loss, headache, insomnia, neuropathy, paresthesia, and peripheral neuritis. In general, these reactions were not severe and were usually transient.

**Interferon Reactions:**
The interferon reactions reported in patients treated with Roferon-A were injection site reactions, injection site pain, systemic flu-like symptoms (fever, chills, myalgia, and headache), fatigue, malaise, myalgia, asthenia, nausea, vomiting, diarrhea, loss of appetite, anorexia, weight loss, headache, insomnia, neuropathy, paresthesia, and peripheral neuritis. In general, these reactions were not severe and were usually transient.

**Hypersensitivity Reactions:**
The hypersensitivity reactions reported in patients treated with Roferon-A were injection site reactions, injection site pain, systemic flu-like symptoms (fever, chills, myalgia, and headache), fatigue, malaise, myalgia, asthenia, nausea, vomiting, diarrhea, loss of appetite, anorexia, weight loss, headache, insomnia, neuropathy, paresthesia, and peripheral neuritis. In general, these reactions were not severe and were usually transient.

**Viral Reactions:**
The viral reactions reported in patients treated with Roferon-A were injection site reactions, injection site pain, systemic flu-like symptoms (fever, chills, myalgia, and headache), fatigue, malaise, myalgia, asthenia, nausea, vomiting, diarrhea, loss of appetite, anorexia, weight loss, headache, insomnia, neuropathy, paresthesia, and peripheral neuritis. In general, these reactions were not severe and were usually transient.

**Drug Interactions:**
The drug interactions reported in patients treated with Roferon-A were injection site reactions, injection site pain, systemic flu-like symptoms (fever, chills, myalgia, and headache), fatigue, malaise, myalgia, asthenia, nausea, vomiting, diarrhea, loss of appetite, anorexia, weight loss, headache, insomnia, neuropathy, paresthesia, and peripheral neuritis. In general, these reactions were not severe and were usually transient.
**Abnormal Laboratory Test Values**

<table>
<thead>
<tr>
<th>Tests</th>
<th>Reference Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hairy Cell Leukemia</strong></td>
<td></td>
</tr>
<tr>
<td>Neutrophils</td>
<td>NA</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>NA</td>
</tr>
<tr>
<td>Platelet</td>
<td>360,000 to 420,000</td>
</tr>
<tr>
<td>LDH</td>
<td>50 to 211</td>
</tr>
<tr>
<td>BUN</td>
<td>5 to 19</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.7 to 1.3</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>0%</td>
</tr>
</tbody>
</table>

*Note: Applicable — Patient's initial hematology laboratory test values were abnormal due to their underlying disorder.*

In increasing tests fasting serum glucose, serum phosphorus and serum uric acid levels and decreases in serum calcium levels were also observed in less than 5% of patients.

**Dosage and Administration:**

- **Hairy Cell Leukemia:** The induction dose of Roferon-A is 3 million IU daily for 16 to 24 weeks. The maintenance dose is administered as a subcutaneous injection or intravenously.
- **Subcutaneous administration:** is particularly suggested for, but not limited to, thrombocytopenic patients (platelet count <50,000/mm³) or patients at risk for bleeding. The recommended maintenance dose is 3 million IU twice per week. Dose reduction by one-half or withholding of individual doses may be necessary for severe adverse reactions occurring in 3 to 5% of patients treated with Roferon-A. Where severe adverse reactions occur, the 3 million IU dose should not be used for the treatment of hairy cell leukemia.
- **AIDS-Related Kaposi’s Sarcoma:** The recommended induction dose of Roferon-A is 36 million IU daily for 10 to 12 weeks, administered as an intramuscular or subcutaneous injection. Subcutaneous administration is particularly suggested for, but not limited to, patients who are thrombocytopenic (platelet count <50,000/mm³) or who are at risk for bleeding. The recommended maintenance dose is 36 million IU, three times per week. Dose reductions by one-half or withholding of individual doses may be necessary for severe adverse reactions occurring. An escalating schedule of maintenance is 36 million IU, 9 million IU and 18 million IU each daily for 3 days followed by 36 million IU daily for the remainder of the 10 to 12 week induction period has also produced equivalent therapeutic results with some amelioration of the hematologic toxicity in some patients.
- **When disease stabilization or a response to treatment occurs, treatment should continue until there is further evidence of tumor growth and stabilization or because of a severe opportunistic infection or adverse effects.** The optimal duration of treatment for this disease has not been determined.

**Parenteral Drug Products:**

- No effective visually clear solution should be used for the treatment of hairy cell leukemia.
- The maximum effective doses of Roferon-A for the treatment of hairy cell leukemia and AIDS-related Kaposi’s sarcoma have not been established.

** references:**

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Finding answers to disease within human physiology rather than chemical pharmacology: this is the Amgen commitment to the practice of medicine. With that purpose in mind, Amgen's more than one hundred molecular biologists, protein chemists, and biochemical engineers are free to explore wherever the scientific imagination leads.

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