Proposal for assessment of new health technologies

Important information – read this first!

- Submitted proposals for national health technologies (HTAs) will be published in full. If the proposer thinks there is information necessary for filling out the form, that should not be made public, please contact the secretariat (Nye Metoder) before submission.

  The proposer is aware that the form will be published in its entirety (tick): ☒

- Proposer has filled out point 19 below «Interests and, if any, conflicts of interest» (tick): ☒
- This form serves the purpose to submit proposals for health technology assessment (HTA) at the national level in Nye Metoder - the national system for managed introduction of new health technologies within the specialist health service in Norway. The form does not apply to proposals for research projects. A health technology assessment is a type of evidence review, and for this to be possible, documentation is required, e.g. from completed clinical trials. Lack of documentation may be one of the reasons why the Commissioning Forum (Bestillerforum RHF) does not assign a health technology assessment.
- If the proposal concerns a medical device, the proposer is familiar with the document «Guidance criteria for management of medical devices in the National System for Managed Introduction of New Health Technologies within the Specialist Health Service in Norway» (link) (tick): ☐

Contact information:

Name of the proposer (organization / institution / company / manufacturer)**:**

CSL Behring AB

Name of proposal contact:

Erik Ahlzén

Telephone number:

+46 8 544 966 70

E-mail address:

erik.ahlzen@cslbehring.com

Date and locality:

7 Feb 2019

1. Proposer's title on the proposal: *
   *This may be changed during the course of the process"

Berinert (C1-esterasehemmer) til subkutan injeksjon for forebygging av tilbakevendende anfall av hereditært angioødem (HAE).

2. Brief description of the health technology proposed to be considered:

Berinert for subcutaneous injection is indicated for prevention of recurrent Hereditary Angioedema (HAE). Berinert 2000/3000 IU is intended for self-administration by subcutaneous injection. The therapeutic effect of Berinert in hereditary angioedema is induced by the substitution of the deficient C1-esterase inhibitor activity.

3. Brief description of current standard of care (SOC) (Which health technology (ies) are currently used. What is the status of the technology (ies)? Whether it provides curative treatment, life extension, etc.)
   Will the proposed technology replace or be a supplement to today's SOC?

Hereditary angioedema is a genetic condition leading to a reduction or loss of function of the important C1 inhibitor enzyme. C1 inhibitor has numerous functions within the immunological as well as the coagulation system. Lack of C1 inhibitor, among other, can lead to acute edema (swelling) of different locations in the body. The disease can be severely debilitating, and potentially life threatening if there is an edema in the laryngeal region. Pharmacological treatment for HAE consist both of treating acute attacks as well as long term prophylaxis to prevent attacks. Acute attacks of HAE can be treated with intravenous C1 inhibitor, restoring the lacking C1 inhibitor and thus resolving the attack. It is also possible to treat the symptoms of the attack by using a bradykinin receptor antagonist, icatibant. Prophylactic treatment is to date possible with intravenous C1 inhibitor as well as less specific treatment such as androgens and tranexamic acid.

4. This proposal concerns:

	Yes	No
A brand new and innovative health technology	☐	☐
Anew application, or a new indication for an established method	☒	☐
A comparison between several methods	☐	☒
A technology that is already in use	☐	☒
If yes – technology used in clinical practice	☐	☐
If yes – technology used in research/clinical trials	☐	☐
A re-evaluation of technology used in clinical practice	☐	☒

The technology is relevant for disinvestment	☐	☒

"Please include further details about any use of the technology"

5. This health technology involves (Multiple ticks are possible)

Pharmaceutical	☒
Medical device/IVD medical device that is CE-marked*	☐

"*If the technology is CE-marked: What is it CE- marked as and for which indication? Please describe"

Medical device/IVD medical device that is not CE-marked	☐
Procedure	☐
Screening	☐
Highly specialized services / national offers	☐
Organization of the health services	☐
Other (describe)	☐

"If relevant, please include who should be responsible for developing the technology."

6. Application of the technology:

Prevention	☒
Assessment and diagnostics	☐
Treatment	☐
Rehabilitation	☐
Specialist health care	☐
Primary health care	☐

"Please give a description here"

7. Responsibility for funding

	Yes	No
Is the specialized health service responsible for financing the technology today?	☒	☐
May the specialized health service become responsible for funding the health technology?	☐	☐

H-resept

8. Is the technology mentioned in the national guidelines or action programs prepared by the Norwegian Directorate of Health?

Yes	No
☐	☒

"Give more details about the relevant national guidelines or action programs."

9. Does the technology involve the use of radiation (ionizing/ non- ionizing)?

Yes	No
☐	☒

"Give a short description of type of radiation source, device and degree of radiation exposure"

10. Which discipline(s) does the health technology apply to, and which patients are affected? (Could the health technology also affect other groups (e.g. health personnel or relatives)?)

Patients affected: Patients with HAE.

