Finally!
On-Demand Treatment
for Acute Abdominal or Facial Attacks of HAE*
in Adults and Adolescents

On-demand means treating patients with Berinert® when an acute abdominal or facial attack occurs. For example, if a patient has 7 abdominal or facial attacks in a year, you treat the patient 7 times.

Important Safety Information
Berinert®, C1 Esterase Inhibitor (Human) is a plasma-derived concentrate of C1 Esterase Inhibitor (Human), indicated for the treatment of acute abdominal or facial attacks of hereditary angioedema (HAE) in adult and adolescent patients. The safety and efficacy of Berinert® for prophylactic therapy have not been established.

Berinert® is contraindicated in individuals who have experienced an anaphylactic or severe systemic reaction to C1 esterase inhibitor preparations.

Monitor patients for early signs of allergic or hypersensitivity reactions (including hives, generalized urticaria, chest tightness, wheezing, hypotension, and anaphylaxis). If hypersensitivity is suspected, immediately discontinue administration and initiate appropriate treatment. Epinephrine should be immediately available for treatment of acute severe hypersensitivity reactions.

Thrombotic events have occurred in patients receiving off-label high doses of Berinert®. Monitor patients with known risk factors for thrombotic events.

Berinert® is derived from human plasma. The risk of transmission of infectious agents, including viruses and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent, cannot be completely eliminated.

The most serious adverse reaction reported in subjects in clinical studies who received Berinert® is an increase in the severity of pain associated with HAE. The most common adverse reactions observed in more than 4% of subjects after Berinert® treatment were headache, abdominal pain, nausea, muscle spasms, pain, diarrhea, and vomiting.

Berinert® has not been evaluated in pregnant women or nursing mothers; benefits of treatment should be weighed against potential risks in pregnant women, and Berinert® should be given to nursing mothers only if clearly needed.

The safety and efficacy of Berinert® have not been established in children (ages 0 through 12) or in the geriatric population.

Please see Brief Summary of Prescribing Information on following pages.
Berinert® Expert Network (B.E.N.™) makes it easy for you and your patients, and helps you:

• Get access to Berinert®
• Navigate insurance issues and questions
• Offer valuable CSL Behring Assurance and Assistance Programs to your patients who need them

Get Started and Prescribe Berinert® Today

Berinert® Expert Network (B.E.N.™) makes it easy for you and your patients, and helps you:

• Get access to Berinert®
• Navigate insurance issues and questions
• Offer valuable CSL Behring Assurance and Assistance Programs to your patients who need them

Berinert® is made by CSL Behring GmbH and distributed by CSL Behring LLC. Berinert® is a registered trademark of CSL Behring GmbH.

Please see Brief Summary of Prescribing Information on following pages.
Berinert® [C1 Esterase Inhibitor (Human)]

Freeze-dried powder

Before prescribing, please consult full prescribing information, a brief summary of which follows. Some text and references refer to full prescribing information.

1 INDICATIONS AND USAGE

Berinert is a plasma-derived concentrate of C1 Esterase Inhibitor (Human) indicated for the treatment of acute abdominal or facial attacks of hereditary angioedema (HAE) in adult and adolescent patients.

The safety and efficacy of Berinert for prophylactic therapy have not been established.

4 CONTRAINDICATIONS

Berinert is contraindicated in individuals who have experienced life-threatening hypersensitivity reactions, including anaphylaxis, to C1 esterase inhibitor preparations.

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity

Severe hypersensitivity reactions may occur. Epinephrine should be immediately available for treatment of acute severe hypersensitivity reaction (see Patient Counseling Information [17]). The signs and symptoms of hypersensitivity reactions may include hives, generalized urticaria, tightness of the chest, wheezing, hypotension, and/or anaphylaxis during or after injection of Berinert. Because hypersensitivity reactions may have symptoms similar to HAE attacks, treatment methods should be carefully considered. In case of suspected hypersensitivity, immediately discontinue administration of Berinert and institute appropriate treatment.

5.2 Thrombotic Events

Thrombotic events have been reported in association with Berinert when used off-label and at higher than labeled doses. Animal studies have confirmed the risk of thrombosis from intravenous administration of C1 esterase inhibitor products (see Overdosage [10] and Animal Toxicology and Pharmacology [13.2]).

5.3 Transmission of Infectious Agents

Because Berinert is made from human blood, it may contain infectious agents (eg, 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 processes demonstrated to inactivate and/or remove certain viruses during manufacturing (see Description [11] and Patient Counseling Information [17]).

Despite these measures, such products may still potentially transmit disease. There is also the possibility that unknown infectious agents may be present in such products.

