hyperphosphatemia, have been reported within 12–24 hours after the first Rituxan infusion. (See WARNINGS and ADVERSE REACTIONS.) Tumor Lysis Syndrome (TLS): Acute renal failure requiring dialysis with instances of hyperuricemia, severe hyperphosphatemia, hyperkalemia, and hypocalcemia, has been reported in patients with malignant lymphoma (MALT) NHL patients with Rituxan. (See WARNINGS. Severe Mucocutaneous Reactions: Severe mucocutaneous reactions, some with fatal outcome, have been reported in patients receiving Rituxan. (See WARNINGS and ADVERSE REACTIONS.)) Lichenoid dermatitis, vesiculobullous dermatitis, and toxic epidermal necrolysis. The development of severe cutaneous reactions may be influenced by several factors including grading, concomitant medications, and underlying disease. Comparison of the incidence of morbilliform eruptions in patients with Rituxan with other therapies is not available. Chloroma has been reported in a patient receiving Rituxan for chronic lymphocytic leukemia who remained on therapy for 6 years. Infections: Serious bacterial infections have been reported in patients undergoing concomitant chemotherapy or immunosuppressive therapy. Patients with pre-existing cardiac conditions including arrhythmias and angina should be closely monitored during therapy. Approximately 80% of serious adverse events associated with fatal infusion reactions occurred in association with the first infusion. (See WARNINGS and ADVERSE REACTIONS.) Infusion Reactions: Severe infusion reactions occurred in patients treated with Rituxan. (See WARNINGS and ADVERSE REACTIONS.) INDICATIONS AND USAGE Non-Hodgkin’s Lymphoma (Rituxan): Indicated in combination with cyclophosphamide, hydroxydaunorubicin (cyclofosfamide), vincristine, and prednisone (CHOP) chemotherapy for the treatment of patients with CD20-positive, B-cell non-Hodgkin’s lymphoma (Rituxan) is indicated for the first-line treatment of follicular and diffuse, large B-cell non-Hodgkin’s lymphoma in combination with standard chemotherapy regimens of low- or high-dose prednisone, or rituximab, given with cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP), specifically in patients with stage III or IV follicular lymphoma, clinical stage I or II diffuse large B-cell lymphoma, or stage IV B-cell chronic lymphocytic leukemia or small lymphocytic lymphoma. The use of rituximab as monotherapy is not approved. The majority of patients with hematologic malignancies diagnosed with PML have had recurrences of these events during Rituxan therapy and should be monitored for hematologic malignancy. Monitoring and reporting of new cases are important in order to detect any potential association between Rituxan and PML, since the latency period for PML after initiation of therapy may be longer than one year. In patients who develop viral hepatitis, Rituxan and any other medications should be discontinued and the patient’s overall health be assessed at each visit. A monoclonal antibody directed against the Epstein-Barr virus (EBV) latency membrane proteins (LMP1 and LMP2) has been reported in a patient treated with rituximab. (See WARNINGS. Hepatitis B Reactivation with Fulminant Hepatitis: Rituxan monotherapy is a risk factor for hepatitis B virus (HBV) reactivation with fulminant hepatitis, including fulminant hepatitis with fatal outcomes. Careful monitoring of liver function tests and patient history should be performed in patients pretreated with antiviral therapy for chronic HBV infection who are subsequently treated with Rituxan. (See PRECAUTIONS and ADVERSE REACTIONS.) Infectious Events: Infection was the most frequent adverse event in clinical studies of Rituxan administered as a single agent. Most patients received Rituxan in combination with chemotherapy. The median time to the diagnosis of hepatitis was approximately 4 months after the first infusion. Most HBV infections were asymptomatic. Persons at high risk of HBV infection should be screened before initiation of Rituxan. Carrier status should be determined based on previous laboratory results or serological testing. In patients with active hepatitis B virus (HBV) infection, HBV reactivation can also occur in patients with inactive hepatitis B. HBsAg. The presence of HBV DNA, even without HBV RNA, can indicate the potential for HBV reactivation. Patients with active chronic hepatitis B, HBV DNA, and HBsAg should be treated with appropriate antiviral therapy. In patients with chronic hepatitis B, passive or active immunity should be established before initiation of therapy. Careful monitoring of liver function tests and patient history should be performed in patients pretreated with antiviral therapy for chronic HBV infection who are subsequently treated with Rituxan. Among patients treated for lymphomas, 95% of patients received Rituxan in combination with chemotherapy or as part of a hematopoietic stem cell transplant. These viral infections included cytomegalovirus, herpes simple virus, parvovirus B19, varicella-zoster virus, and hepatitis A and B. A single viral reactivation event has occurred up to one year following discontinuation of Rituxan and has been observed in 1.7% of patients in the R-CHOP arm compared with those in the CHOP arm: thrombocytopenia (3% vs. 1%), neutropenia (2% vs. 0%), and anemia (3% vs. 3%). Cardiac disorders, with 4.5% vs. 1.0% incidences for R-CHOP and CHOP, respectively. Among patients treated with other rituximab-containing regimens, the incidence of infections was similar for other rituximab-containing regimens. Due to the possibility of anti-drug antibody development with such a long dosing period, the animals were divided into 3 sets of dosing periods: one set (post-partum day 28). Due to the possibility of anti-drug antibody development with such a long dosing period, the animals were divided into 3 sets of dosing periods: one set (post-partum day 28). Due to the possibility of anti-drug antibody development with such a long dosing period, the animals were divided into 3 sets of dosing periods: one set (post-partum day 28). Due to the possibility of anti-drug antibody development with such a long dosing period, the animals were divided into 3 sets of dosing periods: one set (post-partum day 28). 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For the treatment of low-grade, CD20+, B-cell non-Hodgkin's lymphoma (NHL) in patients with stable disease or who achieve a partial or complete response following first-line treatment with CVP chemotherapy

Risk reduction demonstrated with up to 16 doses of RITUXAN following CVP*

Study protocol from “Results of E1496: A phase III trial of CVP with or without maintenance rituximab in advanced indolent lymphoma (NHL)”†

RITUXAN following CVP reduced risk of progression, relapse, or death by 51%‡

- The primary endpoint in this study was progression-free survival (PFS), defined as the time from randomization to progression, relapse, or death
- RITUXAN following CVP doubled reduction in risk related to PFS compared with observation, with a median follow-up of 28 months
- Clinical benefit was consistent across diverse patient subgroups, including age, presence of bulky disease, tumor burden, histology, extent of disease, and best response after CVP induction

SAFETY SUMMARY
WARNING: Fatal Infusion Reactions: Deaths within 24 hours of RITUXAN infusion have been reported. Approximately 80% of fatal infusion reactions occurred in association with the first infusion. Patients who develop severe infusion reactions should have RITUXAN infusion discontinued and receive medical treatment.
Tumor Lysis Syndrome (TLS): Acute renal failure requiring dialysis with instances of fatal outcome has been reported in the setting of TLS following treatment with RITUXAN.
Severe Mucocutaneous Reactions: Severe mucocutaneous reactions, some with fatal outcome, have been reported in association with RITUXAN treatment.
Progressive Multifocal Leukoencephalopathy (PML): JC virus infection resulting in PML and death has been reported in patients treated with RITUXAN. RITUXAN has also been associated with fatal hepatitis B reactivation with related fulminant hepatitis and other serious viral infections, cardiovascular events, renal toxicity, and bowel obstruction and perforation.

Front-line CVP Chemotherapy Followed by RITUXAN in Low-grade NHL: The following common adverse events were reported more frequently (≥5%) in patients receiving RITUXAN following CVP compared with those who received no further therapy: fatigue (39% vs 14%), anemia (35% vs 20%), peripheral sensory neuropathy (30% vs 18%), infections (19% vs 9%), pulmonary toxicity (18% vs 10%), hepatobiliary toxicity (17% vs 7%), rash and/or pruritus (17% vs 5%), arthralgia (12% vs 3%), and weight gain (11% vs 4%). Neutropenia was the only Grade 3 or 4 adverse event that occurred more frequently (≥2%) in the RITUXAN arm compared with those who received no further therapy (4% vs 1%).

References: 1. Data on file, Genentech, Inc. 2. RITUXAN® (Rituximab) full prescribing information, Genentech, Inc., 2007. For more information, please visit www.rituxan.com/lymphoma.

*CVP: Cyclophosphamide, vincristine, and prednisone.
‡Derived from a hazard ratio range up to but not exceeding 0.49.

Please see brief summary of prescribing information on adjacent page.
What could a missed myeloma diagnosis mean?

**ANSWER:**

A. Pathological fractures  
B. Acute renal failure  
C. Paraplegia  
D. All of the above

Could this be avoided?

Early diagnosis of myeloma may prevent progressive bone damage, irreversible renal failure and may contribute to better survival.

The detection rate for plasma cell disorders increased from 48% for serum protein electrophoresis (SPE) alone to 100% when both SPE and Freelite™ Serum Free Light Chain assays were used together.1

Use Freelite™ Serum Free Light Chain assays in your initial evaluation of suspected myeloma.

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www.freelite.co.uk

Freelite™ is a trademark of The Binding Site, Ltd, Birmingham, UK.
Q: What could a missed myeloma diagnosis mean?

A: Pathological fractures

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Use Freelite™ Serum Free Light Chain assays in your initial evaluation of suspected myeloma.

Reference:

www.freelite.co.uk
With a life-threatening acquired hemophilia bleed, every minute counts. Spot it, then stop it with NovoSeven®.

Acquired hemophilia is often difficult to recognize and has a mortality rate of up to 22%. To spot acquired hemophilia, look for spontaneous and uncontrolled bleeding (gastrointestinal, retroperitoneal, purpura, etc) with prolonged PTT. To stop acquired hemophilia bleeding, look to recombinant NovoSeven. NovoSeven has demonstrated 86% efficacy as a first-line therapy and is approved for acquired hemophilia.

For options on how to access NovoSeven, go to accessnovoseven.com or call 1-877-NOVO-777.

For the treatment of bleeding episodes in patients with acquired hemophilia. For the prevention of bleeding in surgical interventions or invasive procedures in patients with acquired hemophilia.

IMPORTANT SAFETY INFORMATION

Most common adverse events: pyrexia, hemorrhage, injection site reaction, arthralgia, headache, hypertension, hypotension, nausea, vomiting, pain, edema, and rash. Patients with disseminated intravascular coagulation (DIC), advanced atherosclerotic disease, crush injury, sepsis, or concomitant treatment with activated or nonactivated prothrombin complex concentrates (aPCCs/PCCs) may have a potential risk of developing thrombotic events in association with NovoSeven treatment. Contraindicated in patients with known hypersensitivity to NovoSeven, its components, or mouse, hamster, or bovine proteins. The risk of potential interaction between NovoSeven and coagulation factor concentrates has not been evaluated. Simultaneous use of aPCCs/PCCs should be avoided. Serious adverse events that may or may not have been related to the use of NovoSeven in acquired hemophilia (10 of 139 patients in the compassionate use program, HTRS registry, and the published literature) may include thrombotic serious adverse events and death. Serious adverse events that may or may not have been related to the use of NovoSeven occurred in 14 of 298 patients with hemophilia A or B with inhibitors in the initial clinical program.

*In the compassionate use program (38/44 bleeding episodes).

Please see brief summary of Prescribing Information at end of advertisement.
Tending the molecules that may transform cancer treatment
...and turning them into practical therapies

Research at Genentech BioOncology that led to important breakthroughs:
- Original research on VEGF, one of the key mediators of angiogenesis
- Original research on the HER2 protein
- Collaborative efforts on the CD20 antigen
- Collaborative research on a HER1/EGFR TK inhibitor

Key molecules now being investigated in our extensive clinical research program include:
- HER dimerization inhibitor
- Recombinant human Apo2L/TRAIL, a pro-apoptotic receptor agonist
- Systemic Hedgehog antagonist
- PARP inhibitor
- HER2 antibody-drug conjugate

For more information, visit www.BioOncology.com or call (800) 551-2231.
Even though your CML patients may be responding to imatinib therapy, are they meeting their recommended treatment goals? If not, they could be imatinib resistant and at increased risk of disease progression. Guidelines for CML management support the urgency of identifying imatinib resistance and taking appropriate action.¹

For more information, call 1-888-294-4664

INVESTIGATING THE ORAL DAC* INHIBITOR LBH589

Two multicenter, phase II studies of oral LBH589 are now enrolling adult patients with relapsed or refractory Chronic Myeloid Leukemia (CML) in:

**Chronic Phase**

For patients who have received treatment with at least 2 Bcr-Abl TKIs**† AND meet any of the following criteria:

- Have demonstrated resistance to prior treatments, including most recent Bcr-Abl TKI
- Have a history of intolerance to at least 1 Bcr-Abl TKI and demonstrate resistance to the most recent Bcr-Abl TKI
- Are intolerant to at least 2 Bcr-Abl TKIs if they also demonstrate resistance to or intolerance of interferon therapy (monotherapy or in combination)

Primary endpoint:
- Major cytogenetic response rate

**Accelerated Phase or Blast Crisis**

For patients who have received treatment with at least 2 Bcr-Abl TKIs† AND meet any of the following criteria:

- Have demonstrated resistance to prior treatments, including most recent Bcr-Abl TKI
- Have a history of intolerance to at least 1 Bcr-Abl TKI and demonstrate resistance to the most recent Bcr-Abl TKI

Primary endpoint:
- Hematologic response (CHR/NEL/RTC)* rate

Oral LBH589
20 mg once daily
Mon, Wed, Fri

ALPHA CML1
Assessment of LBH589 in Patients with Hematologic Advanced cancers
Chronic Myeloid Leukemia-Chronic Phase

ALPHA CML2
Assessment of LBH589 in Patients with Hematologic Advanced cancers
Chronic Myeloid Leukemia-Accelerated Phase/Blast Crisis

Information about these clinical trials, including full inclusion/exclusion criteria, is available at www.novartiscclinicaltrials.com, by calling the Novartis Oncology Clinical Trials Hotline at 1-800-340-6843 (US only), or by visiting www.clinicaltrials.gov.

LBH589 is an investigational medicine. Efficacy and safety have not been established. There is no guarantee that LBH589 will become commercially available.

*DAC = deacetylase; TKI = tyrosine kinase inhibitor; CHR = complete hematologic response; NEL = no evidence of leukemia; RTC = return to chronic phase.
†One of these TKIs must be imatinib.
A Randomized, Open-label Study of Oral CEP-701 Administered in Sequence with Standard Chemotherapy to Patients with Relapsed Acute Myeloid Leukemia (AML) Expressing FLT-3 Activating Mutations

**Primary Objective**
Evaluate whether CEP-701 given in sequence with induction chemotherapy increases the proportion of patients who achieve a second complete remission (CR/CRp)

**Secondary Objectives**
- Overall survival
- Event-free survival
- Remission duration (for patients with CR/CRp)
- Proportion of patients achieving an outcome of CR/CRp/PR (complete remission plus partial response)
- Proportion of patients maintaining an outcome of CR/CRp at day 113

**Eligibility Criteria**
- ≥18 years old
- Cytological confirmation of AML
- Relapsed disease (initial CR of 1-24 months)
- FLT-3 activating mutation positive after point of initial relapse
- >3 months life expectancy
- ECOG performance status 0, 1, 2

For additional information, please visit [www.clinicaltrials.gov/ct/show/NCT00079482](http://www.clinicaltrials.gov/ct/show/NCT00079482)
A Trial in Newly Diagnosed Multiple Myeloma

An open-label, randomized, multicenter, phase 3b trial (Protocol C05009) comparing the efficacy and safety of 3 regimens containing VELCADE® (bortezomib) for Injection in previously untreated multiple myeloma patients not eligible for high-dose chemotherapy and autologous stem cell transplantation (n=approximately 500)

Study Schema

<table>
<thead>
<tr>
<th>Induction Therapy*</th>
<th>Maintenance Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eight 21-day cycles</td>
<td>Five 35-day cycles</td>
</tr>
<tr>
<td>VD&lt;br&gt;VELCADE&lt;br&gt;Dexamethasone</td>
<td>VELCADE&lt;br&gt;VTD&lt;br&gt;Thalidomide&lt;br&gt;Dexamethasone</td>
</tr>
<tr>
<td>VTD&lt;br&gt;VELCADE&lt;br&gt;Thalidomide&lt;br&gt;Dexamethasone</td>
<td></td>
</tr>
<tr>
<td>VMP&lt;br&gt;VELCADE&lt;br&gt;Melphalan&lt;br&gt;Prednisone</td>
<td></td>
</tr>
</tbody>
</table>


*In an interim analysis after the first 70 patients in each arm have completed ≥4 cycles of therapy or discontinued treatment prior to 4 cycles of therapy, the most inferior arm (based on ≥VGPR and toxicity) will be discontinued.

Study Endpoints

- **Primary endpoint:** PFS
- **Secondary endpoints:** ORR, CR, ≥VGPR, duration of response, OS, safety and tolerability, time to alternative therapy, quality of life

Key Eligibility Criteria

- Measurable disease, symptomatic multiple myeloma or asymptomatic multiple myeloma with related organ or tissue damage
- No previous or current systemic therapy for multiple myeloma
- Not a candidate for high-dose chemotherapy and stem cell transplantation
- Karnofsky Performance Status score ≥50%


For more information on VELCADE clinical trials, call 800-589-9005.
The Platelet Elevator

Now, Rhophylac® gives platelet levels a lift with proven efficacy and safety

- Efficacy and tolerability established in a chronic ITP clinical trial
- Demonstrated safety and purity with 3-step viral safety process
- Short infusion and treatment time
- From CSL Behring (formerly ZLB Behring)—over 100 years of experience in plasma protein biotherapeutics

For Important Safety Information, please read the brief summary of Prescribing Information beginning below. Before prescribing, please see full Prescribing Information.

