Ecallantide for treatment of acute attacks of hereditary angioedema

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Hereditary angioedema (HAE) is a rare, autosomal dominant disorder characterized by a deficiency of C1 esterase inhibitor.1 C1 esterase inhibitor is synthesized in the liver and regulates activation of the complement pathway, the contact pathway (involving kallikrein), and the coagulation pathway (involving plasmin, factor IX, and factor XIa).1,4 C1 esterase inhibitor inhibits the activation of these pathways, particularly the kallikrein system, which controls the production and activation of bradykinin. In patients with HAE, the lack of C1 esterase inhibitor promotes the excess activation of bradykinin, which leads to the classic symptom of swelling due to increased vascular permeability (Figure 1).2,4

The prevalence of HAE is approximately 1 in 50,000.1,2 Age, sex, and race appear to have no effect on disease prevalence. Approximately 85% of patients with HAE have type I disease, caused by a deficiency in circulating C1 esterase inhibitor in the plasma.2,5 About 15% of patients have type II disease, in which plasma levels of C1 esterase inhibitor are normal but the protein’s functionality is severely reduced. A third type of HAE has been described, primarily in women and associated with increased estrogen levels, such as during pregnancy or when given exogenous estrogen.4 While not all attacks of HAE have an identifiable trigger, common precipitants include infection, oral contraceptive

Purpose. The pharmacology, pharmacokinetics, efficacy, safety, dosage, administration, adverse effects, and place in therapy of ecallantide, a kallikrein inhibitor for the treatment of hereditary angioedema (HAE), are reviewed.

Summary. Ecallantide is the first member of the kallikrein inhibitor class approved for the treatment of acute attacks of HAE. Ecallantide works by binding to kallikrein, preventing the conversion of kininogen to bradykinin, which reduces vascular permeability, thus reducing the swelling associated with acute attacks of HAE. Ecallantide has been studied for the treatment of HAE in three Phase II studies and two Phase III studies. These studies were collectively known as the EDEMA (Evaluation of DX-88’s Effect in Mitigating Angioedema) studies. Phase III clinical trials found that ecallantide is superior to placebo in ameliorating patient symptoms associated with acute attacks of HAE at any anatomical site. Ecallantide has a favorable safety profile, with the most common adverse effects being gastrointestinal effects, headache, and injection site reactions. The most severe adverse effects of ecallantide are the risk of anaphylaxis and the possible development of antiecallantide antibodies. A risk evaluation and mitigation strategy program has been approved by the Food and Drug Administration to help ensure the safety and efficacy of ecallantide use. The recommended dose is 30 mg given as three separate subcutaneous injections.

Conclusion. Ecallantide is a novel agent approved for the treatment of acute attacks of HAE at any anatomical site. It is one of only three medications approved for this indication in the United States, presents a unique mechanism of action, and appears to be safe and effective when used for its labeled indication.

Index terms: Angioedemas; Dosage; Ecallantide; Enzyme inhibitors; Mechanism of action; Pharmacokinetics; Toxicity

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use, trauma, emotional stress, and angiotensin-converting-enzyme (ACE) inhibitors. In acute attacks, there may be subcutaneous or submucosal, nonpitting, nonpruritic swelling anywhere throughout the body that is unresponsive to antihistamines, epinephrine, or corticosteroids. The swelling usually develops slowly over 24 hours before subsiding within five days. The most common sites affected include the extremities, gastrointestinal tract, and respiratory tract.

Attacks usually develop at a young age and persist throughout life, with variable frequency and severity, ranging from mild discomfort of the extremities to nausea, vomiting, and intestinal obstruction to airway compromise and death.

Treatment for HAE is limited, as there are few therapeutic options available in the United States. Primary prevention includes avoiding the use of ACE inhibitors and estrogen, promptly treating infections to prevent activation of the complement cascade, and controlling physiological and psychological stress. Medical prophylaxis is recommended in patients with a history of HAE who have had more than one episode of severe abdominal pain in one year, any head or neck swelling, or frequent peripheral or genital swelling or who require C1 esterase inhibitor concentrate more than once a year. Tranexamic acid and the 17-α attenuated alkylated androgens (danazol, stanozolol, and oxandrolone) are most commonly used for long-term prophylaxis of HAE. Tranexamic acid is an antifibrinolytic agent; in HAE, it is believed to promote the sparing of C1 esterase inhibitor by reducing peripheral consumption of C1 esterase inhibitor for the activation of plasminogen. The 17-α attenuated alkylated androgens work by increasing hepatic synthesis of C1 esterase inhibitor. However, significant adverse effects such as hepatic dysfunction and thrombus development limit their use.

