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)**:**

Oresund Pharma ApS

Name of proposal contact:

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Date and locality:

23.02.2022 – Copenhagen, Denmark

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

Siklos – Sickle Cell Disease (SCD), Sigdcellesykdom

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

Siklos is a medicine that contains the active substance hydroxycarbamide (HU). Siklos has been developed specifically for Sickle Cell Disease (SCD), where there has been a great unmet need. Siklos is the first and only approved medicine on the market for; The prevention of recurrent painful vaso-occlusive crises (VOC) including Acute Chest Syndrome (ACS) in adults, adolescents and children older than 2 years suffering from symptomatic sickle cell syndrome.

Siklos can optimize the treatment of today by reducing VOC, ACS, hospitalizations, number of days of hospitalizations for SCD, and number of patients with at least one blood transfusion, compared with the current HU 500mg capsules.

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?

The standard treatment of today is HU 500mg capsules (originator brand: Hydrea®), which is not approved for SCD and is therefore used off-label. The physicians are not able to dose accordingly to 15-30mg/kg/day and are therefore either over-dosing (toxicity) or under-dosing (treatment failure) the patients. Hydrea® is approved for Chronic Myeloid leukemia (CML). HU does not cure SCD however, it will extend the life for the patient.

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	☐	☒

HU is the standard care of today however it is used off-label. Siklos (HU) is the first medicine to be approved for the treatment of SCD.

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	☐

HU is the standard care today for the treatment of SCD.

Siklos should only be used when the treatment is performed by doctors/physicians with special knowledge of SCD and its treatment. Siklos is approved for the prevention of recurrent, painful vaso-occlusive crises (VOC). They can include Acute Chest Syndrome (ACS). Siklos reduces VOC, ACS, hospitalizations, number of days of hospitalizations for SCD, and number of patients with at least one blood transfusion.

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?	☒	☐

HU 500mg capsules are not approved for the treatment of SCD, but they are the drug of choice regarding pharmacological treatment of patients with SCD. The specialized health service has the responsibility for financing the technology today.

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

Yes	No
☒	☐

HU is the standard care of today world-wide. Oslo University Hospital has made a guideline for SCD.

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)?)

Siklos is to be used within hematology (including pediatric hematology). SCD is an inherited blood disease affecting the African population (rare disease in Norway).

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.

P: In patients suffering from SCD

I: is Siklos

C: Compared with Hydroxycarbamide 500mg capsules and placebo,

O: effective in reducing numbers of VOC, ACS, bloodtransfusions and hospitalizations?

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

Standard care of today (HU 500mg capsule) is not approved for SCD, which means physicians/doctors are using the medicine off-label (makes them legally liable if the patients suffer any harm). Dosing recommendation is based on 15-30mg/kg/day. It is not possible to dose precisely, and the patient is therefore either over-dosed (toxicity) or under-dosed (treatment failure). *Example: a patient weighing 35kg and is dosed 20mg/kg/day (avg. dosing), would result in a daily dosage of 700mg*. The physician would round up or down to the nearest 500mg, which in this case is 500mg (A negative difference of 200mg HU).

Siklos is made to solve this great medical need by being able to divide the tablets, which results in a treatment where the physicians can dose to the nearest 50mg (precise dosing). Siklos has shown in a large-scale long-term study to be a more effective treatment compared with HU 500mg capsules.

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

Sickle Cell Disease is a serious and lifelong health condition with no cure.

Expected effect

No. Of VOC reduces 50%

No. Of ACS reduces 67%

No. Of Hospitalizations reduces 46%

No. Of days of hospitalization for SCD reduces 46%

No. Of patients with at least one blood transfusion reduces 21%

Safety

Known risk factors are:

Neutropenia, thrombocytopenia and anemia

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

In 1997 there were 15 patients I Norway.

In Denmark the number of children and adolescents with SCD have grown from 20 patients in 2007 to approximately 50 patients in 2015.

It could be estimated that there are approximately 50 patients in Norway.

Consequences for resource use in the public health service

Estimated consequences for resource use in the public health service (based on maksimal utsalgspris for apotek:

1.432.050,00 NOK.

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

Revision of existing guidelines regarding HU treatment.

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):

Escort-HU cohort study – A large-scale and long-term study on Siklos (full article can be send as document if needed).

https://onlinelibrary.wiley.com/doi/10.1002/ajh.26286

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

Addmedica S.A.S.

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

MA date: Siklos 100mg: 28.02.2011 Siklos 1000mg: 29.06.2007

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

"Click in the field and type"

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)

Oresund Pharma ApS is Siklos-distributor for Addmedica in the Nordics