ITP therapy that counts

Rhophylac®
Rh(D) Immune Globulin Intravenous (Human)

For adult chronic Immune Thrombocytopenic Purpura (ITP)

NEW INDICATION

ZLB Behring
BRIEF SUMMARY OF PRESCRIBING INFORMATION
Rhophylac®
Rh(D) Immune Globulin Intravenous (Human)

For Intravenous or Intramuscular Injection
Preservative-free, Latex-free, Ready-to-use Prefilled Syringe

Before prescribing, please consult full prescribing information, a brief summary of which follows. Some text refers to the full prescribing information.

4 CONTRAINDICATIONS
Individuals known to have had an anaphylactic or severe systemic reaction to the administration of human immune globulin products should not receive Rh(D) immune globulin.

5 WARNINGS AND PRECAUTIONS
5.1 Both Indications
Allergic Reactions
Allergic reactions may occur. If symptoms of allergic or early signs of hypersensitivity reactions (including generalized urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis) occur, immediately discontinue administration. The treatment required depends on the nature and severity of the side effect. If necessary, the current medical standards for shock treatment should be observed (see Patient Counseling Information [17.1]).

Selective IgA Deficiency
Individuals with selective IgA deficiency can develop antibodies to IgA and anaphylactic reactions (including anaphylaxis and shock) after administration of blood components containing IgA. Although the concentration of IgA was found to be below the detection limit of 5 mcg/mL, Rhophylac® may contain trace amounts of IgA (see Description [11]). Those with known antibodies to IgA may have a greater risk of developing potentially severe hypersensitivity and anaphylactic reactions. Therefore, the...
physician must weigh the expected benefits of treatment with Rhophylac®. Rh(D) Immune Globulin Intravenous (Human) against the potential risks. Interference With Laboratory Tests

The administration of Rh(D) immune globulin may affect the results of blood typing, the antibody screening test, and the direct antiglobulin (Coombs’) test. Antepartum administration of Rh(D) immune globulin to the mother can also affect these tests in the newborn infant.

Rhophylac® can contain antibodies to other Rh antigens (e.g., anti-C antibodies), which might be detected by sensitive serological tests following administration.

Transmissible Infectious Agents

Rhophylac® is made from human plasma. Products made from human plasma may contain infectious agents, e.g., viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, that can cause disease. The risk that such products will transmit an infectious agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses during manufacturing through solvent/detergent treatment and virus filtration. The solvent/detergent treatment step is effective in inactivating enveloped viruses such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). The virus filtration step is effective in removing both enveloped and non-enveloped viruses (see Description [11], Patient Counseling Information [17.1]).

Despite these measures, such products can still potentially transmit disease. There is also the possibility that unknown infectious agents may be present in such products. All infections thought by a physician possibly to have been transmitted by this product should be reported by the physician or other healthcare provider to ZLB Behring at 1-800-504-5434. The physician should discuss the risks and benefits of this product with the patient.

5.2 Suppression of Rh Isoimmunization

Postpartum Use Following an Rh-incompatible Pregnancy

Rhophylac® should not be given to the newborn infant (see Pediatric Use [8.4] for pediatric use in incompatible transfusions and in ITP).

5.3 ITP

Intravascular Hemolysis

Intravascular hemolysis has occurred in a clinical study with Rhophylac®. All cases resolved completely. However, as reported in the literature, some patients treated with Rh(D) immune globulin (anti-D) developed clinically compromising anemia, acute renal insufficiency, and, very rarely, disseminated intravascular coagulation (DIC) and death.

Following administration of Rhophylac®, patients should be monitored for signs and/or symptoms of intravascular hemolysis and its complications including clinically compromising anemia, acute renal insufficiency, and DIC. Patients experiencing intravascular hemolysis may present with back pain, shaking chills, fever, and, most consistently, hemoglobinuria (see Patient Counseling Information [17.3]).

ITP patients presenting with signs and/or symptoms of intravascular hemolysis and its complications after Rh(D) immune globulin administration should have confirmatory laboratory tests. DIC may be difficult to detect in the ITP population; the diagnosis is dependent mainly on laboratory testing. If patients who develop hemolysis with clinically compromising anemia after receiving Rhophylac® are to be transfused, Rh(D)-negative packed RBCs should be used to avoid exacerbating ongoing hemolysis.

Pre-existing Anemia

The safety of Rhophylac® in the treatment of ITP has not been established in patients with pre-existing anemia. The physician must weigh the benefits of Rhophylac® against the potential risk of increasing the severity of the anemia.

6 ADVERSE REACTIONS

The most serious adverse reactions in patients receiving Rh(D) immune globulin have been observed in the treatment of ITP. These reactions include intravascular hemolysis, clinically compromising anemia, acute renal insufficiency, and, very rarely, DIC and death (see Warnings and Precautions [5.3]).

The most common adverse reactions observed in the use of Rhophylac® for suppression of Rh isoimmunization are nausea, dizziness, headache, injection-site pain, and malaise.

The most common adverse reactions observed in the treatment of ITP are chills, pyrexia/increased body temperature, and headache. Mild extravascular hemolysis (manifested by an increase in bilirubin and a decrease in hemoglobin) was also observed.

6.1 Clinical Studies Experience

Because clinical studies are conducted under different protocols and widely varying conditions, adverse reaction rates observed cannot be directly compared to rates in other clinical trials and may not reflect the rates observed in practice.

Suppression of Rh Isoimmunization

In two clinical studies, 447 Rh(D)-negative pregnant women received either an intravenous or intramuscular injection of Rhophylac® 1500 IU (300 mcg) at Week 28 of gestation. A second 1500 IU (300 mcg) dose was administered to 267 (9 in Study 1 and 258 in Study 2) of these women within 72 hours of the birth of an Rh(D)-positive baby. In addition, 30 women in Study 2 received at least one extra antepartum 1500 IU (300 mcg) dose due to obstetric complications (see Clinical Studies [14.2]).

The most common adverse reactions were nausea (0.7%), dizziness (0.5%), headache (0.5%), injection-site pain (0.5%), and malaise (0.5%). A laboratory finding of a transient positive anti-C antibody test was observed in 0.9% of subjects. All adverse reactions were mild to moderate in intensity.

ITP

In a clinical study, 98 Rh(D)-positive adult subjects with chronic ITP received an intravenous dose of Rhophylac® 250 IU (50 mcg) per kg body weight (see Clinical Studies [14.2]). Premedication to alleviate infusion-related side effects was not used except in a single subject who received acetaminophen and diphenhydramine. Adverse reactions were mild to moderate in intensity with the exception of one case of severe headache. Eighty-four (85.7%) subjects experienced 392 treatment-emergent adverse events (TEAEs). Sixty-nine (70.4%) subjects had 186 drug-related TEAEs (defined as TEAEs with a probable, possible, definite, or unknown relationship to the study drug). Within 24 hours of dosing, 73 (74.5%) subjects experienced 183 TEAEs, and 66 (67%) subjects experienced 156 drug-related TEAEs.

Mild extravascular hemolysis, manifested as an increase in bilirubin, a decrease in hemoglobin, or a decrease in haptoglobin, was observed, as expected when an anti-D product is given to an Rh-positive individual. An increase in blood bilirubin was seen in 21% of subjects. The median decrease in hemoglobin was greatest (0.8 g/dL) at Day 6 and Day 8 following administration of Rhophylac®.

Table 2 shows the most common TEAEs observed in the clinical study.

Table 2: Most Common Treatment-Emergent Adverse Events (TEAEs) in Subjects With ITP

<table>
<thead>
<tr>
<th>TEAE</th>
<th>Number of Subjects (%) With a TEAE</th>
<th>Number of Subjects (%) With a Drug-Related TEAE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chills</td>
<td>34 (34.7%)</td>
<td>34 (34.7%)</td>
</tr>
<tr>
<td>Pyrexia/ Increased body temperature</td>
<td>32 (32.6%)</td>
<td>30 (30.6%)</td>
</tr>
<tr>
<td>Increased blood bilirubin</td>
<td>21 (21.4%)</td>
<td>21 (21.4%)</td>
</tr>
<tr>
<td>Headache</td>
<td>14 (14.3%)</td>
<td>11 (11.2%)</td>
</tr>
</tbody>
</table>

* Defined as TEAEs with a possible, probable, definite, or unknown relationship to the study drug.

Serious adverse events (SAEs) were reported in 10 (10.2%) subjects. SAEs considered to be drug-related were intravascular hemolytic reaction (hypotension, nausea, chills and headache), and a decrease in haptoglobin and hemoglobin in two subjects; headache, dizziness, nausea, pallor, shivering, and weakness requiring hospitalization in one subject; and an increase in blood pressure and severe headache in one subject. All four subjects recovered completely.

6.2 Postmarketing Experience

Because postmarketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to product exposure. Evaluation and interpretation of these postmarketing reactions is confounded by underlying diagnosis, concomitant medications, pre-existing conditions, and inherent limitations of passive surveillance.

Suppression of Rh Isoimmunization

The following adverse reactions have been identified during postapproval use of Rhophylac® for suppression of Rh isoimmunization: hypersensitivity reactions, including rare cases of anaphylactic shock or anaphylactoid reactions, headache, dizziness, vertigo, hypotension, tachycardia, dyspnea, nausea, vomiting, rash, erythema, pruritus, chills, pyrexia, malaise, and, rarely, diarrhea and back pain. Transient injection-site irritation and pain have been observed following intramuscular administration.

ITP

Transient hemoglobinuria has been reported in a patient being treated with Rhophylac® for ITP.

Manufactured by: ZLB Behring AG
Berne, Switzerland
US License No. 1710

Distributed by: ZLB Behring LLC
Kankakee, IL 60901 USA
GAIN Trial

Gemtuzumab Ozogamicin Addition to Induction and Post-Consolidation Therapy in Younger Patients With Newly Diagnosed AML

CRITERIA:
Patient eligibility
Age: < 56 years of age
Therapy: Untreated de novo acute myeloid leukemia (AML)

OBJECTIVES:
1. Determine whether using gemtuzumab ozogamicin in addition to standard treatment with daunorubicin and cytosine arabinoside will increase relapse-free survival
2. Evaluate the safety and tolerability of this regimen

SCHEMA

INDUCTION THERAPY:
Randomization into 2 arms

ARM 1
Daunorubicin 45 mg/m²
Days 1–3, cytosine arabinoside 100 mg/m²
Days 1–7, and gemtuzumab ozogamicin 0 mg/m² Day 4

ARM 2
Daunorubicin 60 mg/m²
Days 1–3, cytosine arabinoside 100 mg/m²
Days 1–7

CONSOLIDATION THERAPY:
3 cycles of high-dose cytosine arabinoside (Ara-C)-HiDaC
(3 g/m² Days 1, 3, 5 every 28 days)

POST-CONSOLIDATION THERAPY:
Randomization into 2 arms

ARM 1
3 doses of gemtuzumab ozogamicin 5 mg/m² at least 28 days apart

ARM 2
No therapy

CONTACT INFORMATION: Go to www.swog.org/visitors/studies.asp. Select “Open Protocols,” then Study no. S0106. Click the “Start Search” button, which retrieves the protocol information. Click on “Where is This Study Open” (bottom right of page), then locate appropriate state and hospital. SWOG telephone number: 1-210-677-8808.
Blood, the Journal of the American Society of Hematology, published in print and online, provides an international forum for the publication of original articles describing basic laboratory, translational, and clinical investigations in hematology. Acceptance of manuscripts is based on the originality and newness of the observation or investigation, the quality of the work described and validity of the evidence presented, the clarity of presentation, and the relevance to our readership. Authors submit a manuscript with the understanding that the manuscript (or its essential substance) has not been published other than as an abstract in any language or format and has not been submitted elsewhere for print or electronic publication consideration. Visit our complete Author Guide online at www.bloodjournal.org/misc/ifora.dtl for information on the following topics:

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Regular Articles. Manuscripts submitted as Regular Articles are expected to be concise, well organized, and clearly written. Acceptance of Regular Articles is based on the originality, definitiveness, and importance of the findings to the field of hematology. Regular Articles will be published under the following scientific categories: Chemokines, Cytokines, and Interleukins; Clinical Trials and Observations; Gene Therapy; Hematopoiesis; Hemostasis, Thrombosis, and Vascular Biology; Immunobiology; Neoplasia; Phagocytes; Red Cells; Stem Cells in Hematology; Transfusion Medicine; and Transplantation. Maximum length for a Regular Article is 5,000 words of text, not counting the abstract, tables, figure legends, and references; abstracts must not exceed 200 words and should be a single paragraph with no subheadings. Submissions are limited to a total of 7 figures and digital images are strongly preferred.

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Review Articles. Review articles are highly desired and are generally solicited by the Editor-in-Chief. A review article should focus on a topic of broad scientific interest, on recent advances in diagnosis and therapy, or on another timely subject relevant to the field of hematology. Such articles must be concise and critical and include appropriate references to the literature. Reviews should not exceed 5,000 words in length, must include abstracts of 200 words or fewer, and must have no more than 100 references. The use of tables and color figures to summarize critical points is encouraged; the Journal offers a service to professionally draw illustrations, if requested. Review Articles are reviewed by the Editors and other expert reviewers before a final publication decision is made, and revisions may be required. The online Author Guide contains separate guidelines for invited reviews.

Reviews in Translational Hematology. These critical reviews describe recent advances in basic science that are moving from the bench to the bedside.

Perspectives. Perspectives on significant topics in the field of hematology are highly desired. Interested authors should correspond with the Editor-in-Chief prior to submission to discuss the suitability of the proposed subject matter. The length should not exceed 2,500 words; the abstract must not exceed 200 words; and references are limited to 50. Typically, Perspectives state the topic concisely, discuss opposing viewpoints, and make recommendations for further investigation.

Inside Blood. These brief capsules written by experts in the field present analyses of specific articles that are deemed particularly noteworthy. Invited by the Editors.

Brief Reports. Short manuscripts definitively documenting either experimental results or informative patient presentations are considered for publication in this category. The authors are asked to document experimental results with a clear question in the introduction and then to present definitive proof in the body of the text. Keep the “Materials and Methods” section succinct, using primarily cited work, but sufficiently informative to allow reproduction of the data. Combine the “Results” and “Discussion” sections and do not repeat the introductory comments. Brief Reports should not exceed 1,200 words of text and 150 words in the abstract and should have no more than 2 figures/tabs and 25 references.

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Please contact the Blood office if you cannot find an answer to your question(s) in our complete Author Guide at www.bloodjournal.org/misc/ifora.dtl or in the Blood Bench>Press Manuscript Processing System at submit.bloodjournal.org: Blood, The American Society of Hematology, 1900 M Street, NW, Suite 200, Washington, DC 20036; phone: 202-776-0548; fax: 202-776-0549

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Recent Advances in the Treatment of
HEMATOLOGIC MALIGNANCIES and
CANCER-ASSOCIATED THROMBOSIS

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August 21

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Use in pregnancy: Use in women of childbearing potential is not recommended because the long-term effects of rFVIIa on human reproduction are not known. FVII is involved in both haemostatic and coagulation pathways.

Pharmacodynamic properties: The pharmacodynamic properties of rFVIIa are dependent on the underlying haemorrhage of the individual patient. The pharmacodynamic properties of rFVIIa in patients with haemophilia A or B patients. Isolated cases of FVII-deficient patients developing antibodies against FVII reported after treatment with NovoSeven. These patients previously treated with human plasma and/or plasma derived FVII. Monitor FVII deficient patients for FVII antibodies. One case angenoendothelial oedema reported in patient with Glanzmann’s thrombasthenia after administration of NovoSeven. The Summary of Product Characteristics should be consulted for a full list of side effects.

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Editor: Sanford J. Shattil, MD
Publisher: American Society of Hematology
Blood Online is sponsored by an unrestricted grant from:
Thrombopoietin tertiary structure
Thrombocytopenia: Fewer Platelets, More Consequences

Thrombocytopenia: The result of platelet destruction and/or impaired production

Thrombocytopenia is commonly encountered across a number of conditions, including immune (idiopathic) thrombocytopenic purpura (ITP). Patients with thrombocytopenia are at increased risk for both minor and major bleeding events. For instance, in ITP, there is a risk of fatal hemorrhage, due mainly to intracranial hemorrhage.

Thrombocytopenia has many causes. These causes include a deficiency in platelet production, excessive platelet destruction, sequestration of platelets by the spleen, or a combination of these.

Thrombopoietin: Essential in stimulating platelet production

Thrombopoietin (TPO) is the primary growth factor regulating platelet production and the proliferation of megakaryocytes. TPO is produced primarily in the liver and binds to the TPO receptor on megakaryocytes. New approaches for treating thrombocytopenia are being investigated.

Increased understanding of hematopoiesis can lead to novel treatment approaches

As a pioneer in hematopoietic research, Amgen has made significant contributions in the field of hematology/oncology and is now investigating the TPO pathway and its potential role in the treatment of thrombocytopenia.