Patients with an acute attack of HAE may be treated with the agents used for prophylaxis at larger doses, but this approach is not recommended, primarily due to a lack of data. Fresh frozen plasma has been used for acute attacks because it contains C1 esterase inhibitor; however, fresh frozen plasma contains high concentrations of complement components that may increase the generation of bradykinin, which could worsen the attack in the short term. In Europe, C1 esterase inhibitor concentrate is the intervention of choice; Berinert (CSL Behring, King of Prussia, PA), the first C1 esterase inhibitor concentrate for use in the United States, was approved in October 2009. A drug targeting the bradykinin system, icatibant, works by blocking bradykinin-2.
receptors; it was recently approved for use in the United States for the treatment of acute attacks of HAE.\(^2^ {,}^7\) Ecallantide (e kal’ lan tide) (Kalbitor, Dyax Corporation, Cambridge, MA), known as DX-88 during development, was approved by the Food and Drug Administration (FDA) on November 27, 2009, for the treatment of acute attacks of HAE.\(^5^ {,}^9 {,}^10\) This article reviews the pharmacology, pharmacokinetics, efficacy, safety, dosage, administration, adverse effects, and place in therapy of ecallantide. PubMed, Ovid MEDLINE, and Google Scholar were searched for all English-language articles containing the terms ecallantide or DX-88. The references cited in the retrieved articles were reviewed for additional literature sources.

**Pharmacology**

Ecallantide, a novel 60-amino-acid recombinant protein produced in *Pichia pastoris* yeast cells, was discovered through phage-display technology.\(^9 {,}^11\) It is a highly selective, potent kallikrein inhibitor that ultimately reduces the production of bradykinin and symptoms of acute HAE attacks. Ecallantide acts by reversibly binding plasma kallikrein, a plasma protease within the contact pathway, with high affinity, preventing the conversion of high-molecular-weight kininogen to bradykinin.

**Pharmacokinetics and pharmacodynamics**

Ecallantide exhibits dose-dependent effects, though no target concentrations have been identified. After a single subcutaneous injection of ecallantide 30 mg, the mean maximum plasma concentration \((C_{\text{max}})\) was 586 ng/mL, the time to \(C_{\text{max}}\) was two to three hours, and the mean area under the plasma concentration–time curve was 3017 ng·hr/mL.\(^10 {,}^{11}\) The absolute bioavailability of ecallantide is approximately 90%.\(^10\) Sex, age, and body weight do not significantly affect exposure to ecallantide. Metabolism of ecallantide has not been studied; however, because it is a small polypeptide molecule, metabolic catabolism is expected.\(^11\) Biologically active metabolites are believed to be formed through glycosylation, oxidation, and amino-terminal truncation.\(^11\) The volume of distribution is 26.4 L, plasma clearance is 153 mL/min, and mean elimination half-life is two hours.\(^10\) Ecallantide is eliminated by the kidneys and has been detected in the urine of subjects treated in clinical trials. Pharmacokinetic data in patients with renal or hepatic impairment are not currently available, nor are data regarding potential drug–drug interactions.\(^10 {,}^{11}\) Because ecallantide is not metabolized through cytochrome P-450 isoenzyme pathways, pharmacokinetic drug interactions with these enzymes are not expected.\(^10\) Of note, ACE inhibitors are contraindicated in patients with HAE due to possible enhancement of bradykinin levels.\(^11 {,}^{12}\)

Ecallantide, administered subcutaneously, affects the contact pathway but has no effect on the coagulation or complement pathway. Therefore, while intravenously administered ecallantide was found to prolong activated partial thromboplastin time (aPTT), subcutaneous ecallantide has not been associated with clinically significant increases in aPTT.\(^11\)

**Clinical efficacy**

Ecallantide has been studied for the treatment of HAE in three Phase II studies and two Phase III studies. These studies were collectively known as the EDEMA (Evaluation of DX-88’s Effect in Mitigating Angioedema) studies.