Since 1979, a few suspected cases of viral transmission have been reported with the use of Berinert outside the US, including cases of acute hepatitis C. From the incomplete information available from these cases, it was not possible to determine with certainty if the infections were or were not related to prior administration of Berinert. The physician should discuss the risks and benefits of this product with the patient before prescribing or administering it to the patient. (See Patient Counseling Information [17.1].)

All infections thought by a physician possibly to have been transmitted by Berinert should be reported by lot number, by the physician, or other healthcare provider to the CSL Behring Pharmacovigilance Department at 1-866-915-6958.

6 ADVERSE REACTIONS

The most serious adverse reaction reported in subjects enrolled in clinical studies who received Berinert was an increase in the severity of pain associated with HAE.

6.1 Clinical Trials Experience

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

Placebo-controlled Clinical Study

In the placebo-controlled clinical study, referred to as the randomized clinical trial (RCT) (see Clinical Studies [14]), 124 subjects experiencing an acute moderate to severe abdominal or facial HAE attack were treated with Berinert (either a 10 unit per kg body weight or a 20 unit per kg body weight dose), or placebo (physiological saline solution).

The treatment-emergent serious adverse reactions/events that occurred in 5 subjects in the RCT were: laryngeal edema, facial attack with laryngeal edema, swelling (shoulder and chest), exacerbation of hereditary angioedema, and laryngospasm.

Table 1: Adverse Reactions Occurring up to 4 Hours After Initial Infusion in More Than 4% of Subjects, Irrespective of Causality

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Number (%) of Subjects Reporting Adverse Reactions: Berinert 20 units/kg (n = 43)</th>
<th>Number (%) of Subjects Reporting Adverse Reactions: Placebo Group (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea*</td>
<td>3 (7%)</td>
<td>5 (11.9%)</td>
</tr>
<tr>
<td>Diarrhea*</td>
<td>2 (4.7%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Abdominal Pain†</td>
<td>2 (4.7%)</td>
<td>2 (4.7%)</td>
</tr>
<tr>
<td>Vomiting†</td>
<td>1 (2.3%)</td>
<td>3 (7.1%)</td>
</tr>
<tr>
<td>Diarrhea†</td>
<td>0 (0)</td>
<td>4 (9.5%)</td>
</tr>
<tr>
<td>Headache</td>
<td>0 (0)</td>
<td>2 (4.8%)</td>
</tr>
</tbody>
</table>

* The study protocol specified that adverse events that began within 72 hours of blinded study medication administration were to be classified as at least possibly related to study medication (ie, adverse reactions).
† The following abdominal symptoms were identified in the protocol as associated with HAE abdominal attacks: abdominal pain, bloating, cramps, nausea, vomiting, and diarrhea.

Table 2: Adverse Reactions Occurring in More Than 4% of Subjects up to 72 Hours After Infusion of Initial or Rescue Medication† by Intent-to-Treat, Irrespective of Causality

<table>
<thead>
<tr>
<th>Adverse Reactions</th>
<th>Number (%) of Subjects Reporting Adverse Reactions: Berinert 20 units/kg (n = 43)</th>
<th>Number (%) of Subjects Reporting Adverse Reactions: Placebo Group (n = 42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>3 (7%)</td>
<td>11 (26.2%)</td>
</tr>
<tr>
<td>Headache</td>
<td>3 (7%)</td>
<td>5 (11.9%)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>3 (7%)</td>
<td>5 (11.9%)</td>
</tr>
<tr>
<td>Diarrhea†</td>
<td>2 (4.7%)</td>
<td>1 (2.4%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>1 (2.3%)</td>
<td>7 (16.7%)</td>
</tr>
<tr>
<td>Headache</td>
<td>1 (2.3%)</td>
<td>4 (9.5%)</td>
</tr>
<tr>
<td>Pain</td>
<td>1 (2.3%)</td>
<td>4 (9.5%)</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>1 (2.3%)</td>
<td>6 (14.3%)</td>
</tr>
<tr>
<td>Back pain</td>
<td>0 (0)</td>
<td>6 (14.3%)</td>
</tr>
<tr>
<td>Facial pain</td>
<td>0 (0)</td>
<td>2 (4.8%)</td>
</tr>
</tbody>
</table>

† The study protocol specified that adverse events that began within 72 hours of blinded study medication administration were to be classified as at least possibly related to study medication (ie, adverse reactions).
† If a subject experienced no relief or insufficient relief of symptoms within 4 hours after infusion, investigators had the option to administer a blinded second infusion (“rescue” treatment) of Berinert 20 units/kg for the placebo group or 10 units/kg for the 10 units/kg group, or placebo (for the 20 units/kg group).