References:
Enter a new world of support for Ph+ CML

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Building on more than 5 years of worldwide experience in improving outcomes in Philadelphia chromosome–positive (Ph+) chronic myeloid leukaemia (CML), Novartis Oncology introduces a new support programme—CML ALLIANCE.

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PROGRAM UNDER DEVELOPMENT AND SUBJECT TO LEGAL AND REGULATORY APPROVAL.
REVLIMID® (lenalidomide) in combination with dexamethasone is indicated for the treatment of multiple myeloma patients who have received at least one prior therapy.

REVLIMID® (lenalidomide) is indicated for patients with transfusion-dependent anemia due to Low- or Intermediate-1–risk myelodysplastic syndromes (MDS) associated with a deletion 5q cytogenetic abnormality with or without additional cytogenetic abnormalities.

<table>
<thead>
<tr>
<th>WARNING</th>
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<tbody>
<tr>
<td>1. POTENTIAL FOR HUMAN BIRTH DEFECTS:</td>
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<tr>
<td>LENALIDOMIDE IS AN ANALOGUE OF THALIDOMIDE. THALIDOMIDE IS A KNOWN HUMAN TERATOGEN THAT CAUSES SEVERE LIFE-THREATENING HUMAN BIRTH DEFECTS. IF LENALIDOMIDE IS TAKEN DURING PREGNANCY, IT MAY CAUSE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. FEMALES SHOULD BE ADVISED TO AVOID PREGNANCY WHILE TAKING REVLIMID® (lenalidomide).</td>
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<tr>
<td>Special Prescribing Requirements</td>
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<tr>
<td>BECAUSE OF THIS POTENTIAL TOXICITY AND TO AVOID FETAL EXPOSURE TO REVLIMID® (lenalidomide), REVLIMID® (lenalidomide) IS ONLY AVAILABLE UNDER A SPECIAL RESTRICTED DISTRIBUTION PROGRAM. THIS PROGRAM IS CALLED “RevAssist™”. UNDER THIS PROGRAM, ONLY PRESCRIBERS AND PHARMACISTS REGISTERED WITH THE PROGRAM CAN PRESCRIBE AND DISPENSE THE PRODUCT. IN ADDITION, REVLIMID® (lenalidomide) MUST ONLY BE DISPENSED TO PATIENTS WHO ARE REGISTERED AND MEET ALL THE CONDITIONS OF THE RevAssist® PROGRAM.</td>
</tr>
<tr>
<td>2. HEMATOLOGIC TOXICITY (NEUTROPENIA AND THROMBOCYTOPENIA):</td>
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<tr>
<td>THIS DRUG IS ASSOCIATED WITH SIGNIFICANT NEUTROPENIA AND THROMBOCYTOPENIA. EIGHTY PERCENT OF PATIENTS WITH DEL 5q MYELODYSPLASTIC SYNDROMES HAD TO HAVE A DOSE DELAY/REDUCTION DURING THE MAJOR STUDY. THIRTY-FOUR PERCENT OF PATIENTS HAD TO HAVE A SECOND DOSE DELAY/REDUCTION. GRADE 3 OR 4 HEMATOLOGIC TOXICITY WAS SEEN IN 80% OF PATIENTS ENROLLED IN THE STUDY. PATIENTS ON THERAPY FOR DEL 5q MYELODYSPLASTIC SYNDROMES SHOULD HAVE THEIR COMPLETE BLOOD COUNTS MONITORED WEEKLY FOR THE FIRST 8 WEEKS OF THERAPY AND AT LEAST MONTHLY THEREAFTER. PATIENTS MAY REQUIRE DOSE INTERRUPTION AND/OR REDUCTION. PATIENTS MAY REQUIRE USE OF BLOOD PRODUCT SUPPORT AND/OR GROWTH FACTORS. (SEE DOSAGE AND ADMINISTRATION)</td>
</tr>
</tbody>
</table>

**ADDITIONAL WARNINGS: HEMATOLOGIC TOXICITY**

**Multiple Myeloma**

In the pooled multiple myeloma studies, Grade 3 and 4 hematologic toxicities were more frequent in patients treated with the combination of REVLIMID® (lenalidomide) and dexamethasone than in patients treated with dexamethasone alone. Patients on therapy should have their complete blood counts monitored every 2 weeks for the first 12 weeks and then monthly thereafter. Patients may require dose interruption and/or dose reduction.

**CONTRAINDICATIONS:**

Hypersensitivity: REVLIMID® (lenalidomide) is contraindicated in any patients who have demonstrated hypersensitivity to the drug or its components.

**PRECAUTIONS:**

Renal impairment: REVLIMID® (lenalidomide) is substantially excreted by the kidney, so the risk of toxic reactions may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection, and it would be prudent to monitor renal function.

Nursing mothers: It is not known whether REVLIMID® (lenalidomide) is excreted in human milk. Because of the potential for adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

**ADVERSE REACTIONS:**

**Multiple Myeloma**

In the REVLIMID® (lenalidomide)/dexamethasone treatment group, 151 patients (45%) underwent at least one dose interruption with or without a dose reduction of REVLIMID® (lenalidomide) compared to 21% in the placebo/dexamethasone treatment group. Of these patients who had one dose interruption with or without a dose reduction, 50% in the REVLIMID® (lenalidomide)/dexamethasone treatment group underwent at least one additional dose interruption with or without a dose reduction compared to 21% in the placebo/dexamethasone treatment group.

Other adverse reactions reported in multiple myeloma patients (REVLIMID® (lenalidomide)/dexamethasone vs dexamethasone/placebo): constipation (39% vs 19%), fatigue (38% vs 37%), insomnia (32% vs 37%), muscle cramp (30% vs 21%), diarrhea (29% vs 25%), neutropenia (28% vs 5%), anemia (24% vs 17%), hyperglycemia (15% vs 14%), hyperlipidemia (15% vs 14%), muscle weakness (15% vs 15%).

**Myelodysplastic Syndromes**

Other adverse reactions reported in del 5q MDS patients (REVLIMID® (lenalidomide)): diarrhea (49%), pruritus (42%), rash (36%), constipation (24%), nausea (24%), nasopharyngitis (23%), arthralgia (22%), pyrexia (21%), back pain (21%), peripheral edema (20%), cough (20%), dizziness (20%), headache (20%), muscle cramp (18%), dyspnea (17%), and pharyngitis (16%).

**DOSE AND ADMINISTRATION:**

Dosing is continued or modified based upon clinical and laboratory findings. Dosing modifications are recommended to manage Grade 3 or 4 neutropenia or thrombocytopenia or other Grade 3 or 4 toxicities judged to be related to lenalidomide. For other Grade 3 or 4 toxicities judged to be related to lenalidomide, hold treatment and restart at next lower dose level when toxicity has resolved to less than or equal to Grade 2.

Please see full Prescribing Information, including Boxed WARNINGS, CONTRAINDICATIONS, PRECAUTIONS, and ADVERSE REACTIONS, on adjacent pages.
The world of options has changed for many patients with multiple myeloma
Significantly superior

In 2 randomized Phase III studies comparing REVLIMID® + dex to placebo + dex in multiple myeloma

Two multicenter, randomized, double-blind, placebo-controlled Phase III studies [Study 1 (North American), Study 2 (international)] compared REVLIMID® plus oral pulse dexamethasone (REVLIMID® + dex) to placebo + dex in patients who have received at least 1 prior treatment.

In the 2 studies, a preplanned interim analysis was conducted when 50% of the patients progressed. This analysis showed superior time to progression with REVLIMID® + dex and led to patient censoring for both arms.

>50% overall response rate*

- 53% vs 16% in Study 1 (P<0.0001)
- 51% vs 19% in Study 2 (P<0.0001)

In Studies 1 and 2, median time to response with REVLIMID® + dex was 54 days

Median follow-up time was approximately 5 months

- 20.1 weeks (Study 1) and 22.3 weeks (Study 2)

* Based on modified EBMT/IBMTR/ABMTR criteria. Adapted from Bladé J, et al. Br J Haematol. 1998. (Overall response = CR + PR. Includes 2 assessments performed 6 weeks apart. Responses must have lasted at least 6 weeks.)
Once-a-day oral dosing in multiple myeloma

25 mg daily starting dose

- **REVLIMID®** — Start at 25 mg/day orally once a day with water for Days 1–21 of repeated 28-day cycles
- **Dex** — Start at 40 mg/day orally:
  - Days 1–4, 9–12, and 17–20 of each 28-day cycle for first 4 cycles
  - Days 1–4 of every 28-day cycle thereafter
- Monitor CBCs every 2 weeks for the first 12 weeks, then monthly thereafter
- Dosing continued/modified based on clinical and laboratory findings
- Dose interruption and/or reduction may be required

Safety: **REVLIMID® + dex vs placebo + dex**

- With **REVLIMID® + dex**, Grade 3 neutropenia occurred in 17% vs 2% and Grade 4 neutropenia occurred in 4% vs 1% of patients; 2% vs 0% of patients had Grade 3/4 febrile neutropenia

- The overall incidence of thrombotic events — including DVT, pulmonary embolism, thrombosis, and thromboembolism — was higher among patients taking REVLIMID® + dex (12%; 43/346) vs placebo + dex (4%; 14/345)

No significant difference between treatment arms in Grade 3/4 constipation, fatigue, and neuropathy

REVLIMID® (lenalidomide) in combination with dexamethasone is indicated for the treatment of multiple myeloma patients who have received at least one prior therapy.

**RevAssist** REVLMID® is only available under a special restricted distribution program

Please see full Prescribing Information, including Boxed WARNINGS, CONTRAINDICATIONS, PRECAUTIONS, and ADVERSE REACTIONS, on adjacent pages.
REVLIMID® (lenalidomide)
5 mg, 10 mg, 15 mg and 25 mg capsules

WARNING: POTENTIAL FOR HUMAN BIRTH DEFECTS

LENALIDOMIDE IS AN ANALOGUE OF THALIDOMIDE. THALIDOMIDE IS A KNOWN HUMAN TERATOGEN THAT CAUSES SEVERE LIFE-THREATENING HUMAN BIRTH DEFECTS. IF LENALIDOMIDE IS TAKEN DURING PREGNANCY, IT MAY CAUSE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. FEMALES SHOULD BE ADVISED TO AVOID PREGNANCY WHILE TAKING REVLIMID® (lenalidomide).

BECAUSE OF THIS POTENTIAL TOXICITY AND TO AVOID FETAL EXPOSURE TO REVLIMID® (lenalidomide), REVLIMID® (lenalidomide) IS ONLY AVAILABLE UNDER A SPECIAL RESTRICTED DISTRIBUTION PROGRAM. THIS PROGRAM IS CALLED “RevAssist®.” UNDER THIS PROGRAM, ONLY PRESCRIBERS AND PHARMACISTS REGISTERED WITH THE PROGRAM CAN PRESCRIBE AND DISPENSE THE PRODUCT. IN ADDITION, REVLIMID® (lenalidomide) MUST ONLY BE DISPENSED TO PATIENTS WHO ARE REGISTERED AND MEET ALL THE CONDITIONS OF THE RevAssist® PROGRAM.

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REVLIMID® (lenalidomide) should be used in sexually active males when the patient MEETS ALL OF THE FOLLOWING CONDITIONS (i.e., she is unable to become pregnant while on lenalidomide therapy)

• she understands and can reliably carry out instructions.
• she is capable of complying with the mandatory contraceptive measures, pregnancy testing, patient registration, and patient survey as described in the RevAssist® program.

Effective contraception must be used by female patients of childbearing potential for at least 4 weeks before starting REVLIMID® (lenalidomide) therapy, during dose interruptions and for 4 weeks following discontinuation of REVLIMID® (lenalidomide) therapy. Reliable contraception is indicated even where there has been a history of infertility, unless due to hysterectomy, as the patient has been postmenopausal naturally for at least 24 consecutive months. Two reliable forms of contraception must be used simultaneously unless continuous abstinence from heterosexual sexual contact is the chosen method. Females of childbearing potential should be referred to a qualified provider of contraceptive methods, if needed. Sexually mature females who have not undergone a hysterectomy, have not had a bilateral oophorectomy or who have not been postmenopausal naturally for at least 24 consecutive months (i.e., who have had menstues at some time in the preceding 24 consecutive months) are considered to be females of childbearing potential.

Before prescribing REVLIMID® (lenalidomide), females of childbearing potential should have 2 negative pregnancy tests (sensitivity of at least 50 mIU/mL). The first test should be performed within 10-14 days, and the second test within 24 hours prior to prescribing REVLIMID® (lenalidomide). A prescription for REVLIMID® (lenalidomide) for a female of childbearing potential must not be issued by the prescriber until negative pregnancy tests have been verified by the prescriber.

Male Patients

Before prescribing REVLIMID® (lenalidomide) treatment, REVLIMID® (lenalidomide) must be discontinued immediately.

Any suspected fetal exposure to REVLIMID® (lenalidomide) should be reported to the FDA via the MedWatch number at 1-800-FDA-1088 and also to Celgene Corporation at 1-888-423-5436. The patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling.

Female Patients

REVLIMID® (lenalidomide) should be used in females of childbearing potential only when the patient MEETS ALL OF THE FOLLOWING CONDITIONS (i.e., she is unable to become pregnant while on lenalidomide therapy)

• he has received and understands both oral and written warnings of the potential risks of taking lenalidomide and exposing a fetus to the drug.
• he has received both oral and written warnings of the risk of possible contraception failure and that it is unknown whether lenalidomide is present in semen. He has been instructed that he must always use a latex condom during any sexual contact with females of childbearing potential, even if he has undergone a successful vasectomy.
• he acknowledges, in writing, his understanding of these warnings and of the need to use a latex condom during any sexual contact with females of childbearing potential, even if he has undergone a successful vasectomy. Females of childbearing potential are considered to be sexually mature females who have undergone a hysterectomy, have not had a bilateral oophorectomy or who have not been postmenopausal for at least 24 consecutive months (i.e., who have had menstues at some time in the preceding 24 consecutive months).

RELATION OF PREGNANCY TESTING (SENSITIVITY OF AT LEAST 50 mIU/mL). The first test should be performed within 10-14 days, and the second test within 24 hours prior to prescribing REVLIMID® (lenalidomide). A prescription for REVLIMID® (lenalidomide) for a female of childbearing potential must not be issued by the prescriber until negative pregnancy tests have been verified by the prescriber.

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Female Patients

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• he understands and can reliably carry out instructions.
• he is capable of complying with the mandatory contraceptive measures that are appropriate for men, patient registration, and patient survey as described in the RevAssist® program.
The efficacy and safety of REVILIMID® (lenalidomide) were evaluated in patients with transfusion dependent anemia in low- or intermediate-1-risk MDS with a 5q (q31-33) cytogenetic abnormality in isolation or with additional cytogenetic abnormalities, at a dose of 10 mg once daily or 10 mg once daily for 21 days every 28 days in an open-label, single-arm, multi-center study. The major study was not designed nor powered to prospectively compare the efficacy of the 2 dosing regimens. Sequential dose reductions to 5 mg daily and 5 mg once daily, other, as well as dose delays, were allowed for toxicity.

This major study enrolled 148 patients who had RBC transfusion dependent anemia. RBC-transfusion dependency was defined as having received ≥2 units of RBCs within 8 weeks prior to study treatment. The study enrolled patients with absolute neutrophil counts (ANC) ≤5000/mm3, platelet counts ≤50,000/mm3, serum creatinine ≥2.5 mg/dL, serum SGOT/AST or SGPT/ALT ≥3.0 x upper limit of normal (ULN), and serum direct bilirubin ≥2.0 mg/dL. Granulocyte colony-stimulating factor was permitted for patients who developed neutropenia or fever in association with neutropenia. Baseline patient and disease-related characteristics are summarized in Table 1.

