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):

Sun Pharmaceutical Industries Europe B.V.

Name of proposal contact:

Ann-Sofie Brandt

Telephone number:

+46 725530252

E-mail address:

marketaccesssweden@gmail.com

Date and locality:

2021-02-05 Malmö, Sweden

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

   Proposal for assessment of Odomzo

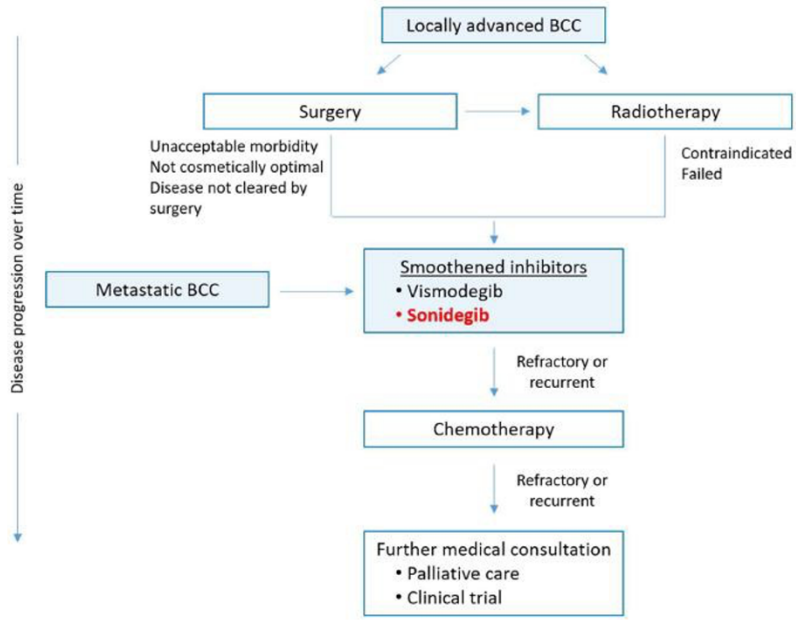
2. Brief description of the health technology proposed to be considered:

   ODOMZO® (sonidegib) is a prescription medicine used to treat adults with basal cell carcinoma (BCC), that has come back following surgery or radiation or that cannot be treated with surgery or radiation.

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?

Due to the pathogenesis of advanced BCC (laBCC and mBCC), treatment options are limited by the type, size, location and depth of penetration of the lesions as well as the extent of disease (e.g. extensive metastases). In some cases surgery and radiotherapy are not an option and these patients are often managed palliatively with best supportive care. Only recently have the hedgehog pathway inhibitors (including sonidegib and vismodegib) provided an alternative, targeted option for treatment of advanced BCC. Vismodegib is already available on the Norwegian market. Sonedigib will be a supplement of today's SOC for patients unable to undergo surgery and radiotherapy.

Figure 1. Current and proposed treatment algorithm for locally advanced BCC



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 ☒ ☐

Because of the longer response duration of treatment with sonedigib vs. vismodegib, and because the benefits of the treatment may last longer after treatment discontinuation, the sonedigib label provides the opportunity to reduce the frequency of administration from once daily to once every two weeks. This can help physicians better manage the side effect associated with the HHI treatment and lower the overall treatment cost.

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	☐

Odomzo is a cancer medicine used to treat adults with basal cell carcinoma (a type of skin cancer) which is locally advanced (has started to spread nearby) and which cannot be treated either by surgery or by radiotherapy (treatment with radiation).

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?	☒	☐

"Please give a further description of responsibility for funding"

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

Yes	No
☐	☒

Europan Guidelines are published by: Peris K, Fargnoli MC, Garbe C, Kaufmann R, Bastholt L, Seguin NB, Bataille V, Marmol VD, Dummer R, Harwood CA, Hauschild A, Höller C, Haedersdal M, Malvehy J, Middleton MR, Morton CA, Nagore E, Stratigos AJ, Szeimies RM, Tagliaferri L, Trakatelli M, Zalaudek I, Eggermont A, Grob JJ; European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO) and the European Organization for Research and Treatment of Cancer (EORTC). Diagnosis and treatme,t of basal cell carcinoma. European consensus-based interdisciplinary guidelines. Eur J Cancer. 2019 Sep;118:10-34.

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)?)

"Sonedigib is a cancer medicine used to treat adults with basal cell carcinoma (a type of skin cancer) which is locally advanced (has started to spread nearby) and which cannot be treated either by surgery or by radiotherapy (treatment with radiation).