EDEMA0 was a small Phase II trial involving seven patients with HAE and two patients with acquired angioedema.\(^13\) The study had an open-label, dose-escalation design. Patients, whose ages ranged from 31 to 67 years, received 10-, 40-, or 80-mg doses of ecallantide as a short i.v. infusion for the treatment of a non-life-threatening attack of angioedema. Areas of angioedema attacks included the face, bowel, hands, and genitals. After the infusion, the time to relief ranged from 25 minutes to 3 hours, with all patients showing clinical improvement by 4 hours postinfusion. Time to resolution of the attack ranged from 2 to 72 hours. One patient with HAE and both patients with acquired angioedema had a relapse of symptoms within 7–15 hours. This study was published only in abstract form, which limits the conclusions that can be drawn from the data.

EDEMA1 was a Phase II, multicenter, randomized, placebo-controlled, double-blind, ascending-dose trial that evaluated four different doses of i.v. ecallantide (5, 10, 20, and 40 mg/m²) in patients experiencing acute attacks of HAE.\(^14\) Ten patients were randomized to receive each of the four different doses of ecallantide, while 8 patients were randomized to receive placebo. Patients age 10 years or older with a diagnosis of HAE were included in the study. Patients were excluded if they had an active infection, any serious concurrent illness, a serum creatinine concentration more than 10% higher than the upper limit of normal, serum hepatic transaminase concentrations more than twice the upper limit of normal, received any investigational intervention within the past 30 days, any previous exposure to ecallantide, or were pregnant or breast-feeding. The primary outcome was the percentage of patients reporting significant improvement at the primary attack location 4 hours after drug infusion. Baseline characteristics were not presented but were described as comparable among treatment groups.

A total of 48 patients were enrolled in the study. Most of the patients were female \((n = 37, 77%)\) and white \((n = 42, 88%)\). Clinical improvement within 4 hours of treatment occurred...
in a greater proportion of patients who received ecallantide (29 [73%] of 40) versus placebo (2 [25%] of 8) (p = 0.0169). The median time to improvement of symptoms was 30.5 minutes in ecallantide-treated patients and 71.5 minutes in the placebo group. Adverse events were reported in similar proportions of patients (32 [78%] of 40 patients receiving ecallantide and 7 [88%] of 8 patients receiving placebo). When the different doses were analyzed for efficacy, only the 40-mg/m² dose was shown to be statistically superior to placebo (p = 0.0128). In the subgroup analysis for efficacy based on primary location of attack, ecallantide (at all doses) was also superior to placebo in treating peripheral attacks (response in 13 [72%] of 18 ecallantide-treated patients and in 0 of 4 patients receiving placebo, p = 0.00172). The small number of patients in this trial, particularly in the placebo group, in addition to the minimal reporting of baseline characteristics, makes some of the results difficult to generalize, particularly the subgroup analyses of the dose effects and adverse effects of ecallantide.

EDEMA2 was a Phase II, open-label, repeat-administration study in which patients received ecallantide at doses of 5, 10, or 20 mg/m² i.v. or 30 mg subcutaneously.15-17 Qualified patients who appeared within 4 hours of the onset of an acute HAE attack of at least moderate severity were treated with a single dose of ecallantide. If no improvement was noted within 4 hours, a second dose could be administered. Patients could receive a maximum of 20 doses for separate attacks. A successful outcome was defined as the onset of resolution within 4 hours of administration that continued for 24 hours after dose administration.

Seventy-seven patients with 240 HAE attacks were treated during this study; 20 patients (26%) had previous exposure to ecallantide. The mean age of patients treated was 33 years, the majority of whom were white (n = 67, 87%) and male (n = 50, 65%). Peripheral HAE attacks were reported as the first study-treated attacks for 35 patients (45%), abdominal attacks for 32 (42%), and laryngeal attacks for 10 (13%).