### Table 1: Baseline Demographic and Disease-Related Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Overall (N=148)</th>
<th>REVLIMID/Dex</th>
<th>Placebo/Dex</th>
<th>REVLIMID/Dex</th>
<th>Placebo/Dex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>71.0</td>
<td>59.0</td>
<td>67.0</td>
<td>59.0</td>
<td>67.0</td>
</tr>
<tr>
<td>Median</td>
<td>37.0</td>
<td>39.0</td>
<td>35.0</td>
<td>37.0</td>
<td>36.0</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>143 (96.6)</td>
<td>76 (54.8)</td>
<td>54 (54.9)</td>
<td>66 (54.8)</td>
<td>65 (54.9)</td>
</tr>
<tr>
<td>Female</td>
<td>5 (3.4)</td>
<td>13 (8.5)</td>
<td>13 (8.5)</td>
<td>14 (9.1)</td>
<td>13 (8.5)</td>
</tr>
<tr>
<td>Duration of MDS (years)</td>
<td>2.3</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
<td>2.5</td>
</tr>
<tr>
<td>Median</td>
<td>0.1, 20.7</td>
<td>0.1, 20.7</td>
<td>0.1, 20.7</td>
<td>0.1, 20.7</td>
<td>0.1, 20.7</td>
</tr>
<tr>
<td>Duration of 5q (q31-33) Cytogenetic Abnormality (days)</td>
<td>118 (79.7%)</td>
<td>62 (42.0%)</td>
<td>56 (56.0%)</td>
<td>56 (46.1%)</td>
<td>52 (41.5%)</td>
</tr>
<tr>
<td>Median</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
<td>10.0</td>
</tr>
<tr>
<td>Other cytogenetic abnormalities</td>
<td>37 (25.2%)</td>
<td>11 (8.3%)</td>
<td>15 (15.2%)</td>
<td>12 (9.8%)</td>
<td>13 (10.5%)</td>
</tr>
<tr>
<td>IPSS Score(4)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low (0)</td>
<td>55 (37.2)</td>
<td>29 (20.0%)</td>
<td>26 (26.0%)</td>
<td>26 (21.6%)</td>
<td>29 (23.3%)</td>
</tr>
<tr>
<td>Intermediate-1 (0.5-1.0)</td>
<td>65 (43.9%)</td>
<td>31 (21.6%)</td>
<td>34 (34.3%)</td>
<td>31 (25.4%)</td>
<td>34 (26.9%)</td>
</tr>
<tr>
<td>Intermediate-2 (1.5-2.0)</td>
<td>6 (4.1)</td>
<td>2 (1.4)</td>
<td>4 (4.1)</td>
<td>2 (1.6)</td>
<td>4 (3.2)</td>
</tr>
<tr>
<td>High(&gt;2.5)</td>
<td>2 (1.4)</td>
<td>1 (0.7)</td>
<td>1 (1.0)</td>
<td>1 (0.8)</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Missing</td>
<td>20 (13.5)</td>
<td>10 (7.1)</td>
<td>10 (10.0)</td>
<td>10 (8.2)</td>
<td>10 (8.2)</td>
</tr>
<tr>
<td>FAB Classification(5) from central review</td>
<td>37 (25.2%)</td>
<td>14 (10.0%)</td>
<td>23 (23.3%)</td>
<td>13 (10.5%)</td>
<td>23 (18.2%)</td>
</tr>
<tr>
<td>RA</td>
<td>177 (52.0)</td>
<td>96 (68.7)</td>
<td>61 (62.5%)</td>
<td>81 (65.3%)</td>
<td>86 (67.2%)</td>
</tr>
<tr>
<td>RARS</td>
<td>16 (10.8)</td>
<td>9 (6.6)</td>
<td>7 (7.2)</td>
<td>9 (7.5)</td>
<td>7 (5.6)</td>
</tr>
<tr>
<td>RAB</td>
<td>30 (20.3)</td>
<td>18 (12.9)</td>
<td>12 (12.5%)</td>
<td>12 (9.8%)</td>
<td>12 (9.5%)</td>
</tr>
<tr>
<td>CMML</td>
<td>3 (2.0)</td>
<td>2 (1.4)</td>
<td>1 (1.0)</td>
<td>2 (1.6)</td>
<td>1 (0.8)</td>
</tr>
</tbody>
</table>

### Table 2: Summary of Efficacy Analysis – Studies 1 and 2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study 1</th>
<th>Study 2</th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall n (%)</td>
<td>90 (53)</td>
<td>34 (19)</td>
<td>90 (51)</td>
<td>34 (19)</td>
</tr>
<tr>
<td>CR (Complete Response) n (%)</td>
<td>14 (8)</td>
<td>1 (1)</td>
<td>14 (8)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>PR (Partial Response) n (%)</td>
<td>76 (44)</td>
<td>27 (16)</td>
<td>76 (44)</td>
<td>27 (16)</td>
</tr>
<tr>
<td>NR (No Response) n (%)</td>
<td>89 (53)</td>
<td>28 (16)</td>
<td>90 (51)</td>
<td>24 (19)</td>
</tr>
<tr>
<td>Overall Response n (%)</td>
<td>90 (53)</td>
<td>34 (19)</td>
<td>90 (51)</td>
<td>34 (19)</td>
</tr>
</tbody>
</table>

The primary efficacy endpoint in both studies was time to progression (TTP). TTP was defined as the time from randomization to the first occurrence of progressive disease or death due to progressive disease.

Preplanned interim analyses of both studies showed that the combination of REVILIMID® (lenalidomide)/dexamethasone was significantly superior to dexamethasone alone for TTP. The studies were unblinded to allow patients in the placebo/dexamethasone group to receive treatment with the REVILIMID® (lenalidomide)/dexamethasone combination.

Table 3 summarizes TTP and response rates based on the best response assessments for Studies 1 and 2.

### Table 3: Summary of Efficacy Analysis – Studies 1 and 2

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study 1</th>
<th>Study 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall n (%)</td>
<td>90 (53)</td>
<td>34 (19)</td>
</tr>
<tr>
<td>CR (Complete Response) n (%)</td>
<td>14 (8)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>PR (Partial Response) n (%)</td>
<td>76 (44)</td>
<td>27 (16)</td>
</tr>
<tr>
<td>NR (No Response) n (%)</td>
<td>89 (53)</td>
<td>28 (16)</td>
</tr>
<tr>
<td>Overall Response n (%)</td>
<td>90 (53)</td>
<td>34 (19)</td>
</tr>
</tbody>
</table>

The p-value is based on a one-tailed unstratified log rank test.

Figure 1: Kaplan-Meier Estimate of Time to Progression — Study 1

The Kaplan-Meier estimate of time to progression for Study 1 is depicted in Figure 1. The log-rank test p-value is less than 0.0001. The p-value is based on a one-tailed unstratified log rank test.
precautions

General
Nonclinical studies have been conducted in patients with renal impairment. This drug is known to be excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function.

Information for Patients
Patients should be counseled on lenalidomide’s potential risk of teratogenicity due to its structural similarity to thalidomide. Patients may only acquire a prescription for REVLIMID® (lenalidomide) therapy through a controlled distribution program (RevAssist®) through contracted pharmacies. Patients must be counseled that the risk of fetal harm associated with lenalidomide therapy is increased when administered during pregnancy. Pregnancy should be avoided in women of childbearing potential while on REVLIMID® (lenalidomide) therapy. If a patient becomes pregnant while receiving lenalidomide, the patient should be informed of the potential hazards to the fetus and how to minimize exposure; the patient should be referred to an obstetrician/gynecologist experienced in reproductive toxicity for further evaluation and counseling. Use of effective contraception is strongly recommended. Any suspected fetal exposure to REVLIMID® (lenalidomide) must be reported to Pfizer, Inc.
Thrombocytopenia (61.5%; 91/148) and neutropenia (58.8%; 87/148) were the most frequently reported adverse events. Table 4 summarizes the adverse events that were reported in ≥5% of the REVLI® (lenalidomide) treated patients in the del 5q MDS clinical study. Table 5 summarizes the most frequently reported Grade 3 and 4 adverse reactions regardless of relationship to treatment with REVLI® (lenalidomide). In the single-arm studies conducted, it is often not possible to distinguish adverse events that are drug-related and those that reflect the patient’s underlying disease.

Table 4: Summary of Adverse Events Reported in ≥8% of the REVLI® (lenalidomide) Treated Patients in del 5q MDS Clinical Study

<table>
<thead>
<tr>
<th>System organ class/Preferred term</th>
<th>10 mg Overall (N=148)</th>
<th>Patients with a specific event</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Blood and Lymphatic System Disorders</strong></td>
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<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>91 (61.5)%</td>
<td></td>
</tr>
<tr>
<td>Neutropenia</td>
<td>87 (58.8)%</td>
<td></td>
</tr>
<tr>
<td>Anemia NOS</td>
<td>17 (11.5)%</td>
<td></td>
</tr>
<tr>
<td>Leukopenia NOS</td>
<td>12 (8.1)%</td>
<td></td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>8 (5.4)%</td>
<td></td>
</tr>
<tr>
<td><strong>Skin and Subcutaneous Tissue Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>62 (41.9)%</td>
<td></td>
</tr>
<tr>
<td>Rash NOS</td>
<td>53 (35.8)%</td>
<td></td>
</tr>
<tr>
<td>Dry Skin</td>
<td>21 (14.2)%</td>
<td></td>
</tr>
<tr>
<td>Contusion</td>
<td>12 (8.1)%</td>
<td></td>
</tr>
<tr>
<td>Night Sweats</td>
<td>12 (8.1)%</td>
<td></td>
</tr>
<tr>
<td>Sweating Increased</td>
<td>10 (6.8)%</td>
<td></td>
</tr>
<tr>
<td>Erythema</td>
<td>8 (5.4)%</td>
<td></td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diarrhea NOS</td>
<td>72 (48.6)%</td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>35 (23.6)%</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>35 (23.6)%</td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain NOS</td>
<td>18 (12.2)%</td>
<td></td>
</tr>
<tr>
<td>Vomiting NOS</td>
<td>15 (10.1)%</td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain Upper</td>
<td>12 (8.1)%</td>
<td></td>
</tr>
<tr>
<td>Dry Mouth</td>
<td>10 (6.8)%</td>
<td></td>
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<tr>
<td>Loose Stools</td>
<td>9 (6.1)%</td>
<td></td>
</tr>
<tr>
<td><strong>Respiratory, Thoracic and Mediastinal Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>24 (16.2)%</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>29 (19.6)%</td>
<td></td>
</tr>
<tr>
<td>Dyspnea NOS</td>
<td>25 (16.9)%</td>
<td></td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>23 (15.5)%</td>
<td></td>
</tr>
<tr>
<td>Epistaxis</td>
<td>22 (14.9)%</td>
<td></td>
</tr>
<tr>
<td>Dyspnea Exertional</td>
<td>10 (6.8)%</td>
<td></td>
</tr>
<tr>
<td>Rhinitis NOS</td>
<td>10 (6.8)%</td>
<td></td>
</tr>
<tr>
<td>Bronchitis NOS</td>
<td>9 (6.1)%</td>
<td></td>
</tr>
<tr>
<td><strong>Musculoskeletal and Connective Tissue Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis</td>
<td>32 (21.6)%</td>
<td></td>
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<tr>
<td>Back Pain</td>
<td>31 (20.9)%</td>
<td></td>
</tr>
<tr>
<td>Muscle Cramp</td>
<td>27 (18.2)%</td>
<td></td>
</tr>
<tr>
<td>Pain in Limb</td>
<td>16 (10.8)%</td>
<td></td>
</tr>
<tr>
<td>Myalgia</td>
<td>13 (8.8)%</td>
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</tr>
<tr>
<td>Peripheral Swelling</td>
<td>12 (8.1)%</td>
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<tr>
<td><strong>Nervous System Disorders</strong></td>
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<tr>
<td>Dizziness</td>
<td>29 (19.6)%</td>
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</tr>
<tr>
<td>Headache</td>
<td>29 (19.6)%</td>
<td></td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>10 (6.8)%</td>
<td></td>
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<tr>
<td>Dysequisia</td>
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<tr>
<td>Perioperative Neuropathy</td>
<td>8 (5.4)%</td>
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<tr>
<td><strong>Metabolic and Nutrition Disorders</strong></td>
<td></td>
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<tr>
<td>Hypokalemia</td>
<td>16 (10.8)%</td>
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<tr>
<td>Anorexia</td>
<td>15 (10.1)%</td>
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<tr>
<td>Hyperuricemia</td>
<td>9 (6.1)%</td>
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<tr>
<td><strong>Investigations</strong></td>
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<td>Alanine Aminotransferase Increased</td>
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<tr>
<td><strong>Psychiatric Disorders</strong></td>
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<tr>
<td>Insomnia</td>
<td>15 (10.1)%</td>
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<tr>
<td>Depression</td>
<td>10 (6.8)%</td>
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<tr>
<td><strong>Vascular Disorders</strong></td>
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<td></td>
</tr>
<tr>
<td>Hypertension NOS</td>
<td>15 (10.1)%</td>
<td></td>
</tr>
<tr>
<td><strong>Renal and Urinary Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dysuria</td>
<td>10 (6.8)%</td>
<td></td>
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<tr>
<td><strong>Cardiac Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Palpitation</td>
<td>8 (5.4)%</td>
<td></td>
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<tr>
<td><strong>Endocrine Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquired Hypothyroidism</td>
<td>10 (6.8)%</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Preferred term</th>
<th>10 mg (N=148)</th>
<th>Patients with at least one Grade 3 or 4 AE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>79 (53.4)%</td>
<td></td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>70 (47.9)%</td>
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</tr>
<tr>
<td>Pneumonia NOS</td>
<td>11 (7.4)%</td>
<td></td>
</tr>
<tr>
<td>Rash NOS</td>
<td>10 (6.8)%</td>
<td></td>
</tr>
<tr>
<td>Anemia NOS</td>
<td>9 (6.1)%</td>
<td></td>
</tr>
<tr>
<td>Leukopenia NOS</td>
<td>8 (5.4)%</td>
<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>7 (4.7)%</td>
<td></td>
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<tr>
<td>Back Pain</td>
<td>7 (4.7)%</td>
<td></td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>6 (4.1)%</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>6 (4.1)%</td>
<td></td>
</tr>
<tr>
<td>Diabetes NOS</td>
<td>5 (3.4)%</td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>5 (3.4)%</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td>4 (2.7)%</td>
<td></td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (2.7)%</td>
<td></td>
</tr>
<tr>
<td>Granulocytopenia</td>
<td>3 (2.0)%</td>
<td></td>
</tr>
<tr>
<td>Chest Pain</td>
<td>3 (2.0)%</td>
<td></td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>3 (2.0)%</td>
<td></td>
</tr>
<tr>
<td>Respiratory Distress</td>
<td>3 (2.0)%</td>
<td></td>
</tr>
<tr>
<td>Pruritus</td>
<td>3 (2.0)%</td>
<td></td>
</tr>
<tr>
<td>Pancytopenia</td>
<td>3 (2.0)%</td>
<td></td>
</tr>
<tr>
<td>Muscle Cramp</td>
<td>3 (2.0)%</td>
<td></td>
</tr>
<tr>
<td>Respiratory Tract Infection</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Multi-organ Failure</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Epistaxis</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Hypoesthesia</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Pleural Effusion</td>
<td>2 (1.4)%</td>
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</tr>
<tr>
<td>Pneumonitis NOS</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Pulmonary Hypertension NOS</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Vomiting NOS</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Sweating Increased</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Anemia NOS</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Pain in Limb</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
<tr>
<td>Syncope</td>
<td>2 (1.4)%</td>
<td></td>
</tr>
</tbody>
</table>

(1) Preferred Terms are coded using the MedDRA dictionary. A patient with multiple occurrences of an AE is counted only once in the Preferred Term category.

In other clinical studies of REVLI® (lenalidomide) in MDS patients, the following serious adverse events (regardless of relationship to study drug treatment) not described in Table 4 or 5 were reported:

**Blood and lymphatic system disorders:** Warm type hemolytic anemia, splenic infarction, bone marrow depression NOS, coagulopathy, hemolysis NOS, hemolytic anemia NOS, refractory anemia NOS

**Cardiac disorders:** Cardiac failure, congestive atrial fibrillation, anemia pectoris, cardiac arrest, cardiac failure NOS, cardio-respiratory arrest, cardiomyopathy NOS, myocardial infarction, myocardial ischemia, atrial fibrillation aggravated, bradycardia NOS, cardiogenic shock, pulmonary edema NOS, supraventricular arrhythmia NOS, tachyarrhythmia, ventricular dysfunction

**Endocrine disorders:** Basedow's disease

**Gastrointestinal disorders:** Gastrointestinal hemorrhage NOS, colitis ischemic, intestinal perforation NOS, rectal hemorrhage, colonic polyp, diverticulitis NOS, dysphagia, gastritis NOS, gastritis NOS, hemorrhagic reflux disease, obstructive inguinal hernia, irritable bowel syndrome, melanoma, pancreatitis due to biliary obstruction, pancreatitis NOS, perirectal abscess, small intestinal obstruction NOS, upper gastrointestinal hemorrhage

**General disorders and administration site conditions:** Disease progression NOS, fatigue, gait abnormal, intermittent pyrexia, nodule, rigors, sudden death

**Hepatobiliary disorders:** Hepatitis A NOS, cholestasis acute NOS, cholestasis NOS, hepatic failure

**Immune system disorders:** Hypersensitivity NOS

**Infections and infestations:** Infection NOS, bacteremia, central line infection, circulatory shock NOS, ear infection NOS, Enterobacter species, fungal infection NOS, herpes viral infection NOS, influenza, kidney infection NOS, Klebsiella species, lobar pneumonia NOS, localized infection, oral infection, Pseudomona NOS, infection NOS, septic shock, sinusitis acute NOS, sinusitis NOS, Staphylococcal infection, uresepsis

**Injury, poisoning and procedural complications:** Femur fracture, transfusion reaction, cerebral vertebral fracture, femoral neck fracture, fractured pelvis, hip fracture, overdose NOS, post procedural hemorrhage, rib fracture, road traffic accident, spinal compression fracture

**Investigations:** Blood creatinine increased, culture NOS negative, hemoglobin decreased, liver function tests NOS abnormal, troponin I increased

**Metabolism and nutrition disorders:** Dehydration, gout, hypernatremia, hypoglycemia NOS

**Musculoskeletal and connective tissue disorders:** Arthritis NOS, arthritis NOS aggravated, gouty arthritis, neck pain, chondrocalcinosis, pyrophosphate

**Neoplasms benign, malignant and unspecified:** Acute leukemia NOS, acute myeloid leukemia NOS, bronchoalveolar carcinoma, lung cancer metastatic, lymphoma NOS, prostate cancer metastatic

**Nervous system disorders:** Cerebrovascular accident, aphasia, cerebellar infarction, depressed level of consciousness, dysarthria, migraine NOS, spinal cord compression NOS, subarachnoid hemorrhage NOS, transient ischemic attack

NOS, not otherwise specified

(2) System organ classes and preferred terms are coded using the MedDRA dictionary. System organ classes and preferred terms are listed in descending order of frequency for the Overall column. A patient with multiple occurrences of an AE is counted only once in the AE category.
Studies 1 and 2.