Table 3 lists the adverse events that occurred in more than 4% of the subjects 7 to 9 days after the end of a Berinert infusion, irrespective of causality.

Table 3: Adverse Events Occurring in More Than 4% of Subjects’ Receiving Berinert at Either 10 Units/kg or 20 units/kg 7 to 9 Days after Infusion, Irrespective of Causality

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Number (%) of Subjects Reporting Adverse Events (n=108)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hereditary angioedema</td>
<td>12 (11.1%)</td>
</tr>
<tr>
<td>Headache</td>
<td>12 (11.1%)</td>
</tr>
<tr>
<td>Abdominal pain†</td>
<td>7 (6.5%)</td>
</tr>
<tr>
<td>Nausea†</td>
<td>7 (6.5%)</td>
</tr>
<tr>
<td>Muscle spasms</td>
<td>6 (5.6%)</td>
</tr>
<tr>
<td>Pain</td>
<td>6 (5.6%)</td>
</tr>
<tr>
<td>Diarrhea†</td>
<td>5 (4.6%)</td>
</tr>
<tr>
<td>Vomiting†</td>
<td>5 (4.6%)</td>
</tr>
</tbody>
</table>

† Includes subjects in the placebo group who received Berinert 20 units/kg rescue study medication.

These symptoms were identified in the protocol as related to the underlying disease. Any increase in intensity or new occurrence of these symptoms after study medication administration was considered to be an adverse event.

Subjects were tested at baseline and after 3 months for possible exposure to Parvovirus B19, hepatitis B, hepatitis C, and HIV-1 and HIV-2. No subject who underwent testing evidenced seroconversion or treatment-emergent positive polymerase chain reaction testing for these pathogens.

Extension Study

In an interim safety analysis, of the ongoing open-label extension study, 56 subjects with 559 acute moderate to severe abdominal, facial, peripheral and/or laryngeal attacks received a 20 units/kg body weight dose of Berinert (see Clinical Studies [14]). This study...
provides additional safety data in subjects who received multiple infusions of the product for sequential HAE attacks (one infusion per attack). Table 4 lists the adverse events that occurred in this interim safety analysis of the ongoing open-label extension study in more than 4% of subjects up to 72 hours or 9 days after the end of a Berinert infusion, irrespective of causality.

Table 4: Incidence of Adverse Events by Descending Frequency Occurring in More Than 4% of Subjects Receiving Berinert up to 72 Hours or 9 Days After Infusion, Irrespective of Causality

<table>
<thead>
<tr>
<th>Adverse Events</th>
<th>Number (%) of Subjects Reporting Adverse Events up to 72 hours (n=56)</th>
<th>Number (%) of Subjects Reporting Adverse Events up to 9 Days (n=56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>3 (5.4%)</td>
<td>4 (7.1%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>3 (5.4%)</td>
<td>3 (5.4%)</td>
</tr>
<tr>
<td>Hereditary angioedema</td>
<td>2 (3.6%)</td>
<td>4 (7.1%)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>2 (3.6%)</td>
<td>3 (5.4%)</td>
</tr>
</tbody>
</table>

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 the frequency of these reactions or establish a causal relationship to product exposure. Adverse reactions reported in Europe since 1979 in patients receiving Berinert for treatment of HAE include hypersensitivity/anaphylactic reactions, a few suspected cases of viral transmission, including cases of acute hepatitis C, injection-site pain, injection-site redness, chills, and fever.

The following adverse reactions, identified by system organ class, have been attributed to Berinert during post-approval use outside the US:
- **Immune System Disorder:** Hypersensitivity/anaphylactic reactions, and shock
- **General Body as a Whole:** Pain on injection, redness at injection site, chills, and fever

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category C. Animal reproduction studies have not been conducted with Berinert. It is not known whether Berinert can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Berinert should be given to a pregnant woman only if clearly needed. In a retrospective case collection study, 20 pregnant women ranging in age from 20 to 35 years received Berinert with repeated doses up to 3,500 units per attack; these women reported no complications during delivery and no harmful effects on their 34 neonates.

8.2 Labor and Delivery
The safety and effectiveness of Berinert administration prior to or during labor and delivery have not been established. Use only if clearly needed.

8.3 Nursing Mothers
It is not known whether Berinert is excreted in human milk. Because many drugs are excreted in human milk, use only if clearly needed when treating a nursing woman.

8.4 Pediatric Use
Safety and efficacy of Berinert in children (ages 0 through 12) have not been established. The clinical studies included an insufficient number of subjects in this age group to determine whether they respond differently from older subjects. The safety and efficacy of Berinert were evaluated in 5 children (ages 3 through 12) and in 8 adolescent subjects (ages 13 through 16) (see Pharmacokinetics [12.3]).

