October 2, 2017

Dear Medical and Pharmacy Directors, Policy/Utilization Management Departments:

We are the Medical Advisory Board for the US Hereditary Angioedema Association (HAEA). The Association is a non-profit charitable organization that serves the HAE community. We are writing today regarding the negative impact of an ongoing outage of Cinryze®, an intravenous plasma-based C1-esterase inhibitor (Human) prescribed to prevent painful and potentially fatal HAE attacks. Shire, the manufacturer of Cinryze, halted production in mid-August 2017 due to manufacturing issues.

Numerous patients have already been hospitalized for HAE attacks due to the unavailability of Cinryze. We urge you to help us prevent patient suffering, costly hospitalizations, and decrease the risk of potentially fatal laryngeal attacks by (1) providing expedited processing and approval of HAE medication prescriptions and (2) doing whatever is necessary to facilitate swift patient access to one of the FDA-approved acute attack HAE therapies.

While HAEGARDA® (subcutaneous C1-esterase inhibitor [human] manufactured by CSL Behring) was recently approved for routine prevention of HAE attacks, availability of this therapy may, unfortunately, be limited in the near term. The company has advised that delays are likely for new patients starting HAEGARDA over the next few months, and there will not be a sufficient supply of HAEGARDA in the near-term to accommodate the entire population of patients seeking alternatives to Cinryze.

FDA approved acute attack treatments are:

BERINERT® --intravenous C1-inhibitor for acute attacks in adults and pediatric patients manufactured by CSL Behring. This medicine is approved for on-demand self-administration. We are aware of at least one Specialty Pharmacy that is experiencing what they describe as a temporary shortage of Berinert®.

RUCONEST®-- intravenous plasma-free recombinant human C1-inhibitor for treating acute attacks in adults and adolescents. Manufactured by Pharming, this medicine is approved for self-administration.

KALBITOR® --subcutaneous kallikrein inhibitor for acute attacks in patients 12 years of age and older. Manufactured by Shire, this medicine must be administered by a healthcare

professional.

FIRAZYR® --subcutaneous B2 bradykinin receptor antagonist for acute attacks in patients 18 years and older. Manufactured by Shire, this medicine is approved for self-administration.

Payer Considerations Requests

We understand your plan may already have a coverage policy and/or prior authorization criteria in place for all HAE products. We also understand that other agreements or entities may help determine coverage parameters or utilization restrictions to help ensure appropriate use of these medications.

The US HAEA Medical Advisory Board urges you to revisit your clinical criteria during this Cinryze outage and waive any existing restrictions for that would prevent Cinryze patients from getting immediate access to an alternative HAE therapy.

Please consider the following coverage and approval allowances during this critical and dangerous period for our HAE patients:

1. **Accelerate the prior authorization process for any prescribed HAE treatment and eliminate the administrative burden of unnecessary and redundant documentation.**
    - Use the same documentation (lab results, C1 levels, C4 functioning level, chart notes, etc.) that resulted in approval for Cinryze.

2. **Revisit or temporarily remove any quantity limits set by medical/pharmacy policy.**
    - Update pharmacy and medical claim limits to allow for the specific quantity prescribed by the physician.

3. **Allow coverage for more than one acute therapy.**
    - Some of the current therapies approved for acute attacks only provide limited relief, with some patients experiencing rebound or break-through attacks
    - Medical or pharmacy policies, as currently written, may limit or delay the option to add a secondary product and put patients at risk of not obtaining a much-needed secondary option prior to another HAE attack.

During this stressful time for our HAE patients, we ask that your health plan work with prescribing physicians to minimize the profound risk our patients now face during the Cinryze outage. We ask you to temporarily ease restrictions on access to therapy for those previously treated with Cinryze.

Sincerely,

Bruce L. Zuraw
Chair, US HAE Association Medical Advisory Board

Signed by Affirmation:
Aleena Banerji, MD
Jonathan Bernstein, MD
Paula Busse, MD
Timothy Craig, DO
Sandra Christiansen, MD
Mark Davis-Lorton, MD
Michael Frank, MD
Henry Li, MD, PhD
William Lumry, MD
Marc Riedl, MD
Members of the Medical Advisory Board

Enclosures (these can be accessed at https://www.haea.org/EmailDocs092717/**)**

- Accredo Special Pharmacy Fax Announcement on Cinryze shortage
- Shire Health Care Provider communication on Cinryze shortage
- Shire Patient communication on Cinryze shortage
- HAEGARDA letter to physicians
- EU Cinryze Shortage Communication
- FDA Website Product Shortage List
- FDA Recommendations for Prophylaxis and Treatment of Hereditary Angioedema (HAE) Attacks