Multiple Myeloma

Vascular system disorders: deep vein thrombosis, hypotension NOS, aortic disorder, ischemia NOS, thromboembolic superficial, thromboembolism superficial, thrombosis.

Multiple Myeloma

Table 7: Adverse Events with NCI CTC Grades 3 and 4 Reported In At Least 2% of Patients by Preferred Term and Treatment Group – (Safety Population)

<table>
<thead>
<tr>
<th>System organ class/Preferred term</th>
<th>Revlimid/Dex (N=346)</th>
<th>Placebo/Dex (N=345)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neutropenia</td>
<td>96 (27.7)</td>
<td>16 (4.6)</td>
</tr>
<tr>
<td>Anemia NOS</td>
<td>84 (24.3)</td>
<td>60 (17.4)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>59 (17.1)</td>
<td>34 (9.4)</td>
</tr>
<tr>
<td>Vision Blurred</td>
<td>51 (14.7)</td>
<td>36 (10.4)</td>
</tr>
<tr>
<td>Constipation</td>
<td>134 (38.7)</td>
<td>64 (18.6)</td>
</tr>
<tr>
<td>Diarrhea NOS</td>
<td>101 (29.2)</td>
<td>85 (24.6)</td>
</tr>
<tr>
<td>Nausea</td>
<td>76 (22.0)</td>
<td>66 (19.1)</td>
</tr>
<tr>
<td>Vomiting NOS</td>
<td>48 (13.9)</td>
<td>46 (13.3)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>39 (11.0)</td>
<td>28 (8.1)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>153 (43.8)</td>
<td>129 (37.4)</td>
</tr>
<tr>
<td>Anemia NOS</td>
<td>81 (23.4)</td>
<td>86 (24.9)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>59 (17.1)</td>
<td>57 (17.1)</td>
</tr>
<tr>
<td>Edema Peripheral</td>
<td>73 (21.1)</td>
<td>65 (18.8)</td>
</tr>
<tr>
<td>Infections and infestations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper Respiratory Tract</td>
<td>47 (13.6)</td>
<td>43 (12.5)</td>
</tr>
<tr>
<td>Pneumonia NOS</td>
<td>39 (11.3)</td>
<td>26 (7.5)</td>
</tr>
<tr>
<td>Investigations</td>
<td>64 (18.2)</td>
<td>48 (13.9)</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>9 (2.6)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Hypocalcemia</td>
<td>8 (2.3)</td>
<td>5 (1.4)</td>
</tr>
<tr>
<td>Hypotension NOS</td>
<td>4 (1.2)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Muscle Weakness NOS</td>
<td>18 (5.2)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Confusional State</td>
<td>6 (1.7)</td>
<td>3 (0.9)</td>
</tr>
<tr>
<td>Ataxia</td>
<td>6 (1.7)</td>
<td>3 (0.9)</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>7 (2.0)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>2 (0.6)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Vascular Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deep Vein Thrombosis</td>
<td>23 (6.6)</td>
<td>1 (0.3)</td>
</tr>
<tr>
<td>Pulmonary Embolism</td>
<td>2 (0.6)</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

Table 7 summarizes the Grade 3/4 adverse events reported in ≥2% of patients in either treatment group in Studies 1 and 2.

*See WARNINGS
Neutrophil counts (ANC)*

If neutrophilia develops WITHIN 4 weeks of starting treatment at 10 mg daily

If baseline ANC <1,000/mcL

When Neutrophils Recommended Course

When Neutrophils

If baseline ANC <1,000/mcL

When Neutrophils

If neutrophilia develops AFTER 4 weeks of starting treatment at 10 mg daily

If baseline ANC <1,000/mcL

When Neutrophils

If platelet transfusions

Return to baseline ANC

Reulenimad® at 5 mg every other day

Patients who are dosed initially at 10 mg and experience neutropenia should have their dosage adjusted as follows:

Dose Adjustments During Treatment

When Neutrophils

Recommend Course

Return to baseline ANC

Reulenimad® at 5 mg daily

Patients who experience neutropenia at 5 mg daily should have their dosage adjusted as follows:

Other Grade 3/4 Toxicities

For other Grade 3/4 toxicities judged to be related to lenalidomide, hold treatment and restart at next lower dose level when toxicity has resolved to <Grade 2.

How Supplied

REVLIMID® (lenalidomide) is supplied as:

White opaque capsules imprinted “RE” on one half and “5 mg” on the other half in black ink:

5 mg bottles of 100 (NDC 59572-450-30)

5 mg bottles of 100 (NDC 59572-450-90)

Blue/green and pale yellow opaque capsules imprinted “RE” on one half and “10 mg” on the other half in black ink:

10 mg bottles of 30 (NDC 59572-410-30)

10 mg bottles of 100 (NDC 59572-410-90)

Powder blue and white opaque capsules imprinted “RE” on one half and “15 mg” on the other half in black ink:

15 mg bottles of 30 (NDC 59572-415-21)

15 mg bottles of 100 (NDC 59572-415-90)

White opaque capsules imprinted “RE” on one half and “25 mg” on the other half in black ink:

25 mg bottles of 25 (NDC 59572-425-25)

25 mg bottles of 100 (NDC 59572-425-90)

Storage and Dispensing

Drug no more than a 28-day supply.

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F). [See USP Controlled Room Temperature].

Rx only.

Manufactured for Celgene Corporation

86 Morris Avenue

Summit, NJ 07901

Important Information and Warnings for All Patients Taking REVLIMID® (lenalidomide)

WARNING: POTENTIAL FOR HUMAN BIRTH DEFECTS.

LENALIDOMIDE IS AN ANALOGUE OF THALIDOMIDE. THALIDOMIDE IS A KNOWN HUMAN TERATOGEN THAT CAUSES LIFE-THREATENING HUMAN BIRTH DEFECTS. IF LENALIDOMIDE IS TAKEN DURING PREGNANCY, IT MAY CAUSE BIRTH DEFECTS OR DEATH TO AN UNBORN BABY. FEMALES SHOULD BE ADVISED TO AVOID PREGNANCY WHILE ON LENALIDOMIDE.

All Patients

• The patient understands that birth defects may occur with the use of REVLIMID® (lenalidomide).

• The patient has been named by his/her doctor that an unborn baby may have birth defects and can even, if a female is pregnant or becomes pregnant while taking REVLIMID® (lenalidomide).

• REVLIMID® (lenalidomide) will be prescribed ONLY for the patient and must NOT be shared with ANYONE, even someone who has similar symptoms.

• REVLIMID® (lenalidomide) must be kept out of the reach of children and should NEVER be given to females who are able to have children.

• The patient cannot donate blood while taking REVLIMID® (lenalidomide).

• The patient has read the REVLIMID® (lenalidomide) patient brochure and understands the contents, including other possible health problems from REVLIMID® (lenalidomide), “side effects.”

• The patient’s doctor has answered any questions the patient has asked.

• The patient must participate in a telephone survey and patient registry, while taking REVLIMID® (lenalidomide).

Female Patients of Childbearing Potential

• The patient must not take REVLIMID® (lenalidomide) if she is pregnant, breast-feeding a baby, or able to get pregnant and not using the required two methods of birth control.

• The patient confirms that she is not now pregnant, nor will she try to become pregnant during REVLIMID® (lenalidomide) therapy, during therapy interruption and for at least 4 weeks after she has completely finished taking REVLIMID® (lenalidomide).

• If the patient is able to become pregnant, she must use at least one highly effective method and one additional effective method of birth control (contraception) AT THE SAME TIME.

At least one highly effective method AND One additional effective method

• IUD

• Hormonal (birth control pills, injections, patch or implants)

• Cervical cap

• Tubal ligation

• Partner’s vasectomy

• These birth control methods must be used for at least 4 weeks before beginning REVLIMID® (lenalidomide) therapy, during REVLIMID® (lenalidomide) therapy, during therapy interruption and for 4 weeks following discontinuation of REVLIMID® (lenalidomide) therapy.

• The patient must use these birth control methods unless she completely abstains from heterosexual sexual contact.

• If a hormonal method (birth control pills, injections, patch or implants) or IUD is not medically possible for the patient, she may use another highly effective method or two barrier methods AT THE SAME TIME.

• The patient must have a pregnancy test done by her doctor within 10-14 days and 24 hours before REVLIMID® (lenalidomide) therapy, then weekly during the first 4 weeks of REVLIMID® (lenalidomide) therapy.

• Thereafter, the patient must have a pregnancy test every week if she has regular menstrual cycles, or every 2 weeks if her cycles are irregular while she is taking REVLIMID® (lenalidomide).

• The patient must immediately stop taking REVLIMID® (lenalidomide) and inform her doctor:

• If she becomes pregnant while taking the drug.

• If she misses her menstrual period, or experiences unusual menstrual bleeding.

• If she stops using birth control.

• If she thinks FOR ANY REASON that she may be pregnant.

• The patient understands that if her doctor is not available, she can call 1-888-668-2538 for information on emergency contraception.

Female Patients Not of Childbearing Potential

The patient certifies that she is not now pregnant, nor of childbearing potential as she has been postmenopausal naturally for at least 24 months (been through the change of life); or she has had a hysterectomy or bilateral oophorectomy.

The patient or guardian certifies that a prepubertal female child is not now pregnant, nor is of childbearing potential as menstruation has not yet begun, and/or the child will not be engaging in heterosexual sexual contact for at least 4 weeks before REVLIMID® (lenalidomide) therapy, during REVLIMID® (lenalidomide) therapy, during therapy interruption and for at least 4 weeks after stopping therapy.

Male Patients

The patient has been told by his doctor that he must NEVER have unprotected sexual contact with a female who can become pregnant.

Because it is not known whether REVLIMID® (lenalidomide) is present in semen, his doctor has explained that he must either completely abstain from sexual contact with females who are pregnant or able to become pregnant, or he must use a latex condom EVERY TIME he engages in any sexual contact with females who are pregnant or may become pregnant while he is taking REVLIMID® (lenalidomide) and for 4 weeks after he stops taking the drug, even if he has had a successful vasectomy.
• The patient should inform his doctor:
  - if he has had unprotected sexual contact with a female who can become pregnant.
  - if he thinks FOR ANY REASON, that his sexual partner may be pregnant.
  - the patient understands that if his doctor is not available, he can call 1-888-668-2528 for information on emergency contraception.
  - the patient cannot donate semen or sperm while taking REVLIMID® (lenalidomide).

Know the medicines you take. Keep a list of them to show your healthcare provider and pharmacist.

How should I take REVLIMID®?
• Take REVLIMID® exactly as prescribed. You must also follow all the instructions of the RevAssist® program. Before prescribing REVLIMID®, your healthcare provider will:
  - explain the RevAssist® program to you
  - have you sign the Patient-Physician Agreement Form

You will not be prescribed REVLIMID® if you cannot agree to or follow all of the instructions of the RevAssist® program.

You will get no more than a 28-day supply of REVLIMID® at one time. This is to make sure you follow the RevAssist® program.

• If you miss a dose of REVLIMID®, take it as soon as you remember that day. If you miss taking your dose for the entire day, go back to taking your regular dose the next day. Do not take 2 doses at the same time.
• If you take too much REVLIMID® or overdose, call your healthcare provider or poison control center right away.
• You will have regular blood tests during your treatment with REVLIMID®. If you are being treated for del 5q myelodysplastic syndromes (MDS) you should have your blood tested every week during your first 8 weeks of treatment, and at least monthly after that. If you are being treated for multiple myeloma, your blood counts should be checked every two weeks for the first 12 weeks and then at least monthly thereafter. That your healthcare provider may adjust your dose of REVLIMID® or interrupt your treatment based on the results of your blood tests and on your general condition.
• Female patients who can get pregnant will get regular pregnancy testing.
  - get a pregnancy test weekly for 4 weeks.
  - Female patients who can become pregnant must agree to use 2 separate forms of effective birth control at the same time, 4 weeks before, while taking, and for 4 weeks after stopping REVLIMID®.
• Male patients, even those who have had a vasectomy, must agree to use a latex condom during sexual contact with a pregnant female or a female who can become pregnant.

What should I avoid while taking REVLIMID®?
• Do not get pregnant while taking REVLIMID® and for 4 weeks after stopping REVLIMID®. See “What is the most important information I should know about REVLIMID®?”
• Do not breastfeed while taking REVLIMID®. We do not know if REVLIMID® passes into your milk and harms your baby.
• Do not share REVLIMID® with other people. It may cause birth defects and other serious problems.
• Do not give blood while you take REVLIMID® and for 4 weeks after stopping REVLIMID®. If someone who is pregnant gets your donated blood, her baby may be exposed to REVLIMID® and may be born with birth defects.

What are the possible side effects of REVLIMID®?
• REVLIMID® may cause serious side effects including:
  - birth defects
  - low white blood cells and platelets
  - blood clots in veins and in the lungs
• Other common side effects of REVLIMID® are:
  - diarrhea
  - itching
  - rash
  - tiredness

Tell your healthcare provider about any side effect that bothers you or that does not go away. These are not all the side effects with REVLIMID®. Ask your healthcare provider or pharmacist for more information.

How should I store REVLIMID®?
Store REVLIMID® at room temperature, 59°F to 86°F (15°C to 30°C).

Keep REVLIMID® and all medicines out of the reach of children.

General information about the safe and effective use of REVLIMID®
Medicines are sometimes prescribed for conditions that are not mentioned in Medication Guides. Do not take REVLIMID® for conditions for which it was not prescribed. Do not give REVLIMID® to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide provides a summary of the most important information about REVLIMID®. If you would like more information, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about REVLIMID® that is written for healthcare professionals. You can also call 1-888-423-5436 or visit www.REVLIMID.com.

What are the ingredients in REVLIMID®?
REVLIMID® (lenalidomide) capsules contain 5 mg, 10 mg, 15 mg or 25 mg of lenalidomide and are available as gelatin capsules for oral administration.

The inactive ingredients of REVLIMID® capsules are: lactose anhydrous, microcrystalline cellulose, croscarmellose sodium, and magnesium stearate.

The 5 mg and 25 mg capsule shells contain gelatin, titanium dioxide and black ink. The 10 mg capsule shell contains gelatin, FD&C blue no. 2, yellow iron oxide, titanium dioxide and black ink. The 15 mg capsule shell contains gelatin, FD&C blue no. 2, titanium dioxide and black ink.

Manufactured for Celgene Corporation Summit, NJ 07901
This Medication Guide has been approved by the US Food and Drug Administration.

RevPyPhG.005/MG.005 03/07

Information for patients and caregivers: MEDICATION GUIDE REVLIMID® (rev-t-mid) (lenalidomide)

Read the Medication Guide that comes with REVLIMID®: before you start taking it and each time you get a new prescription. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about REVLIMID®?
• REVLIMID® is only for patients who understand and agree to all of the instructions in the RevAssist® program.
• REVLIMID® may cause serious side effects including:
  1. birth defects
  2. low white blood cells and platelets
  3. blood clots in veins and in the lungs

1. Possible birth defects (deformed babies) or death of an unborn baby. Female patients who are pregnant or who plan to become pregnant must not take REVLIMID®.

REVLIMID® is similar to the medicine thalidomide (THALIDOMIDE). We know thalidomide causes life-threatening birth defects. REVLIMID® has not been tested in pregnant women. REVLIMID® has harmed unborn animals in animal testing.

Female patients must not get pregnant:
• for 4 weeks before starting REVLIMID®
• while taking REVLIMID®
• during dose interruptions of REVLIMID®
• for 4 weeks after stopping REVLIMID®

It is not known if REVLIMID® passes into semen, so:
• Male patients, including those who have had a vasectomy, must use a latex condom during any sexual contact with a pregnant female or a female that can become pregnant while taking REVLIMID® and for 4 weeks after stopping REVLIMID®.

If you get pregnant while taking REVLIMID®, stop taking it right away and call your healthcare provider. Female partners of males taking REVLIMID® should call their healthcare provider right away if they get pregnant. Healthcare providers and patients should report all cases of pregnancy to:
• FDA MedWatch at 1-800-FDA-1088, and
• Celgene Corporation at 1-888-423-5436

2. Low white blood cells (neutropenia) and low platelets (thrombocytopenia). REVLIMID® causes low white blood cells and low platelets in most patients. You may need a blood transfusion or certain medicines if your blood counts drop too low. If you are being treated for del 5q myelodysplastic syndromes (MDS) your blood counts should be checked weekly during the first 8 weeks of treatment with REVLIMID® and at least monthly thereafter. If you are being treated for multiple myeloma, your blood counts should be checked every 2 weeks for the first 12 weeks and then at least monthly thereafter.

