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.

Berinert® has not been evaluated in children (ages 0 through 12) or in the geriatric population.

Please see Brief Summary of Prescribing Information on following pages.
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

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Please see Brief Summary of Prescribing Information on following pages.
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. The most common adverse reactions that have been reported in greater than 4% of the subjects who received Berinert in clinical studies were subsequent HAE attack, headache, abdominal pain, nausea, muscle spasms, pain, diarrhea, and vomiting.

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.

Pharohe-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.

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 and administering it to the patient. (See Patient Counseling Information [17]).

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.

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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/or Pharmacology [13.2]).

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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


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Distributed by:

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Produced in barley, these proteins are animal, bacterial, and viral free, and are ultra pure, with extremely low endotoxin.

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- Animal, bacterial & viral free
- Extremely low endotoxin (<0.005 ng/ug)
- Highly biologically active
- Easier regulatory clearance
- Perfect for cell culture, drug development, stem cell research, animal research
- For use in all in vitro cellular studies
- For use in all in vivo animal studies

Ultra pure cytokines & growth factors

- FGF1, human
- FGF2, human
- FLT3 ligand, human
- GCSF, human
- IFNA2, human
- IFN gamma, human
- IGF1, human
- IL1-alpha, human
- IL2, human
- IL3, human
- IL4, human
- IL5, human
- IL6, human
- IL7, human
- IL9, human
- IL16, human
- IL22, human
- KGF, human
- M-CSF, human
- NRG1/HRG beta 2, human
- SCF, mouse
- SF20/IL25, human
- TNF-alpha, human
- TNF-beta, human
- VEGF121, human
- VEGF165, human
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AAI is pleased to offer a program to match new PI’s with established PI’s who have significant, successful grant writing careers. The Grant Review for Immunologists Program (GRIP) invites new PI’s to submit an outline or NIH-style abstract to the GRIP coordinator who, with the assistance of a small volunteer subcommittee, will attempt to match the topic of the proposal with the research experience of an established PI. Matches will be made as quickly as possible to allow new PI’s to meet upcoming NIH grant deadlines. Participation is strictly voluntary and is not intended to supplant internal mentoring programs.

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