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Institute for Clinical and Economic Review  
Attn: Matt Seidner, Program Manager  
2 Liberty Square, 9<sup>th</sup> Floor  
Boston, MA 02109

Dear Mr. Seidner:

CSL Behring appreciates the opportunity to comment during ICER's Draft Scope Response period regarding its planned assessment of the comparative clinical effectiveness and value of therapies for Hereditary angioedema (HAE). It is our understanding that the stated focus of ICER's review only involves the prophylactic therapies in the US (current and in-development) for the prevention of Hereditary angioedema attacks, including CSL Behring's HAEGARDA<sup>®</sup> (C1-INH Esterase Inhibitor Subcutaneous (Human)).

HAEGARDA is the only subcutaneous injection for the prevention of HAE attacks. In the pivotal trial, HAEGARDA demonstrated a 95% median reduction of HAE attacks compared to placebo per month and showed a  $\geq 99\%$  median reduction in number of uses of rescue medication per month compared to placebo by the subjects in the 60 IU/kg treatment arm (as per the FDA indication). CSL Behring chose to price HAEGARDA at an acquisition cost of 15% discount as compared to the lower fixed dose of prophylaxis therapy (CINRYZE) for an average 80kg patient.

The HAE patient population is less than 6,300 diagnosed in the U.S.A. with  $\sim 1/3^{\text{rd}}$  of those patients being appropriate for prophylactic therapy. The scoping document refers to "*Data permitting, we intend to compare all the agents to one another and to no prophylaxis*". We do not believe a comparison of prophylaxis therapy to no prophylaxis is appropriate for many clinical reasons. The nature of HAE attacks are unpredictable and vary from patient to patient with many suffering debilitating and potentially life-threatening angioedema attacks (laryngeal asphyxiation). These attacks are often/commonly associated with HRQoL impairment and substantial medical cost

Routine prophylaxis is an essential treatment decision between the Healthcare Provider and the HAE patient (or parents), especially those patients with high disease burden, lack of access to care, severity of the attacks, HRQoL impairment in between attacks and during attacks. Some of these factors do not lend itself to inclusion in cost or QOL. The purpose of HAE prophylaxis is to mitigate, or literally prevent angioedema attacks from occurring, thus allowing HAE patients to live, as closely as possible, to a "normal" life. The 2017 World Allergy Organization HAE guideline recommends that HAE patients are to be evaluated for long-term prophylaxis therapy at every visit. Thus we strongly recommend only comparing among the products that have been studied for prophylactic therapy.

In the scoping document, table 1.1: Key Outcomes and Harms, lists the many endpoints that would be included in assessing the value of various therapies. We would like to recommend inclusion of

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cost (both direct and indirect) for the site of infusion of prophylactic therapy as well as ports used for the intravenous products. Data suggests that at least 30% of CINRYZE users have used ports.

We also re-iterate the importance of including only pivotal trial results (phase 3 clinical trials) across the four prophylactic HAE therapies, which will provide the best comparison, although an indirect comparison. Three of the four prophylactic therapies being considered will not have published open label study results in time for consideration during this assessment. Therefore CSL Behring would like to request that your organization notify us if any open label study results will be included in the analysis, since we would consider providing unpublished data under a confidentiality agreement.

Finally I would like to draw your attention to an additional Cost effectiveness analysis that has been presented at both AMCP and ACAAI 2017 comparing CINRYZE to HAEGARDA, which is the only model that has been published comparing prophylactic therapies.

We welcome the opportunity to continue the dialogue with ICER and provide information as appropriate moving forward.

Sincerely,

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