3. An increased chance for blood clots in veins and in the lungs. Call your healthcare provider or get emergency medical care right away if you get the following signs or symptoms:
• shortness of breath
• chest pain
• arm or leg swelling

What is REVLIMID® and what is it used for?
REVLIMID® is a medicine taken by mouth to treat certain patients who have myelodysplastic syndromes (MDS). Patients with MDS have bone marrow that does not produce enough mature blood cells. This causes a lack of healthy blood cells that can function properly in the body. There are different types of MDS. REVLIMID® is for the type of MDS with a chromosome problem where part of chromosome 5 is missing. This type of MDS is known as deletion 5q MDS. Patients with this type of MDS may have low red blood cell counts that require treatment with blood transfusions.

REVLIMID® is also used with dexamethasone to treat patients with multiple myeloma who have already had another treatment. Multiple myeloma is a cancer of plasma cells. Plasma cells are found in the bone marrow. Plasma cells produce a protein called antibodies. Some antibodies can attack and kill disease causing germs. Patients with this type of cancer may have low blood cell counts and immune problems giving them a higher chance for getting infections such as pneumonia. The bones can be affected leading to bone pain and breaks (fractures).

REVLIMID® can only be:
• prescribed by healthcare providers who are registered in the RevAssist® program
• dispensed by a pharmacy that is registered in the RevAssist® program
• given to patients who are registered in the RevAssist® program and who agree to do everything required in the program

REVLIMID® has not been studied in children under 18 years of age.

Who should not take REVLIMID®?
• Do not take REVLIMID® if you are pregnant, plan to become pregnant, or become pregnant during REVLIMID® treatment. REVLIMID® may cause birth defects. See “What is the most important information I should know about REVLIMID®?”
• Do not take REVLIMID® if you are allergic to anything in it. See the end of this Medication Guide for a complete list of ingredients in REVLIMID®.

What should I tell my healthcare provider before taking REVLIMID®?
Tell your healthcare provider about all of your medical conditions, including if you:
• are pregnant or breastfeeding. REVLIMID® must not be used by women who are pregnant or breastfeeding.

Tell your healthcare provider about all the medicines you take including prescription and non-prescription medicines, vitamins and herbal supplements. It is possible that REVLIMID® and other medicines may affect each other causing serious side effects.

RevPyPhG.005/MG.005 03/07
Important Safety Information

Humate-P® is contraindicated in individuals with a history of anaphylactic or severe systemic response to antihemophilic factor or von Willebrand factor preparations or to any of its components.

Thromboembolic events have been reported in VWD patients receiving coagulation factor replacement, especially in the setting of known risk factors for thrombosis. Caution should be exercised and antithrombotic measures considered.

Humate-P® is derived from human plasma. As with all plasma-derived products, the risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.
In the treatment of VWD, Humate-P® stands alone

Humate-P® is the only von Willebrand factor (VWF) concentrate that:

- Is approved for the treatment of von Willebrand disease (VWD) and the prevention of excessive bleeding during and after surgery
- Can even be used for prevention of bleeding during and after surgery in all VWD types and for all procedures
- Contains high molecular weight multimers of VWF—important for correcting the coagulation defect in patients with VWD

In over 20 years and more than one-half billion units infused, there is no documented evidence of viral transmission with Humate-P®.

Visit us at www.HumateP.com

Close as it gets to normal VWF

HUMATE-P®
Antihemophilic Factor/von Willebrand Factor Complex (Human), Dried, Pasteurized

Although few adverse reactions have been reported in patients receiving Humate-P®, the most commonly reported are allergic-anaphylactic reactions, including urticaria, chest tightness, rash, pruritus, edema, shock, chills and fever, and hypervolemia. For patients undergoing surgery, the most common adverse reactions are postoperative wound or injection-site bleeding.

Please see brief summary of prescribing information on page 3 of this ad.

Reference: 1. Data on file, CSL Behring LLC.
BRIEF SUMMARY OF PRESCRIBING INFORMATION

CSL Behring
Humate-P
Antihemophilic Factor/von Willebrand Factor Complex (Human), Dried, Pasteurized

Manufactured by: CSL Behring GmbH
6045 Marburg, Germany
US License No. 1765

Distributed by: CSL Behring LLC
Kankakee, IL 60901 USA

It only
Before prescribing, please consult full prescribing information, a brief summary of which follows:

CONTRAINDICATIONS
Humate-P, Antihemophilic Factor/von Willebrand Factor Complex (Human), Dried, Pasteurized, is contraindicated in individuals with a history of anaphylactic or severe systemic response to antihemophilic factor or von Willebrand factor products. It is also contraindicated in individuals with a known hypersensitivity to any of its components.

WARNINGS
Thromboembolic events have been reported in WVD patients receiving Antihemophilic Factor/von Willebrand Factor Complex (Human), Dried, Pasteurized. Thromboembolic events should be considered in the differential diagnosis of patients on treatment with Humate-P®. Early reports might indicate a higher incidence in females. In addition, endogenous high levels of FVIII have also been associated with thromboembolic events. In some cases, increased SGPT/ALT levels have been observed in patients receiving antihemophilic factor/von Willebrand factor products. Because Humate-P® and Hemate-P® are made from the same raw material, patients with a history of Hepatitis B virus exposure should be monitored for this condition.

Humate-P® and Hemate-P®, Antihemophilic Factor/von Willebrand Factor Complex (Human), Dried, Pasteurized, is made from human plasma. As a result, the risk of transmitting viral agents, including those not yet known to science, is inherent. These products are sterilized by heat treatment of the purified, stabilized aqueous solution at 60°C for 10 hours (i.e., pasteurization). In addition, the purification procedure, which includes several precipitation steps and an adsorption step, is used in the manufacture of Humate-P® and Hemate-P®. Additional virus reduction steps (see DOSAGE AND ADMINISTRATION) have been employed to reduce the risk of virus transmission. The primary virus reduction step of the Hemate-P® manufacturing process is the heat treatment of the purified, stabilized aqueous solution at 60°C for 10 hours (i.e., pasteurization). In addition, the purification procedure, which includes several precipitation steps and an adsorption step, is used in the manufacture of Humate-P® and Hemate-P®. Additional virus reduction steps (see DOSAGE AND ADMINISTRATION) have been employed to reduce the risk of virus transmission. The primary virus reduction step of the Hemate-P® manufacturing process is the heat treatment of the purified, stabilized aqueous solution at 60°C for 10 hours (i.e., pasteurization). The primary virus reduction step of the Humate-P® manufacturing process is the heat treatment of the purified, stabilized aqueous solution at 60°C for 10 hours (i.e., pasteurization).

The following table lists the non-hemorrhagic adverse events reported in at least two subjects, regardless of causality, and the adverse events that were possibly related to Humate-P®. Pulmonary embolism was considered related possibly to Humate-P® occurred in one elderly subject who underwent bilateral laparoscopic surgery.

<table>
<thead>
<tr>
<th>Body System</th>
<th>Adverse Event</th>
<th>Number of Subjects with an AE Possibly Related to Humate-P®</th>
<th>Number of Subjects with an AE Regardless of Causality*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body as a Whole</td>
<td>Pain</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Fever</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Back pain</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Headache</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Vomiting</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Sore throat</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Hemic and lymphatic System</td>
<td>Anemia</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Decreased Hemoglobin</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Metabolic/Nutritional</td>
<td>Increased Uric acid</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nervous</td>
<td>Decreased</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Digestive</td>
<td>Nausea</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Urinary</td>
<td>Vomiting</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Skin and Appendages</td>
<td>Rash</td>
<td>1</td>
</tr>
</tbody>
</table>

* Occurring in two or more subjects

Thromboembolic events are reported frequently in WVD patients receiving Humate-P®. Although the overwhelming number of hepatitis A and parvovirus B19 cases are community acquired, there have been reports of transmission of hepatitis A virus (HAV) and parvovirus B19 (B19V) in patients with hemophilia. However, no inhibitor is known other than the immune complexes of the humoral immune response. However, no inhibitor is known other than the immune complexes of the humoral immune response.

Adverse Reactions in Clinical Trials

Because clinical trials are conducted under widely varying conditions, the adverse reaction rates observed cannot be directly compared to rates in other clinical trials and may not reflect the rates observed in practice.

von Willebrand Disease
Treatment of WVD

4 Hemophilia A patients, including allergic reaction, urticaria, chest tightness, rash, pruritus, and edema, were reported in 2 of 97 (2%) subjects in a Canadian retrospective study. Four of 97 (4%) subjects experienced seven adverse events that were considered to have a possible or probable relationship to the product. These included pruritis, anaphylaxis, asso...
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PNH is a disabling and life-threatening disease

The clinical sequelae of PNH can result in severe complications and death¹

- Patients experience pain, disabling fatigue, and severe anemia, often requiring transfusions²-⁴
- Approximately 40% of patients experience a thrombotic event*¹
- Thrombosis has been reported to increase the risk of death ten-fold⁶
- The median survival rate for patients is as low as 10 years¹

*Reported in Hillmen, et al. 1995¹

Visit www.PNHSource.com, an educational resource for PNH.

CLINICAL TRIAL PATIENT RECRUITMENT

Two open-labeled, randomized, two-dose, parallel group trials of ofatumumab, a fully human monoclonal anti-CD20 antibody:

- **Trial Hx-CD20-407: Ofatumumab with FC in previously untreated B-CLL patients**
  
  **Primary Outcome Measures**
  - Complete remissions measured from start of treatment until 3 months after last infusion

  **Inclusion Criteria**
  - Patients with active B-CLL with an indication for treatment
  - Patients 18 years and above

  **Exclusion Criteria**
  - Any previous treatment for B-CLL with any cell depleting aim
  - Patients who at the time of inclusion are not expected to be able to complete the ofatumumab-FC treatment
  - Current participation in any other interventional clinical study

- **Trial Hx-CD20-409: Ofatumumab with CHOP in previously untreated FL patients**
  
  **Primary Outcome Measures**
  - Objective response rate measured from start of treatment until 3 months after last infusion

  **Inclusion Criteria**
  - Patient with Follicular Lymphoma grade 1 – 3, stage III-IV, or Bulky disease stage II
  - Patients 18 years and above

  **Exclusion Criteria**
  - Any previous treatment for Follicular Lymphoma
  - Clinical suspicion that the Follicular Lymphoma has transformed to aggressive lymphoma
  - Current participation in any other interventional clinical study

For more information, please call: 866-887-1291.
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Publisher: American Society of Hematology

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THE 22nd ANNUAL COURSE AND MEETING OF THE CLINICAL CYTOMETRY SOCIETY

Hyatt Regency Capitol Hill
Washington, DC
Course dates: October 5-7, 2007
Meeting Dates: October 7-9, 2007

The Clinical Cytometry Society is pleased to announce its annual course and meeting to be held at the Hyatt Regency in Washington, DC, on October 5-9, 2007. The course, which precedes the meeting, provides in-depth training for practical analysis of clinical specimens by flow cytometry. The meeting provides supplemental training, as well as updates on topics of interest to clinical cytometrists and hematopathologists. Sessions at this meeting will include regulatory affairs, rare event analysis in the clinical laboratory, assessment of targeted therapy, hematopath updates, and new developments in dendritic cells, as well as practical case study interpretations, and luncheon workshops. The meeting and course may be registered for separately.

For further information, please visit http://www.cytometry.org.

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For further information on program and registration can be found at http://www.nocancer.ephe.fr
Penn State College of Medicine  
Penn State Milton S. Hershey Medical Center

DIRECTOR-HEMOSTASIS/THROMBOSIS PROGRAM
We are seeking a full-time hematologist at the rank of associate professor/professor with an established track record of research in hemostasis, thrombosis or endothelial cell biology to head the Section of Hemostasis/Thrombosis in the Division of Hematology/Medical Oncology of the Department of Medicine in Hershey, PA. This is a tenure track clinician-scientist position supported by an endowed professorship in hematology. This individual will hold a joint appointment in the Department of Pathology and Laboratory Medicine as the Medical Director of the Special Hematology and Hemostasis Laboratories.

The candidate will expand the existing federal and state funded Central Pennsylvania Hemophilia Center into a Hemophilia and Thrombophilia Center to provide comprehensive care, clinical research and education in disorders of hemostasis and thrombosis. The candidate is expected to develop a multi-disciplinary research program in the areas of hemostasis, thrombosis or endothelial cell biology. There are multiple opportunities for collaboration within the College of Medicine, other colleges at University Park, and the newly constructed Hershey Center for Applied Research adjacent to the Medical Center.

Penn State Milton S. Hershey Medical Center is an Affirmative Action, Equal Opportunity Employer. Women and minorities are encouraged to apply.

Interested individuals should send, email or fax their CV to: Hamid Al-Mondhiry, MD, Chair, Search Committee, Division of Hematology/Oncology, Penn State Milton S. Hershey Medical Center, 500 University Drive (H046), Hershey, PA 17033-0850, Fax 717-531-0647, halmondhiry@psu.edu

The Norris Cotton Cancer Center, the Dartmouth Medical School and the Dartmouth-Hitchcock Clinic are seeking applications for a Hematology/Oncology position. This physician will join the regional program based at the Lebanon campus of Norris Cotton Cancer Center and provide consultative service and primary oncology care to patients in the northern New England Region. Minimum requirements include completion of an approved fellowship program and board certification/eligibility in medical oncology. Additional certification in Hematology and post-fellowship experience are preferred. The successful candidate will be expected to become integrated into the academic and teaching activities of the Section of Hematology/Oncology and the cancer programs based within the Norris Cotton Cancer Center, an NCI-designated comprehensive cancer center.

Please send letters of inquiry and CV to:
Brenda A. Kline, Academic Assistant
Dartmouth-Hitchcock Medical Center
One Medical Center Drive
Lebanon, NH 03756
Fax: 603-650-5830
E-mail: Brenda.A.Kline@Hitchcock.ORG

Dartmouth-Hitchcock Medical Center
Dartmouth-Hitchcock Medical Center is an affirmative action/equal opportunity employer and is especially interested in identifying female and minority candidates.

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To place an advertisement in Blood’s Classified Advertising section, please contact Valerie Marvin at the following address: Blood, 180 Old Tappan Road, Old Tappan, NJ 07675. Phone: 201-767-4170; fax: 201-767-8065; e-mail: vmarvin@cunnasso.com.

Academic Hematologist/Oncologist
New Hampshire

The Norris Cotton Cancer Center, the Dartmouth Medical School, and the Dartmouth-Hitchcock Clinic are seeking applications for a Hematology/Oncology position. This physician will join the regional program based at the Lebanon campus of Norris Cotton Cancer Center and provide consultative service and primary oncology care to patients in the northern New England Region. Minimum requirements include completion of an approved fellowship program and board certification/eligibility in medical oncology. Additional certification in Hematology and post-fellowship experience are preferred. The successful candidate will be expected to become integrated into the academic and teaching activities of the Section of Hematology/Oncology and the cancer programs based within the Norris Cotton Cancer Center, an NCI-designated comprehensive cancer center.

Please send letters of inquiry and CV to:
Brenda A. Kline, Academic Assistant
Dartmouth-Hitchcock Medical Center
One Medical Center Drive
Lebanon, NH 03756
Fax: 603-650-5830
E-mail: Brenda.A.Kline@Hitchcock.ORG

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www.Dartmouth-Hitchcock.org

Academic Community-Based Medical Hematologist/Oncologist
Southern New Hampshire

The Norris Cotton Cancer Center, the Dartmouth Medical School and the Dartmouth-Hitchcock Clinic are seeking applications for a Hematology/Oncology position. This physician will provide consultative service and primary oncology care within a multi-specialty practice in the Dartmouth-Hitchcock Clinic System. Minimum requirements include completion of an approved fellowship program and board certification/eligibility in medical oncology. Additional certification in Hematology and post-fellowship experience are preferred. The successful candidate will be able to participate in the academic activities of the site-specific cancer programs based within the Section of Hematology/Oncology of the Norris Cotton Cancer Center, an NIH designated comprehensive cancer center. The practice is located in an urban, southern NH community with a strong school system and located near Boston, the ocean and white mountains.

Please send letters of inquiry and CV to:
Brenda A. Kline, Academic Assistant
Dartmouth-Hitchcock Medical Center
One Medical Center Drive
Lebanon, NH 03756
Fax: 603-650-5830
E-mail: Brenda.A.Kline@Hitchcock.ORG

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**Faculty Position**

**Hematology Division & Cardeza Foundation for Hematologic Research**

**Jefferson Medical College, Philadelphia**

The Division of Hematology and the Cardeza Foundation for Hematologic Research in the Department of Medicine at Jefferson Medical College are seeking Hematologists with an interest in academic benign Hematology. The Hematology Division and Cardeza have an outstanding Hemophilia Treatment Center, and clinical programs in Transfusion Medicine and Sickle Cell disease. The Cardeza also directs the Special Coagulation Laboratory for the Hospital, enabling unique teaching and clinical research opportunities, and efficient evaluation of patients with bleeding and clotting disorders. The Hematology Division has a combined fellowship program with Medical Oncology and the Bone Marrow Transplant Program in the Kimmel Cancer Center.

The new faculty member will have responsibilities on the Jefferson Medical College Hematology service and would be expected to have and develop an academic focus in hemostasis-thrombosis, Transfusion Medicine or hemoglobinopathies. Research support is available for candidates with on-going research programs. Applicants must be Board certified or eligible in Hematology, have excellent interpersonal and communication skills, and should be eligible for appointment at the rank of Assistant or Associate Professor of Medicine. The Cardeza Foundation provides on-going faculty and infrastructure support for Cardeza academic programs.