Of the 240 treated attacks, 165 (69%) were reported to have a successful outcome. Eighteen patients (24 total attacks) received ecallantide 5 mg/m² i.v., 55 patients (141 attacks) received 10 mg/m² i.v., 9 patients (15 attacks) received 20 mg/m² i.v., and 31 patients (60 attacks) received 30 mg subcutaneously. The highest response rate (occurring in 49 [82%] of 60 attacks) was seen with the 30-mg subcutaneous dose. The 10-mg/m² i.v. dose had a 67% response rate (96 of 144 attacks), the 20-mg/m² i.v. dose had a 60% response rate (9 of 15 attacks), and the 5-mg/m² i.v. dose had a 46% response rate (11 of 24 attacks). The 30-mg subcutaneous dose had the highest maintenance of response (no relapses or rebounds in the 24 hours after dose administration). Adverse effects were reported to be mild. Based on the results of this study, the 30-mg subcutaneous dose was used for Phase III studies. No p values were reported for any of the outcome measures. This study report is only available in abstract form, which limits the conclusions that can be drawn from the data. In addition, the lack of a validated, formal symptom scoring system, such as the treatment outcome score (TOS) or mean symptom complex severity (MSCS) score, for use in evaluating efficacy limits the generalizability of the results.

EDEMA3 was a Phase III randomized, multicenter, double-blind, placebo-controlled trial.18 Patients were included if they were at least 10 years old with a diagnosis of HAE and were seen within 8 hours of an acute attack of moderate-to-severe acuity. Patients were excluded if they were pregnant or breast-feeding, had received any investigational intervention within the past 30 days, or had received ecallantide within the past 7 days. Patients were permitted to use prophylactic androgen therapy during the study. Patients were randomized in a 1:1 ratio to receive either ecallantide 30 mg subcutaneously or placebo. For patients with severe upper-airway compromise, an open-label dose of 30 mg of ecallantide subcutaneously was permitted.

The primary outcome was a change in the TOS at 4 hours. The TOS is a patient-reported score based on the site of symptoms, severity, and response to treatment.19 Scores can range from –100 to 100, with positive scores indicating improvement and negative scores indicating worsening of symptoms. The secondary outcome was the change from baseline in the MSCS score. The MSCS score is also a patient-reported score comparing symptom site and severity before and after treatment. MSCS scores can range from 0 to 3, with higher scores indicating a greater severity of symptoms. Other endpoints included the time to significant improvement in overall response, improvement as determined by the TOS and MSCS at 24 hours after treatment, and time to improvement within 4 hours after treatment for at least 45 minutes. A power calculation was performed, which indicated that 62 patients would be needed for 90% power to detect a difference in the distribution of the TOS at 4 hours after treatment administration. The study results were reported as an intent-to-treat analysis. A total of 72 patients, 36 of whom received ecallantide and 36 of whom received placebo, were enrolled in this study. There were no significant differences in baseline characteristics between the placebo and intervention groups. The majority of the patients were female (n = 47, 65%) and white (n = 65, 90%), with a mean age of 35.4 years; 9 patients were between the ages of 10 and 17 years. Ecallantide was associated with a
higher median TOS (indicating more improvement) at 4 hours compared with placebo (TOS, 50 and 0, respectively; \( p = 0.004 \)) and at 24 hours after drug administration (TOS, 75 and 0, respectively; \( p = 0.007 \)). Ecallantide was also associated with more improvement in the median MSCS at 4 hours compared with placebo (change in MSCS, \(-1.00 \) and \(-0.50 \), respectively; \( p = 0.01 \)) and at 24 hours after administration (\(-1.00 \) and \(-0.50 \), respectively; \( p = 0.04 \)). Patients who received ecallantide appeared more likely to experience an adverse event (56% \([ n = 20 \] versus 33% \([ n = 12 \])\), though no \( p \) values were provided for adverse events. Data analyses were performed by the sponsor or a contract research organization paid by the sponsor.

EDEMA4 was a Phase III, randomized, double-blind, placebo-controlled study very similar to EDEMA3. Inclusion criteria, exclusion criteria, and randomization procedures were identical to those in EDEMA3. For patients with severe upper-airway compromise, an open-label dose of 30 mg of ecallantide administered subcutaneously was permitted. In both groups, patients whose attacks did not improve, incompletely resolved, or relapsed 4–24 hours after administration were permitted a single open-label dose of 30 mg of subcutaneous ecallantide and standard of care treatment. The primary efficacy endpoint was change from baseline in the mean MSCS score at 4 hours after dose administration. Secondary efficacy endpoints included the TOS 4 hours after dose administration and maintenance of overall improvement for up to 24 hours.

