For your patients with chronic granulomatous disease (CGD)

Provide protection with ACTIMMUNE® (Interferon gamma-1b)
in conjunction with prophylactic antibiotic and antifungal oral therapies

INDICATIONS AND USAGE
ACTIMMUNE® is indicated:
• For reducing the frequency and severity of serious infections associated with Chronic Granulomatous Disease
• For delaying time to disease progression in patients with severe, malignant osteopetrosis

Select Safety Information
ACTIMMUNE® is contraindicated in patients who develop or have known hypersensitivity to interferon-gamma, E. coli-derived products, or any component of the product.

Please see Important Safety Information on page 7 and the enclosed ACTIMMUNE® Full Prescribing Information.
ACTIMMUNE® significantly reduced the frequency and risk of serious infections in patients with CGD in the pivotal trial1,2

In the clinical trial, ACTIMMUNE® (Interferon gamma-1b) demonstrated significant reductions in total number, rate, and relative risk of serious infections vs placebo.*

Select Safety Information

Patients begun on ACTIMMUNE® before age 1 year should receive monthly assessments of liver function. If severe hepatic enzyme elevations develop, ACTIMMUNE® dosage should be modified.

Study methods

Design 12-month multicenter, randomized, double-blind, placebo-controlled clinical trial in the United States and Europe

Subjects 128 patients (age range: 1 to 44 years) with various types of CGD

Treatment arms Patients were randomized to receive ACTIMMUNE® (n = 63) or placebo (n = 65) administered subcutaneously 3 times weekly for up to 1 year. Although designed as a placebo-controlled trial, more than 85% of study patients were receiving prophylactic antibiotics (trimethoprim-sulfamethoxazole or dicloxacillin) in addition to either ACTIMMUNE® or placebo.

Mean duration of treatment 8.9 months

Primary end point Time to serious infection, defined as a clinical event requiring hospitalization and the use of intravenous antibiotics.

The study reported early results following demonstration of a statistically significant benefit of ACTIMMUNE® therapy compared to placebo with respect to time to serious infection (P = .0036).1,2

ACTIMMUNE® reduced length of stay and helped keep patients free of serious infection for up to 12 months in the pivotal trial1,2

In the clinical trial, ACTIMMUNE® treatment resulted in significantly fewer hospitalization days vs placebo*.

In patients who did need to be hospitalized, the average length of stay was 33% shorter (32 days in the ACTIMMUNE® group vs 48 days in the placebo group; P = 0.02).

In the clinical trial, more than twice as many patients treated with ACTIMMUNE® remained free of serious infection for up to 12 months compared to patients treated with placebo*.

Select Safety Information

The most common adverse experiences occurring with ACTIMMUNE® therapy are “flu-like” symptoms such as fever, headache, chills, myalgia, or fatigue, which may decrease in severity as treatment continues, and may be minimized by bedtime administration of ACTIMMUNE. Acetaminophen may be used to prevent or partially alleviate the fever and headache.

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**ACTIMMUNE® delivers efficacy across various patient types**

In subgroup analyses, ACTIMMUNE® (Interferon gamma-1b) was beneficial regardless of age or type of CGD inheritance.*2

There was a 67% reduction in relative risk of serious infection in patients receiving ACTIMMUNE® compared to placebo across all groups.1,2

*Most patients in a clinical trial also received prophylactic antibiotics.

†Serious infection was defined as a clinical event requiring hospitalization and intravenous antibiotics.

<table>
<thead>
<tr>
<th>SIDE EFFECTS</th>
<th>PERCENTAGE OF PATIENTS</th>
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<tbody>
<tr>
<td></td>
<td>ACTIMMUNE® (n = 63)</td>
</tr>
<tr>
<td>Fever</td>
<td>52</td>
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<tr>
<td>Headache</td>
<td>33</td>
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<tr>
<td>Rash</td>
<td>17</td>
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<td>Chills</td>
<td>14</td>
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<td>Injection site erythema or tenderness</td>
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<tr>
<td>Fatigue</td>
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<td>Nausea</td>
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<tr>
<td>Myalgia</td>
<td>6</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>2</td>
</tr>
</tbody>
</table>

Isolated cases of acute serious hypersensitivity reactions have been observed in patients receiving ACTIMMUNE®. Reversible neutropenia, thrombocytopenia, and elevations of AST and/or ALT have been observed during ACTIMMUNE® therapy. At doses 10 times greater than the weekly recommended dose, ACTIMMUNE® may exacerbate pre-existing cardiac conditions or may cause reversible neurological effects, such as decreased mental status, gait disturbance, and dizziness.1

**TIP**

**MANAGING CERTAIN SIDE EFFECTS**

Some of the “flu-like” symptoms may be minimized by administering ACTIMMUNE® at bedtime. Acetaminophen may be used to prevent or partially alleviate the fever and headache.1

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Your patients are in good hands

TranscendRare™, a HorizonCares program, is dedicated to improving the lives of patients with chronic granulomatous disease (CGD) by providing them and their families with access to a comprehensive network of services and support.