Located in Center City Philadelphia, Jefferson Medical College is one of the oldest and most highly respected medical schools in the U.S. Founded in 1824, the Medical College is part of Thomas Jefferson University and is affiliated with Thomas Jefferson University Hospital and the Jefferson Hospital for the Neurosciences. Interested candidates should send a CV, names of 3 references and a letter of interest to: Paul F. Bray, MD, Director of the Hematology Division and the Cardeza Foundation for Hematologic Research, Jefferson Medical College, 1015 Walnut Street – Curtis 705, Philadelphia, PA 19107. E-mail: paul.bray@jefferson.edu.

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**UNIVERSITY OF SOUTHERN CALIFORNIA**

**Keck School of Medicine**

**HEMATOLOGIC ONCOLOGIST**

The USC/Norris Comprehensive Cancer Center and the Department of Medicine of the Keck School of Medicine at the University of Southern California (USC) seek an outstanding physician (M.D. or M.D./Ph.D.) to join the Division of Cancer Medicine and Blood Diseases. We are seeking candidates with a successful track record in patient care and clinical/translational research in hematologic malignancies. The successful candidate will be nominated for the Ronald H. Bloom Family Chair and recommended for appointment as Associate or Full Professor. We offer a highly competitive salary package with excellent benefits, outstanding infrastructural research support and high quality laboratory space in the new 175,000 sq ft Harlyne Norris Research Tower.

Hematology and hematologic malignancy diagnostics and therapeutics have had a prominent history at USC. The patient population at USC/Norris Cancer Hospital, USC University Hospital and LAC+USC Medical Center is large, diverse and provides an outstanding resource for clinical research, including clinical trials and translational science. Significant growth in clinical, population-based, translational and basic research, in laboratory resources, and in faculty and support staff will occur in the next decade as a high priority of USC.

Qualifications: Candidates must be board-certified (or equivalent) in Internal Medicine and board eligible/certified (or equivalent) in Hematology. A strong background in patient care and clinical/translational research in hematologic malignancy is essential, along with a track record of peer-reviewed clinical or laboratory funding and strong mentoring credentials.

Please send letter of interest and curriculum vitae to:

Search Committee - Ronald H. Bloom Family Chair  
Division of Cancer Medicine and Blood Diseases  
USC/Norris Comprehensive Cancer Center  
University of Southern California  
1441 Eastlake Avenue, #3470  
Los Angeles, CA 90033  
Attn: Gloria Reyes (email: gloriare@usc.edu)

The University of Southern California is an EOE/AA
Pediatric Hematology/Oncology Faculty Position
Clinician/Clinical Investigator
Penn State Children’s Hospital
Pennsylvania State University College of Medicine

The Division of Pediatric Hematology/Oncology at the Penn State Children’s Hospital is recruiting a Clinician/Clinical Investigator. Candidates with an interest in designing and performing clinical trials related to childhood leukemia or lymphoma are particularly encouraged to apply. Applicants with an established track record in clinical investigation will be candidates for an Endowed Chair and appointment as Director of the Pediatric Hematopoietic Malignancy Program. Generous ongoing support for clinical research is provided by the Four Diamond’s Fund of the Penn State College of Medicine. Rank is at the Assistant to Full Professor level commensurate with the applicant’s experience and accomplishments.

The Division of Pediatric Hematology/Oncology currently has 8 full-time Pediatric Hematologists/Oncologists and 4 Ph.D. faculty. Over 100 new oncology patients are seen annually, and there are programs in pediatric stem cell transplantation, neuro-oncology, hemophilia, and sickle cell disease. The division has an accredited Pediatric Hem/Onc fellowship program and is an active member of COG. The endowed Four Diamonds Pediatric Cancer Research Institute includes NIH-funded basic science and translational research in vaccine therapy, immune modulation after BMT, hematopoesis, and leukemia. The Four Diamonds Fund, an NIH-supported General Clinical Research Center, and Pediatric Clinical Trials office support pediatric clinical investigation. The inpatient and outpatient facilities have been recently expanded and provide an excellent environment for patient care and clinical research.

Please submit a current CV and letter of interest to: Barbara Miller, M.D. (bmiller3@psu.edu), Chief, Division of Pediatric Hematology/Oncology, Penn State Children’s Hospital, the Pennsylvania State University College of Medicine, Box 850, MC H085, Hershey, Pennsylvania 17033. Applications are accepted until position is filled.

Penn State Milton S. Hershey Medical Center and the College of Medicine are Equal Opportunity/Affirmative Action employers and encourage applications from women and members of minority groups.

Pediatric Hematologists
University of Pennsylvania School of Medicine, Department of Pediatrics
Assistant Professor – Clinician-Educator

The Division of Hematology in the Department of Pediatrics at the University of Pennsylvania's School of Medicine seeks candidates for several Assistant Professor positions in the non-tenure clinician-educator track. Applicants must have an M.D. degree, have demonstrated excellent qualifications in education, research, and clinical care, and be board certified/eligible in pediatric hematology/oncology.

Successful applicants will have experience in the field of pediatric hematology. We are seeking a candidate with demonstrated expertise in clinical issues related to platelet number and function and research interest and expertise in the molecular basis and treatment of thrombocytopenias. We are also seeking a candidate with demonstrated clinical expertise in hemostasis and thrombosis and clinical research interest and expertise in the complications of the hemophilia and other bleeding disorders.

The University of Pennsylvania is an equal opportunity, affirmative action employer. Women and minority candidates are strongly encouraged to apply.

Please submit curriculum vitae and a letter of interest to:

Mortimer Poncz, M.D.
Professor of Pediatrics, University of Pennsylvania School of Medicine
Chief, Division of Hematology
The Children's Hospital of Philadelphia
34th Street & Civic Center Blvd.
Philadelphia, PA 19104
DIRECTOR OF CLINICAL RESEARCH

The Cancer Therapy & Research Center Institute for Drug Development, a premier cancer research organization focusing on the early development and optimal use of novel anticancer therapeutics, is seeking candidates for the position of Director of Clinical Research and John E. Freeman Chair. The Director will provide scientific leadership and assist in management of operations of the Department of Clinical Research including design and conduct of clinical protocols, with an emphasis on Phase I trials. The Director will be key to maintaining relationships with our academic partners including the NCI and pharmaceutical industry research sponsors. The Director will have a major role in recruiting and mentoring faculty and fellows. The Director, who will report to Dr. Giles, is a member of the senior management team at IDD and will participate in the strategic direction and day-to-day management of the Institute.

Candidates must have a strong record of accomplishment in designing and conducting clinical trials of novel anti-cancer agents. Also important is demonstrated ability to manage a large team and coordinate multiple clinical studies, interface with cross-functional teams, effectively interact with sponsor organizations, and conduct complex research involving several drug types and patient profiles. IDD faculty will work within the San Antonio Cancer Institute, an NCI-designated Cancer Center, and be integral to the CTRC and University of Texas Health Science Center programs being expanded in preparation for application for Comprehensive Cancer Center designation. Candidates should hold an M.D. or M.D. /Ph.D., and be board certified or eligible in medical oncology and/or hematology.

CVs should be sent to:

Francis Giles, M.D.
Director and AT&T Chair
CTRC Institute for Drug Development
Chief, Division of Hematology and Medical Oncology
University of Texas Health Science Center at San Antonio
C/o Angie Bunch
7979 Wurzbach Drive, Ste U612
San Antonio, TX 78229
HR@ctrc.net

Candidates may also visit our website at www.ctrc.net.

Owing to the nature of our mission, only non-smoking candidates will be considered. EOE/AA.

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DIRECTOR OF PHARMACOLOGY

The Cancer Therapy & Research Center Institute for Drug Development, a premier cancer research organization focusing on the early development and optimal use of novel anti-cancer therapeutics, is seeking candidates for the position of Director of Pharmacology and Zachry Chair. The Director is responsible for the scientific leadership, operations, and financial performance of the Department of Pharmacology, including the Preclinical Research In vivo and In vitro Laboratories, the GLP Bioanalytical Laboratory and the Pharmacokinetics/Pharmacodynamics Unit. The Director is also responsible for establishing new peer-reviewed translational programs in one or more areas related to cancer drug development, and for interfacing these and all IDD pharmacology programs to the greatest extent possible, with multidisciplinary, disease specific clinics at CTRC. The Director of Pharmacology, who will report to Dr. Giles, is a member of the senior management team at IDD, thus participating in the strategic direction and day-to-day management of the Institute.

Candidates should possess a strong record of accomplishment in originating and conducting preclinical and clinical research in developing anti-cancer agents, with a focus on animal tumor models, bioanalytical chemistry, and Phase I PK/PD studies. Demonstrated ability to manage and coordinate multiple clinical studies with translational components, interface with cross-functional teams, effectively interact with sponsor organizations, and conduct complex research involving several drug types. IDD faculty will work within the San Antonio Cancer Institute, an NCI-designated Cancer Center, and be integral to the CTRC and University of Texas Health Science Center programs being expanded in preparation for application for Comprehensive Cancer Center designation. Candidates should hold a Ph.D. or M.D./Ph.D. in Pharmacology.

CVs should be sent to:

Francis Giles, M.D.
Director and AT&T Chair
CTRC Institute for Drug Development
Chief, Division of Hematology and Medical Oncology
University of Texas Health Science Center at San Antonio
C/o Angie Bunch
7979 Wurzbach Drive, Ste U612
San Antonio, TX 78229
HR@ctrc.net

Candidates may also visit our website at www.ctrc.net.

Owing to the nature of our mission, only non-smoking candidates will be considered. EOE/AA.

11070507
Two Postdoctoral Positions in the Division of Hematology at The Children's Hospital of Philadelphia and The University of Pennsylvania are available immediately. One position will be devoted to studying the biological effects of long-term expression and immune responses to transgene and/or vectors in hemophilia animals and thrombosis models using gene therapy strategies. Applicants for this position should have a strong background in molecular biology and have experience working with transgenic/gene targeted mouse models.

The second position will examine mechanisms contributing to blood coagulation factor specificity and function. Biochemical approaches both in vitro and in vivo are employed to characterize recombinant blood clotting proteins. Applicants for this position should have a strong background in protein biochemistry and have tissue culture and molecular biology experience. Experience with murine models is also desirable. Candidates for both positions should have a Ph.D. or M.D. degree, have good communications skills, be highly motivated and be willing to work on a multidisciplinary team. Highly competitive salary and benefits are offered. Curriculum vitae and three references should be sent to: Drs. Valder Arruda and Rodney M. Camire, The Children's Hospital of Philadelphia, ARC, Rm. 302, Philadelphia, PA 19104. Email: arruda@email.chop.edu, rcamire@mail.med.upenn.edu

Cerus Corporation
Scientist/Sr. Scientist, Red Blood Cell Physiology

Improving the quality and safety of the world's blood supply is our mission at Cerus Corporation, a public biotechnology company located in Concord, CA. Cerus is actively seeking a Scientist with expertise in red blood cell (RBC) biology, immunohematology or a related field. In this position you will initiate, direct and execute scientific research strategies through critical individual studies supporting our current approaches of viral/bacterial inactivation to ensure a safe and adequate blood supply. You will serve as the in-house expert on questions of RBC physiology and immunohematology.

Qualifications: Ph.D. (or demonstration of equivalent expertise) with a minimum of 3 years blood related experience in an academic or industrial setting. A well-rounded understanding of the principles of red blood cell physiology and metabolism, including morphology and function, immunology and pre-transfusion testing. Knowledge of blood banking/transfusion medicine or related field and current/projected trends is highly desirable.

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Translational Hematology and Transplant Immunology

The Department of Gene and Cell Medicine at Mount Sinai School of Medicine has excellent space and financial resources to recruit two outstanding scientists interested in the development of experimental therapeutics for immunotherapy, translational hematology and transplant immunology. Successful candidates should have an outstanding record in both publications and extramural funding, and may be at the assistant/associate/full professor levels. This interdisciplinary Department currently has 27 faculty members who are actively conducting independent and integrative basic and translational research in various inter-related fields, including immunology, hematology, transplantation, gene therapy, virology and stem cells. Outstanding institutional shared resources to support translational research include, but are not limited to, a state-of-the-art flow cytometry facility, live cell imaging with time-lapse photography, micro-array and high throughput bioinformatics, chemical biology for small molecules screening in target cells, a microvascular surgery core, and transgenic and knock-out mouse services in a VAF barrier rodent facility with an irradiator and an optical imaging system for live laboratory animals. The Mount Sinai School of Medicine, an equal opportunity employer, is situated along the Museum Mile on the Upper Eastside of Manhattan. Interested applicants should electronically submit their updated CV’s and Bibliographies to Miriam Merad, MD, PhD, Chair of the Search Committee, at miriam.merad@mssm.edu.

American Red Cross

Executive Medical Officer

The American Red Cross seeks an Executive Medical Officer to promote the medical mission of the Red Cross by providing expertise, oversight and leadership to Biomedical Headquarters and Blood Regions. Responsibilities include: participation in policy and procedure development, oversight of the Red Cross CME program, design and execute educational meetings with hospital physician and technical staff, and conduct evaluation and planning groups to discuss topics of medical interest or importance to current operations.

Position requires a MD or DO with a specialty in hematology, pathology or other related discipline; 7 – 10 years of work experience with 3 – 5 years of supervisory experience, preferably in a transfusion service or blood center environment. Experience in a hospital setting is desired. This position will require occasional travel.

For more information or to apply, visit the Jobs page of the American Red Cross website at www.redcross.org/jobs and search for keyword 448889R. EOE, M/F/D/V

www.redcross.org
### Academic Bone Marrow Transplant Physician

The Division of Hematology/Oncology at Loyola University Chicago, Stritch School of Medicine/Cardinal Bernardin Cancer Center seeks candidates with expertise in autologous and allogeneic bone marrow transplants for a faculty position as Assistant or Associate Professor in the expanding Bone Marrow Transplant Program. This position will be required to develop and coordinate a clinical program for autologous and/or allogeneic bone marrow transplantation of hematologic malignancies.

Candidates should have a strong commitment to the care of patients with hematologic malignancies including allogeneic and autologous stem cell transplantation. The Division includes a robust Phase I/II network. Successful candidates will actively participate in the education of residents and fellows. The University of Chicago is an Equal Opportunity/Affirmative Action Employer.

Interested individuals should contact:

Dr. James Vardiman, Section of Hematopathology
Department of Pathology • The University of Chicago
5841 S. Maryland Ave., MC0008 Chicago, IL 60637
drjv@chla.usc.edu

A competitive salary, benefits, and support package will be provided. Inquiries should be directed to:

Patrick Stiff, MD, Director, Division of Hematology/Oncology, Loyola University Chicago, Cardinal Bernardin Cancer Center, 2160 South First Avenue, Maywood, IL 60153 FAX 708-327-2210

Loyola University Chicago is an Equal Opportunity/Affirmative Employer and Educator with a strong commitment to diversifying its faculty.

### Childrens Hospital Los Angeles

**Pediatric BMT Physician/Scientist**

The Division of Research Immunology/Bone Marrow Transplantation of Childrens Hospital Los Angeles is recruiting a new faculty member at the Assistant, Associate or Full Professor level. Candidates should have clinical experience in hematopoietic stem cell transplantation and an established research record documented by publications and extramural funding in the fields of cellular therapy, gene therapy, immunology, or stem cell biology. The successful candidate will be expected to lead an extramurally funded research program and will receive an appointment at the Assistant/Associate or Full Professor level at the Keck School of Medicine of the University of Southern California in the Department of Pediatrics.

Interested individuals should contact:

Donald B. Kohn, MD
Search Director
Division of Research Immunology
Bone Marrow Transplantation
Childrens Hospital Los Angeles
4650 Sunset Boulevard #62
Los Angeles, California 90027
dkohn@chla.usc.edu

and include a copy of their Curriculum Vitae, a statement of research interests and the names of three references.

Both the Childrens Hospital Los Angeles and the University of Southern California Keck School of Medicine are Equal Opportunity and Affirmative Action Employers. Women and minorities are encouraged to apply.

### Department of Pathology

**Hematopathology – Immunohistochemistry – Molecular Diagnostics**

The Department of Pathology at The University of Chicago is seeking a hematopathologist at the Instructor level. Candidates must be board certified or board eligible in anatomic and/or clinical pathology as well as in hematopathology, and have qualifications for an Illinois license. The candidate should have broad training and capabilities in all service aspects of Laboratory Hematology/Hematopathology. The duties require that 20-30% effort be devoted to participation in clinical activities that may include interpretation of abnormal peripheral blood smears, bone marrow biopsies and aspirate smears as well as lymph node biopsies and lymphoid-related specimens. Familiarity with interpretation of flow cytometry and molecular studies will be necessary for their integration into the final report. The candidate must also be able to provide periodic coverage for a busy clinical hematology laboratory and for the coagulation service laboratory. The remaining 70-80% of time will be devoted to laboratory investigation, with a strong commitment to the molecular mechanisms of drug resistance of leukemia. A commitment to resident and medical student education is essential. The position will be available February 2008. Applicants should submit a CV, a brief description of career goals, their research experience, and names of three references to:

Dr. James Vardiman, Section of Hematopathology
Department of Pathology • The University of Chicago
5841 S. Maryland, MC0008 • Chicago, IL 60637

Web Link:

jobopportunities.uchicago.edu/applicants/Central?quickFind=195087

The University of Chicago is an Equal Opportunity/Affirmative Action Employer.
The Division of Hematology/Oncology, Department of Medicine at the University of Wisconsin School of Medicine and Public Health, is seeking applicants for several full-time faculty positions in the area of leukemia bone marrow transplant, benign hematology, outreach, and combined VA/UW appointment to serve the needs of hematology and oncology. Position responsibilities include clinical, research, and teaching activities. Clinical activities include those of inpatient, consult, and outpatient at the University of Wisconsin Hospital and Clinics in Madison, WI.