A total of 96 patients, 48 of whom received ecallantide and 48 of whom received placebo, completed the study. Baseline characteristics were similar between groups except for sex, with the placebo group having more males (20 [42%]) than the ecallantide group (11 [23%]). Significantly greater improvements in the MSCS score were seen in the ecallantide group compared with placebo at 4 hours (mean change, \(-0.8 \) and \(-0.4 \), respectively; \( p = 0.01 \)) and at 24 hours after dose administration (mean change, \(-1.5 \) and \(-1.1 \), respectively; \( p = 0.04 \)). The mean TOS was significantly greater with ecallantide treatment compared with placebo 4 hours after dose administration (53.4 and 8.1, respectively; \( p = 0.003 \)) and 24 hours after administration (88.8 and 55.1, respectively; \( p = 0.03 \)). More patients in the ecallantide group (21 [44%]) than in the placebo group (10 [21%]) maintained significant overall improvement through 24 hours (\( p = 0.02 \)). Ecallantide benefit became statistically significant over placebo at 3, 4, and 24 hours after dose administration. Fifteen patients in the ecallantide group (31%) and 22 patients in the placebo group (46%) received an additional open-label dose of ecallantide. Eight ecallantide-treated patients (17%) experienced at least one adverse event related to treatment versus 19 placebo-treated patients (40%). Nausea, headache, and dizziness were the most frequent adverse events observed. No patient developed antiecallantide antibodies over the seven-day follow-up period.

Further trials of ecallantide in HAE are ongoing to study the efficacy and safety of the drug in pediatric patients, the efficacy and safety of repeated doses of ecallantide, and the development of antiecallantide antibodies, allergic reactions, and coagulation abnormalities.

Ecallantide is currently under investigation for the prevention of blood loss during surgical procedures, treatment of ACE-induced angioedema, and treatment of macular edema with associated central retinal vein occlusion. Published data on these trials are still pending.

**Safety**

A black box warning has been issued for ecallantide due to reports of anaphylaxis. Only health care professionals equipped to manage both anaphylaxis and HAE should administer this medication, because it is often difficult to distinguish between the two conditions. During clinical trials, 5 (3%) of 187 patients treated with subcutaneous ecallantide developed anaphylaxis. In all patients who experienced anaphylaxis, symptoms occurred within the first hour after administration of ecallantide. The most common adverse reactions observed in clinical trials with subcutaneous ecallantide are summarized in Table 1.

As with many biological agents, the development of antibodies to ecallantide is a concern. With repeated exposure, the rate of seroconversion increases, as may the risk of hypersensitivity reactions. In 216

Table 1.

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>No. (%) Pts With Reaction</th>
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<tbody>
<tr>
<td><strong>Ecallantide (n = 100)</strong></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>8 (8)</td>
</tr>
<tr>
<td>Nausea</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>4 (4)</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>3 (3)</td>
</tr>
<tr>
<td><strong>Placebo (n = 81)</strong></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>6 (7)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3 (4)</td>
</tr>
<tr>
<td>Pyrexia</td>
<td>0</td>
</tr>
<tr>
<td>Injection site reaction</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>0</td>
</tr>
</tbody>
</table>

*Includes only reactions that occurred more frequently with ecallantide than with placebo. From reference 10, summarizing data from references 18 and 20.
patients treated with ecallantide, 36 (17%) developed antiecallantide antibodies.\textsuperscript{17,22} In addition, anti-\textit{P. pastoris} immune globulin antibodies have been detected in patients treated with ecallantide. The long-term effects of these antibodies are unknown; more studies are needed to adequately describe the immunogenic potential and long-term safety of this drug.

A risk evaluation and mitigation strategy (REMS) program has been approved by FDA to help ensure the safety and efficacy of ecallantide approved by FDA to help ensure strategy (REMS) program has been included in EDEMA.\textsuperscript{3} Use in patients older than 65 years has not been extensively studied and should be approached cautiously.

**Dosage and administration**

The recommended dose of ecallantide is 30 mg (3 mL) administered subcutaneously as three 10-mg (1-mL) injections.\textsuperscript{10} An additional dose of 30 mg can be administered subcutaneously within 24 hours if the attack recurs. Currently, there are no published reports of ecallantide overdosage. During clinical trials, patients were treated with doses as high as 90 mg of i.v. ecallantide without evidence of dose-related toxicity.