The TranscendRare support team consists of case managers, dedicated nurse educators, and other representatives of Horizon Pharma who work directly with patients and their caregivers. The complimentary services provided by TranscendRare guide patients through every step of their journey—from initiating treatment to determining insurance coverage, connecting with others living with CGD, and establishing habits for lifelong adherence. Our services are based on 3 key pillars: guide, support, and connect.

A case manager will:
• Work with your office to secure any insurance authorizations that may be necessary to start or continue ACTIMMUNE™
• Limit financial barriers to treatment by determining insurance coverage and connecting patients with financial assistance options, if necessary
• Coordinate with the specialty pharmacy to schedule shipments of ACTIMMUNE™
• Send patients refill reminders via email and/or text
• Help patients enroll in a sharps disposal program
• Make adjustments, as needed, when patients experience life changes such as moving or losing insurance or employment

A dedicated CGD nurse educator will:
• Serve as the main point of contact for all your patients’ needs related to treatment
• Assist with disease education, day-to-day questions, and treatment challenges
• Provide injection training and support
• Work collaboratively with patients’ healthcare team

Horizon Pharma will:
• Connect patients and their caregivers with communities of people living with CGD and other rare diseases using social media platforms, peer mentor programs, and live events, where families can share stories, tips, and resources with each other
• Introduce patients to advocacy groups and other community resources

For more information, call 1 (877) 305-7704 or visit ACTIMMUNE.com/support.

INDICATIONS AND USAGE
ACTIMMUNE® (Interferon gamma-1b) is indicated:
• For reducing the frequency and severity of serious infections associated with Chronic Granulomatous Disease
• For delaying time to disease progression in patients with severe, malignant osteopetrosis

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
• In patients who develop or have known hypersensitivity to interferon-gamma, E coli-derived products, or any component of the product

WARNINGS AND PRECAUTIONS
• ACTIMMUNE should be used with caution in patients with:
  - Pre-existing cardiac conditions, including ischemia, congestive heart failure, or arrhythmia
  - Seizure disorders or compromised central nervous system function; reduce dose or discontinue
  - Myelosuppression, or receiving other potentially myelosuppressive agents; consider dose reduction or discontinuation of therapy
  - Severe renal insufficiency
  - Age <1 year

• Monitoring:
  - Patients begun on ACTIMMUNE before age 1 year should receive monthly assessments of liver function. If severe hepatic enzyme elevations develop, ACTIMMUNE dosage should be modified
  - Monitor renal function regularly when administering ACTIMMUNE in patients with severe renal insufficiency; accumulation of interferon gamma-1b may occur with repeated administration. Renal toxicity has been reported in patients receiving ACTIMMUNE
  - Pregnancy, Lactation, and Fertility:
    • ACTIMMUNE should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus
    • Use of ACTIMMUNE by lactating mothers is not recommended. ACTIMMUNE or nursing should be discontinued dependent on the importance of the drug to the mother
    • Long-term effects of ACTIMMUNE on fertility are not known

DRUG INTERACTIONS
• Concomitant use of drugs with neurotoxic, hematotoxic, or cardiotoxic effects may increase the toxicity of interferons
• Avoid simultaneous administration of ACTIMMUNE with other heterologous serum protein or immunological preparations (eg, vaccines)

ADVERSE REACTIONS
• The most common adverse experiences occurring with ACTIMMUNE therapy are “flu-like” symptoms such as fever, headache, chills, myalgia, or fatigue, which may decrease in severity as treatment continues, and may be minimized by bedtime administration of ACTIMMUNE. Acetaminophen may be used to prevent or partially alleviate the fever and headache
• Isolated cases of acute serious hypersensitivity reactions have been observed in patients receiving ACTIMMUNE
• Reversible neutropenia, thrombocytopenia, and elevations of AST and/or ALT have been observed during ACTIMMUNE therapy
• At doses 10 times greater than the weekly recommended dose, ACTIMMUNE may exacerbate pre-existing cardiac conditions, or may cause reversible neurological effects such as decreased mental status, gait disturbance, and dizziness

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In the treatment of chronic granulomatous disease (CGD)

Complete your anti-infection strategy with the efficacy of ACTIMMUNE® (Interferon gamma-1b)

- ACTIMMUNE® is recommended by the American Academy of Allergy, Asthma & Immunology; the American College of Allergy, Asthma & Immunology; and the Immune Deficiency Foundation as part of a combination treatment regimen along with prophylaxis therapy:
  - Daily oral antibiotic
  - Daily oral antifungal
  - ACTIMMUNE® 3x weekly
- In the clinical trial, ACTIMMUNE® has been proven to:
  - Help reduce the risk of serious infection†,1,2
  - Help reduce hospitalization days1,2
  - Help reduce the number of serious infections1,2

*Most patients in the clinical trial also received prophylactic antibiotics.
†Serious infection was defined as a clinical event requiring hospitalization and intravenous antibiotics.

Select Safety Information
Isolated cases of acute serious hypersensitivity reactions have been observed in patients receiving ACTIMMUNE®.

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