Candidates should be board eligible/certified in Medical Oncology and/or Hematology. The division of Hematology/Oncology is part of the Department of Medicine and the NCI-designated UW Paul P. Carbone Comprehensive Cancer Center. The Division is active in all phases of cancer therapy development and evaluation.

Please send letter of interest and curriculum vitae to:

Dr. George Wilding
The University of Wisconsin
School of Medicine and Public Health
600 Highland Ave., Room K4/610 (6164)
Madison, WI 53792

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**Director, Center of Hemostasis, Thrombosis and Vascular Biology (CHTVB)**

The University of Pittsburgh, the Institute for Transfusion Medicine and the Hemophilia Center of Western Pennsylvania are jointly establishing a new Center of Hemostasis, Thrombosis and Vascular Biology (CHTVB) and are recruiting a Director for the CHTVB. The Director will provide leadership for all research, educational, clinical, and training aspects of the Center. Applicants should be a MD or MD, PhD with an outstanding track record as an academic research scientist. The applicants should have completed training in hematology, preferably in hemostasis, thrombosis, and/or vascular biology and have a minimum of 8-10 years post-training experience. Preference is given to individuals with a demonstrated track record of sustained NIH funding.

Interested individuals should send their curriculum vitae to: G. David Roodman, MD, PhD, c/o Ms. Rosemarie Catley, University of Pittsburgh, Department of Medicine, 3347 Forbes Avenue, Suite 100, Pittsburgh, PA 15213. Electronic applications should be sent to email address: catleyr@upmc.edu. The University of Pittsburgh is an Affirmative Action, Equal Opportunity Employer.

**Northwestern University, Feinberg School of Medicine**

**ACADEMIC HEMATOPATHOLOGIST**

The Department of Pathology, Northwestern University Feinberg School of Medicine, Chicago, invites applications for a full-time faculty position in the Division of Hematopathology. Applicants must hold MD or MD/PhD degrees and be board certified in AP/CP from the American Board of Pathology, as well as be eligible for an unrestricted medical license in the State of Illinois. Fellowship training in hematopathology is required. Rank and remuneration will be determined by qualification and experience.

Excellence in diagnostic hematopathology and teaching is expected. The hematopathology service includes the clinical hematology laboratory, bone marrow aspirates and biopsies, lymph node biopsies, and flow cytometry. Molecular analysis and cytogenetic studies are performed as indicated. The Division actively participates in medical student teaching, the pathology residency program, and the hematopathology fellowship program. A record of demonstrated productivity and scholarship in Hematopathology is required. The environment for hypothesis driven basic research, and for translational and collaborative research at Northwestern University and the Northwestern Memorial Hospital is outstanding. Interested applicants should submit a letter of interest, curriculum vitae, and names of three references via e-mail to nstarks@northwestern.edu by October 1, 2007.

Northwestern University is an equal opportunity/affirmative action employer. Women and minority candidates are encouraged to apply. Hiring is contingent upon eligibility to work in the United States.
Important Announcement to Authors

*Blood* is pleased to announce its new online manuscript processing system, *Blood Bench>Press*, which launched February 1, 2006, at the following URL:

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**New Submissions:** All new manuscripts must be submitted through the *Blood Bench>Press* system at http://submit.bloodjournal.org.

**Revisions:** All revised manuscripts must be submitted to http://submit.bloodjournal.org. Manuscripts originally submitted to *Blood Manuscript Central* need also be submitted to http://submit.bloodjournal.org, but the authors must use the “Submit New Manuscript” option. The website instructions will guide the authors through the process, and the manuscript submission payment will be waived for revisions coming from *Blood Manuscript Central*.


If you have questions, please contact the *Blood* Editorial Office at editorial@hematology.org or at 202-776-0548.
Transfusion Medicine Fellowship
Department of Pathology
The Methodist Hospital
Houston, Texas

The Methodist Hospital (TMH) Department of Pathology offers an ACGME-accredited fellowship in transfusion medicine. The program is designed for trainees to develop the competency necessary for certification by the American Board of Pathology certification in Blood Banking / Transfusion Medicine. Fellows rotate through required disciplines at TMH and affiliated hospitals, as well as at the Gulf Coast Regional Blood Center.

The Methodist Hospital is affiliated with the Weill Medical College of Cornell University, one of the nation’s leading centers for medical education and research. TMH has over 1000 beds and the blood bank provides over 70,000 blood products per year. The hospital is a leading center for cardiology and cardiac surgery, neurology and neurosurgery, urology and renal disease, ophthalmology, obstetrics and gynecology, oncology and orthopedics. The hospital is building a 560,000 SF outpatient facility and a 300,000 SF research building.

Major components of the transfusion medicine training program include:

- Orientation to transfusion medicine
- Blood bank organization and management
- Hemotherapy, including therapeutic apheresis
- Histocompatibility and hemopoietic stem cell services
- Evaluation and management of bleeding problems
- Evaluation and management of transfusion reactions
- Performance and interpretation of blood bank technical procedures, including antibody identification
- Evaluation and management of alloimmunized patients
- Quality assurance and regulatory requirements
- Blood center operations, including blood donor management and consultation with hospitals on transfusion therapy and blood utilization
- Attendance and participation in conferences, rounds and symposia

Requirements include Texas licensure or training certification and board certification or eligibility in clinical pathology, anesthesiology or hematology.

Applicants should send a letter of interest and Curriculum Vitae to: Richard J. Davey, MD, Director Transfusion Medicine, Department of Pathology, B 250, The Methodist Hospital, 6565 Fannin Street MS 205, Houston, TX 77030.
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The Washington DC Principles is a commitment from 50 (and growing) not-for-profit medical/scientific societies and publishers to provide free access and wide dissemination of published research findings.

The DC Principles provide what has been called the needed “middle ground” in the increasingly heated debate between those who advocate immediate unfettered online access to medical and scientific research findings and advocates of the current journal publishing system. The document was drafted in response to recent claims that these publishers’ practices hinder the public’s ability to access published scientific research.

The 7 Principles

1. As not-for-profit publishers, we see it as our mission to maintain and enhance the independence, rigor, trust, and visibility that have established scholarly journals as reliable filters of information emanating from clinical and laboratory research.

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   b. The full text of our journals is freely available to everyone worldwide either immediately or within months of publication, depending on each publisher’s business and publishing requirements;
   c. The content of our journals is available free to scientists working in many low-income nations;
   d. Articles are made available free online through reference linking between these journals;
   e. Our content is available for indexing by major search engines so that readers worldwide can easily locate information.

4. We will continue to work to develop long-term preservation solutions for online journals to ensure the ongoing availability of the scientific literature.

5. We will continue to work with authors, peer-reviewers, and editors for the development of robust online and electronic tools to improve efficiency of their important intellectual endeavors.

6. We strongly support the principle that publication fees should not be borne solely by researchers and their funding institutions, because the ability to publish in scientific journals should be available equally to all scientists worldwide, no matter what their economic circumstances.

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PROCRIT® (epoetin alfa)

hemoglobin levels between 12 and 14 g/dL or hemoglobin between 36% and 42%). The study was terminated prematurely when interim results demonstrated a significant difference in mortality and/or tumor progression in patients with advanced cancer. The study was not different between the two groups. In a Phase III, multicenter, randomized (epoetin alfa vs. placebo), double-blind, placebo-controlled study in 898 anemic patients with active malignant disease neither requiring nor planning to receive chemotherapy or radiotherapy therapy, there was no evidence of a statistically significant reduction in proportion of patients receiving RBC transfusions. In addition, there were more deaths in the epoetin alfa group at 4 months (7.7%) than in the placebo group (5.4%) at 4 months (7.7%). There was no evidence of a statistically significant reduction in proportion of patients requiring anticoagulant therapy, embolic event including pulmonary embolism, left ventricular failure and thrombocytopenia. A definitive relationship between the rate of hemoglobin increase and the occurrence of clinically significant thrombotic events could not be evaluated due to the limited size of hemoglobin measurements in this study.

Increased Mortality and/or Tumor Progression

Erythropoietin-stimulating agents, when administered to target a hematocrit of greater than 12 g/dL, shortened the time to tumor progression and/or death in patients receiving chemotherapy or radiotherapy. ESAs also shortened survival time in patients with metastatic breast cancer who were not receiving chemotherapy when administered to target a hematocrit of greater than 12 g/dL.

The ENHANCE study was a randomized controlled study in 351 head and neck cancer patients who were not taking chemotherapy or radiotherapy. It was a randomized, double-blind, placebo-controlled, multicenter study that enrolled 681 patients. The patients were randomized to receive placebo or PROCRIT® (150 Units/kg). The study was terminated prematurely when interim results demonstrated a significant difference in mortality and/or tumor progression in patients with advanced cancer. The study was not different between the two groups. In a Phase III, multicenter, randomized (epoetin alfa vs. placebo), double-blind, placebo-controlled study in 898 anemic patients with active malignant disease neither requiring nor planning to receive chemotherapy or radiotherapy therapy, there was no evidence of a statistically significant reduction in proportion of patients requiring anticoagulant therapy, embolic event including pulmonary embolism, left ventricular failure and thrombocytopenia. A definitive relationship between the rate of hemoglobin increase and the occurrence of clinically significant thrombotic events could not be evaluated due to the limited size of hemoglobin measurements in this study.

Likelihood of Response:

In a Phase III, multicenter, randomized controlled study of PROCRIT® in adult patients who were undergoing coronary artery bypass surgery (74 deaths in 126 patients randomized to PROCRIT®; 71 deaths in 122 patients randomized to placebo). The cumulative incidence of the endpoint of death or nonfatal myocardial infarction was 36% in the PROCRIT® group and 33% in the placebo group. The difference did not reach statistical significance.

In a Phase III, multicenter, randomized controlled study (referred to as the ‘SPINE’ study), 681 adult patients with metastatic breast cancer who were not receiving chemotherapy were randomized to placebo or PROCRIT® (150 Units/kg). The study was terminated prematurely when interim results demonstrated a significant difference in mortality and/or tumor progression in patients with advanced cancer. The study was not different between the two groups.

In a Phase III, randomized, double-blind, placebo-controlled study in 222 anemic, metastatic breast cancer patients ages 5 to 88 receiving treatment for a variety of primary tumor types and histologies where the heterogeneity of the underlying malignancies and of anti-angiogenic agents being used was determined, a deterioration of the benefit seen on the primary endpoint of time to tumor progression in patients with metastatic breast cancer who were not receiving chemotherapy was not observed. In patients with metastatic breast cancer who were not receiving chemotherapy the incidence of thrombotic events could not be performed. In the PROCRIT® controlled trial, 5% (11/222) of patients treated with PROCRIT® had 1 or more thrombotic events (p=0.06) and the incidence of serious or life-threatening events was 7.2%.

Adverse Reactions

As with all therapeutic proteins, there is the potential for immunogenicity. Neutralizing antibodies have been observed in some patients receiving ESA or severe anemia (with or without other cytophenias), have been reported in patients receiving PROCRIT® (see WARNINGS: PROCRIT® may cause anaphylactic or anaphylactoid reactions)(see WARNINGS: PROCRIT® may cause anaphylactic or anaphylactoid reactions) during double-blind, placebo-controlled studies of up to 3 months duration involving 131 cancer patients, adverse events with an incidence >1% included: injection site reactions (15%), arthralgia and back pain (13%), headache (8%), hypertension, associated with a significant increase in hemoglobin, has been noted rarely in patients treated with PROCRIT®. Neutralizing antibodies in patients treated with PROCRIT® should be monitored carefully, particularly in patients with an underlying history of thrombotic events.

OVERDOSAGE

In double-blind, placebo-controlled studies of up to 4 months duration involving 131 cancer patients, adverse events with an incidence >1% included: injection site reactions (15%), arthralgia and back pain (13%), headache (8%), hypertension, associated with a significant increase in hemoglobin, has been noted rarely in patients treated with PROCRIT®. Neutralizing antibodies in patients treated with PROCRIT® should be monitored carefully, particularly in patients with an underlying history of thrombotic events.

OVERDOSAGE

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PROCRIT Usage—Oncology

• PROCRIT is indicated for the treatment of anemia in patients with nonmyeloid malignancies where anemia is due to the effect of concomitantly administered chemotherapy. PROCRIT is indicated to decrease the need for transfusions in patients who will be receiving concomitant chemotherapy for a minimum of 2 months.

• PROCRIT is not indicated in patients with active malignant disease not receiving chemotherapy. PROCRIT is also not indicated for the treatment of anemia due to other factors such as iron or folate deficiencies, hemolysis or gastrointestinal bleeding, which should be managed appropriately.

Important Safety Information

From the Boxed WARNINGS

• Use the lowest dose of PROCRIT that will gradually increase the hemoglobin (Hb) concentration to the lowest level sufficient to avoid the need for red blood cell (RBC) transfusion.

• PROCRIT and other erythropoiesis-stimulating agents (ESAs) increased the risk for death and for serious cardiovascular events (including serious arterial and venous thromboembolic events, myocardial infarction, stroke, congestive heart failure) when administered to target a Hb of greater than 12 g/dL. A rate of hemoglobin rise of greater than 1 g/dL over 2 weeks may also contribute to these risks.

• Cancer patients: Use of ESAs:
  — Shortened the time to tumor progression in patients with advanced head and neck cancer receiving radiation therapy when administered to target a Hb of greater than 12 g/dL.
  — Shortened overall survival and increased deaths attributed to disease progression at 4 months in patients with metastatic breast cancer receiving chemotherapy when administered to target a Hb of greater than 12 g/dL.
  — Increased the risk of death when administered to target a Hb of 12 g/dL in patients with active malignant disease receiving neither chemotherapy nor radiation therapy. ESAs are not indicated for this population.

• Patients receiving PROCRIT pre-operatively for reduction of allogeneic RBC transfusions: A higher incidence of deep venous thrombosis was documented in patients receiving PROCRIT who were not receiving prophylactic anticoagulation. Antithrombotic prophylaxis should be strongly considered when PROCRIT is used to reduce allogeneic RBC transfusions.

Contraindications

• PROCRIT is contraindicated in patients with uncontrolled hypertension or with known hypersensitivity to albumin (human) or mammalian cell-derived products.

Additional Important Safety Information

• The rate of Hb increase should not exceed 1 g/dL in any two-week period and the Hb concentration should not exceed 12 g/dL.

• If the Hb approaches 12 g/dL or increases by more than 1 g/dL in a 2-week period, the dose should be reduced by 25%. Withhold the dose of PROCRIT if the Hb exceeds 12 g/dL until the Hb falls below 11g/dL; restart dose at 25% below the previous dose.

• Monitor Hb regularly during therapy, weekly until Hb becomes stable.

• Cases of pure red cell aplasia (PRCA) and of severe anemia, with or without other cytopenias, associated with neutralizing antibodies to erythropoietin have been reported in patients treated with PROCRIT; predominantly in patients with chronic renal failure receiving PROCRIT by subcutaneous administration. If any patient develops a sudden loss of response to PROCRIT, accompanied by severe anemia and low reticulocyte count, and anti-erythropoietin antibody-associated anemia is suspected, withhold PROCRIT and perform assays for binding and neutralizing antibodies. If erythropoietin antibody-mediated anemia is confirmed, PROCRIT should be permanently discontinued and patients should not be switched to other erythropoietic proteins.

• The safety and efficacy of PROCRIT therapy have not been established in patients with a known history of a seizure disorder or underlying hematologic disease (eg, sickle cell anemia, myelodysplastic syndromes, or hypercoagulable disorders).

• In some female patients, menses have resumed following PROCRIT therapy; the possibility of pregnancy should be discussed and the need for contraception evaluated.

• Prior to and regularly during PROCRIT therapy monitor iron status; transferrin saturation should be ≥20% and ferritin should be ≥100 ng/mL. During therapy absolute or functional iron deficiency may develop and all patients will eventually require supplemental iron to adequately support erythropoiesis stimulated by PROCRIT.

• Treatment of patients with grossly elevated serum erythropoietin levels (e.g., >200 mUnits/mL) is not recommended.

• During PROCRIT therapy, blood pressure should be monitored carefully and aggressively managed, particularly in patients with an underlying history of hypertension or cardiovascular disease.

• Seizures in PROCRIT-treated patients have been reported in the context of a significant increase in hemoglobin from baseline; increases in blood pressure were not always observed; and patients may have had other underlying central nervous system pathology.

• The most commonly reported side effects (>10%) for PROCRIT in clinical trials were pyrexia, diarrhea, nausea, vomiting, edema, asthenia, fatigue, shortness of breath, paresthesia, and upper respiratory infection.

Please see adjacent page for Brief Summary of Prescribing Information, including Boxed WARNINGS.