8.5 Geriatric Use
Safety and efficacy of Berinert in the geriatric population have not been established. Clinical studies with Berinert included four subjects older than 65 years. The clinical studies included an insufficient number of subjects in this age group to determine whether they respond differently from younger subjects.

15 REFERENCES

Manufactured by:
CSL Behring GmbH
35041 Marburg, Germany
US License No. 1765
Distributed by:
CSL Behring LLC
Kankakee, IL 60901 USA

The safety and effectiveness of Berinert administration prior to or during labor and delivery have not been established. Use only if clearly needed.

8.3 Nursing Mothers
It is not known whether Berinert is excreted in human milk. Because many drugs are excreted in human milk, use only if clearly needed when treating a nursing woman.

8.4 Pediatric Use
Safety and efficacy of Berinert in children (ages 0 through 12) have not been established. The clinical studies included an insufficient number of subjects in this age group to determine whether they respond differently from older subjects. The safety and efficacy of Berinert were evaluated in 5 children (ages 3 through 12) and in 8 adolescent subjects (ages 13 through 16) (see Pharmacokinetics [12.3]).

8.5 Geriatric Use
Safety and efficacy of Berinert in the geriatric population have not been established. Clinical studies with Berinert included four subjects older than 65 years. The clinical studies included an insufficient number of subjects in this age group to determine whether they respond differently from younger subjects.

15 REFERENCES

Manufactured by:
CSL Behring GmbH
35041 Marburg, Germany
US License No. 1765
Distributed by:
CSL Behring LLC
Kankakee, IL 60901 USA
Induce, differentiate and analyze your mouse and human Th17 cells with novel reagents that are:

- **Well-characterized in relevant models**
- **Both specific and sensitive**

**Flow Cytometry Antibodies:**
- Act1
- CD161
- CD196
- IL-1RA
- IL-6
- IL-6Ra
- IL-17A
- IL-17F
- IL-21
- IL-22
- IL-23/12 p40
- RORγ(t)

**ELISA Kits:**
- IL-6
- IL-17A
- IL-17F
- IL-17AF
- IL-21
- IL-22
- IL-23
- TGFβ
- TNFα

**Recombinant Proteins:**
- IL-6
- IL-17A
- IL-17F
- IL-17AF
- IL-21

Discover more at www.eBioscience.com
The VeriKine-HSTM Human IFN-β Serum ELISA kit sets new standards for sensitivity and reliability in the measurement of Human Interferon-Beta (IFN-β) levels in different sample matrices, such as serum, plasma, and cell culture supernatants. Additionally, this kit:

- Detects as little as 1.5 pg/ml (0.5 IU/ml)
- Maintains <8% inter- and intra-assay CV
- Exhibits a high signal-to-noise ratio
- Does not react with heterophilic antibodies, clotting factors, or serum proteins, minimizing false positive results.

This increased sensitivity allows the detection and quantification of basal human IFN-β enabling greater insight into the early immune response.

Call now +1.732.777.9123 or visit us at www.interferonsource.com/beta for more information.
PerkinElmer puts faster, easier inflammation assays within reach.

AlphaLISA® is a homogeneous alternative to conventional ELISA, enabling you to eliminate tedious wash steps without sacrificing high sensitivity or wide dynamic range. And with our expanding line of AlphaLISA kits for research on cancer, inflammation and other disease areas, we’re bringing this highly efficient Alpha Technology to more labs than ever before. Learn more about our Alpha Technology assays, and all the ways we can give you a hand with your research.

www.perkinelmer.com/nowashELISA
INTRODUCING OUR NEW
2010 PROTEOMICS RESEARCH PRODUCTS CATALOG

FROM THE LEADING SUPPLIER OF PROTEOMICS RESEARCH PRODUCTS:
- over 16,450 monoclonal and 32,930 polyclonal antibodies
- over 135,300 siRNA and shRNA (plasmid and lentivirus) products
- UltraCruz®, ExactaCruz®, and CrystalCruz® brand labware
- over 48,000 ChemCruz® specialty biochemicals
- broad range of support products and secondary antibodies
- website updated daily with new antibodies, biochemicals, labware, product citations and support data.

www.scbt.com

© 2010 Santa Cruz Biotechnology, Inc., the Santa Cruz Biotechnology, Inc. logo, UltraCruz™, ExactaCruz™, ChemCruz™, ImmunoCruz™ and CrystalCruz™ are registered trademarks of Santa Cruz Biotechnology, Inc.