Disciplines: Dermatologists, allergologists, hematologists, anesthesiologists and pulmonologists

11. Which aspects are relevant to the assessment? (Multiple ticks are possible)

Clinical efficacy	☒

Safety/adverse effects	☒
Costs/resource use	☒
Cost-effectiveness	☒
Organizational consequences	☐
Ethical	☐
Legal	☐

12. Please suggest the main scope/objective for the health technology assessment, as well as secondary scopes/objectives (in compliance with question 10). For those familiar with "PICO" (Patient, Intervention, Comparator, Outcome) – please include tentative suggestions for PICO.

Population: Adolescent and adult patients with C1-esterase inhibitor deficiency.

Intervention: The recommended dose of Berinert s.c. is 60 IU/kg body weight twice weekly (every 3-4 days)

Comparator: SoC described in point 3

Outcomes:

- HAE attack frequency
- Percentage of patients responding to treatment
- Rescue medication used
- Adverse events

13. Please give a brief explanation of why it is important that the health technology assessment proposed should be conducted.

Berinert 2000/3000 IU s.c offers a new treatment regime for patients diagnosed with HAE type I and II. HAE is a potentially life treating rare disease with a prevalence of 2-3 in 100 000.

The root cause of HAE is missing or dysfunctional C1-esterase inhibitor and repeated administration with Berinert 2000/3000 IU s.c increases and maintains steady levels of functioning C1-esterase inhibitor above 40%. This restores the body's natural ability to regulate the kallikrein-kinin cascade involved in HAE and the complement, coagulation and fibrinolytic systems as well. HAE attacks are prevented and the approved dose of 60 IU/kg has been shown to reduce the number of HAE attacks by a median of 95 percent relative to placebo as shown in the COMPACT study.

Until now HAE patients have been dependent on on-demand treatment administered intravenously or subcutaneous or prophylactic treatment administrated administered intravenously. Long term home-treatment with intravenous administration is challenging for many patients. Berinert 2000/3000 IU s.c is the first C1-inhibitor esterase concentrate that comes with a subcutaneous regime and are indicated for prophylactic treatment. This is a great improvement for patient convenience and fills an unmet medical need in severe patient groups where HAE patients can have up to two attacks per week with a big impact on their quality of life.

In addition, a Hurtig metodevurdering is currently being conducted for Takhzyro (lanadelumab), ref Metodevarsel LM nr 066 2018. This product is indicated for the same patient population as Berinert 2000/3000 IU s.c and therefore the two treatments should be evaluated in parallel.

14. Please comment on the technology that is proposed to be assessed with regard to the following points:

The severity of the disease/condition the health technology targets

Severe

Expected effect

Pivotal clinical study demonstrated a median reduction in HAE attack frequency of 95% relative to placebo.

In the treatment period of 14 weeks 40% of the patients were attack-free. In an open-label extension study 54% of the patients were attack-free month 1-6 after starting treatment and 83% were attack-free month 25-30 after starting treatment.

Safety

The long-term safety and tolerability profile has been demonstrated to be favorable. The incidence of adverse events in the studies was low and the majority of reported adverse events in the studies were mild. Most reported adverse events were injection-site reaction with the majority of these reported as mild and resolved within 24 hours after onset. No anaphylactic reactions or inhibitory anti-C1 inhibitor antibodies were detected.

Total number of patients in Norway the health technology is applicable to

Approximately 100 patients with HAE in Norway

Ref:

Hereditært angioødem, Norsk helseinformatikk [oppdatert 30. desember 2015]. Tilgjengelig fra: https://nhi.no/sykdommer/hud/rode-hudutslett/angioodem-hereditart/

Consequences for resource use in the public health service

"Click in the field and type"

Need for revision of existing national guidelines or preparation of new guidelines

National:

Hereditært angioødem, ICD: T78.3. Den norske legeforeningen [revidert 08. april 2005]. Tilgjengelig fra: http://legeforeningen.no/Fagmed/Norsk-forening-for-dermatologi-og-venerologi/Veiledere/metodeboker-og-veiledere/hereditart-angioodem-icdt783/

International:

The international WAO/EAACI guideline for the management of hereditary angioedema – the 2017 revision and update

15. Please provide references to documentation of the health technology's effect and safety (i.e. previous technology assessments). (Up to 10 key references can be provided, please do not send attachments in this step of the process):

No HTA assessments on Berinert s.c published in EU yet to our knowledge

16. Please provide the name of the marketing authorization holder/manufacturer/supplier of the health technology (if applicable/available):

CSL Behring AB

17. Marketing Authorization Status (MA) or CE-marking: When is MA or CE- marking expected? If possible, provide the time of planned marketing:

MA granted in Norway on 2018-08-10

18. Additional relevant information (up to 300 words.)

N/A

19. Interests and potential conflicts of interests

Please describe the proposer's relationships or activities that may affect, be influenced by, or be perceived by others to be important for further management of the health technology that is proposed assessed. (E.g. proposer has financial interests in the matter. Proposer has or has had assignments in connection with the technology or to other actors with interest in the technology)

CSL Behring is MA holder of Berinert in Norway.