The drug concentration of each vial of ecallantide is 10 mg/mL; the formulation is a clear, colorless liquid containing no preservatives and should be kept refrigerated and protected from light.\textsuperscript{10} Once removed from the refrigerator, the drug is stable for 14 days. Vials with discoloration or any particulate matter should be discarded and not administered to patients. Aseptic technique should be used to withdraw 1 mL of drug from each vial. Subcutaneous administration should occur in the abdomen, thigh, or upper arm, and the same site can be used for all three injections. At least 2 inches should separate the injection site from the anatomical site of attack. Home administration is not recommended due to the potential risk of anaphylaxis.

**Formulary considerations**

Currently, there are no published economic evaluations of ecallantide or other agents used to treat acute attacks of HAE. The average wholesale price (AWP) of a single treatment of ecallantide is $9540.\textsuperscript{23} The AWP of the C1 esterase inhibitor concentrate Berinert is $2070 per 500 units; for a 70-kg patient receiving 20 units/kg, a single treatment costs $5796.\textsuperscript{23,24} The AWP of a single treatment of icatibant is $6800.\textsuperscript{23} For patients who need help affording ecallantide, the Kalbitor Access Program provides financial assistance, including copayment reductions or provision of the drug free of charge.\textsuperscript{25} Shire, the manufacturer of icatibant, also offers financial assistance through the OnePath program, including copayment assistance or provision of the drug free of charge.\textsuperscript{26}

Ecallantide, C1 esterase inhibitor, and icatibant are three novel agents for the treatment of acute attacks of HAE. Their characteristics are summarized in Table 2. Icatibant is currently the only agent indicated for self-administration for acute attacks of HAE in the United States.\textsuperscript{27} None

### Table 2.

**Comparison of Agents for Acute Treatment of Hereditary Angioedema (HAE)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Mechanism</th>
<th>Indication</th>
<th>Dose</th>
<th>Adverse Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ecallantide\textsuperscript{17,22}</td>
<td>Kallikrein inhibition</td>
<td>Acute attacks of HAE at any location in patients &gt;16 yr of age</td>
<td>30 mg s.c.</td>
<td>Headache, nausea, vomiting, diarrhea, injection-site reactions, anaphylaxis, antibody development</td>
</tr>
<tr>
<td>C1 esterase inhibitor (human)\textsuperscript{23}</td>
<td>Replacement of C1 esterase inhibitor; inhibits bradykinin activation</td>
<td>Acute abdominal or facial attacks of HAE in adults</td>
<td>20 units/kg i.v.</td>
<td>Headache, nausea, vomiting, diarrhea, anaphylaxis, transmission of infectious agents</td>
</tr>
<tr>
<td>Icatibant\textsuperscript{11}</td>
<td>Bradykinin-2 receptor antagonist</td>
<td>Acute attacks of HAE at any location in adults</td>
<td>30 mg s.c.</td>
<td>Dizziness, headache, injection site reactions, rash</td>
</tr>
</tbody>
</table>
of these agents is indicated in pediatric patients, though ecalledante is indicated in patients at least 16 years old. In addition, none have been extensively studied in pregnant women, and all are labeled pregnancy category C by the FDA, though the European Medicines Agency recommends to use icatibant only if the benefits outweigh the risks. Administration of all three agents is recommended only under the guidance of a health care professional.

There are no comparative efficacy studies of any of the three FDA-approved agents for the acute treatment of HAE. Ecalledante does pose a risk of anaphylaxis, as well as the possibility of developing antibodies with repeated exposure; however, it holds several advantages over C1 esterase inhibitor. C1 esterase inhibitor is only approved for treatment of acute attacks of abdominal or facial HAE, whereas ecalledante is approved for attacks at any location. Because C1 esterase inhibitor is derived from human plasma, it carries the potential risk of infectious transmission, whereas ecalledante does not carry this risk. Another advantage of ecalledante is that it is given via subcutaneous injection while C1 esterase inhibitor is given as an i.v. infusion.

Conclusion

Ecalledante is a novel agent approved for the treatment of acute attacks of HAE at any anatomical site. It is one of only three medications approved for this indication in the United States, presents a unique mechanism of action, and appears to be safe and effective when used for its labeled indication.

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