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 Adult patients with locally advanced basal cell carcinoma (BCC) who are not amenable to curative surgery or radiation therapy.
I Odomzo (Sonidegib) 200 mg
C Erivedge (Vismodegib) 150 mg
O Objective response rate (ORR), Duration of response (DOR), Progression free survival (PFS), Overall survival (OS), Adverse events*, Death, Quality of life (QoL), Treatment discontinuation, Time to tumor response (TTR)
*Any AE related to treatment
Muscle spasms
Alopecia
Dysgeusia
Fatigue
Weight decreased
Nausea
Diarrhea
Appetite decreased
CK elevated

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

Sonidegib and vismodegib are hedgehog pathway inhibitors (HHIs) approved for the treatment of locally advanced basal cell carcinoma (la BCC). Vismodegib is currently the only targeted treatment available in Norway for patients with locally advanced BCC (laBCC) in cases where surgery and radiotherapy are inappropriate.

Despite the approval and launch of vismodegib, unmet treatment needs remain for patients with laBCC. Vismodegib demonstrated an Objective Response Rate (ORR) of 47.6% in patients with laBCC. In addition, there are safety concerns associated with the use of vismodegib. The efficacy profile of sonidegib is at least non-inferior to vismodegib with significantly improved safety. Sonidegib also is the first HHI to report QoL data, with over 80% of patients showing maintenance or improvement in QoL via EORTC QLQ-C30 as well as EORTC-H&N35 criteria.

Because of the longer response duration of treatment with sonedigib vs. vismodegib, and because the benefits of the treatment may last longer after treatment discontinuation, the sonedigib label provides the opportunity to reduce the frequency of administration from once daily to once every two weeks. This can help physicians better manage the side effect associated with the HHI treatment and lower the overall treatment cost.

Therefore, sonedigib provides an additional treatment option for HCPs and patients with a strong efficacy/safety profile and improved QoL.

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

Basal cell carcinoma (BCC) is the most common form of skin cancer. The prognosis for uncomplicated BCC is good. In a few cases, BCC cases can develop into advanced form that has a very high degree of difficulty. The disease is then called either locally advanced BCC (laBCC) or metastatic BCC (mBCC).

Expected effect

The Phase II randomized double-blind study (BOLT) demonstrated clinically meaningful responses to sonidegib 200 mg in patients with laBCC after 6-months of follow-up in the primary analysis. Longer-term follow-up at 42-months, corresponding to an overall median duration of follow-up of 50.2 months, continues to support that sonidegib is an effective treatment for patients with laBCC who are not amenable to curative surgery or radiation therapy.

The following efficacy results were demonstrated in the study:

- Tumour shrinkage is observed in 92% of the patients in the 42-month analysis.
- A disease control rate (complete response + partial response + stable disease) of 91% is shown in the 42-month analysis.
- Clinically relevant objective response rates (ORRs) are demonstrated in the 200-mg arm of 56.1% (central review based on mRECIST) and 71.2% (investigator review based on mRECIST) in the 42-month analysis
- Estimated median duration of response (DOR) was 26.1 months (central review) and 15.7 months (investigator review).
- The median progression-free survival (PFS) was 22.1 months per central review and 19.4 months per investigator review.
- Six (9.1%) patients with laBCC died within the 42-month analysis, none were suspected to be related to the study drug. Median overall survival (OS) was non-estimable, with 90.9% of patients censored. The estimated 12-month survival rate was 100%.

Safety

The safety profile of sonidegib 200 mg in patients with laBCC has been well characterized in the phase II, randomized double-blind study (BOLT). Overall, AE results suggest that sonidegib is associated with an acceptable and manageable safety profile in the intended target population. The AE profile is characterized by predictable, primarily low-grade events. These events are generally reversible and noncumulative[1]. The percentage of grade 3-4 adverse events was 43% after 42-month analysis of which 32% were related to the treatment. However, discontinuations due to adverse events were low in the BOLT study

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

5 patients

Consequences for resource use in the public health service

None

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

N/A

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):

BOLT

Migden MR, Guminski A, Gutzmer R, Dirix L, Lewis KD, Combemale P, Herd RM, Kudchadkar R, Trefzer U, Gogov S, Pallaud C, Yi T, Mone M, Kaatz M, Loquai C, Stratigos AJ, Schulze HJ, Plummer R, Chang AL, Cornélis F, Lear JT, Sellami D, Dummer R. Treatment with two different doses of sonidegib in patients with locally advanced or metastatic basal cell carcinoma (BOLT): a multicentre, randomised, double-blind phase 2 trial. Lancet Oncol. 2015 Jun;16(6):716-28. doi: 10.1016/S1470-2045(15)70100-2. Epub 2015 May 14.

Dummer R, Guminski A, Gutzmer R, Dirix L, Lewis KD, Combemale P, Herd RM, Kaatz M, Loquai C, Stratigos AJ, Schulze HJ, Plummer R, Gogov S, Pallaud C, Yi T, Mone M, Chang AL, Cornélis F, Kudchadkar R, Trefzer U, Lear JT, Sellami D, Migden MR. The 12-month analysis from Basal Cell Carcinoma Outcomes with LDE225 Treatment (BOLT): A phase II, randomized, double-blind study of sonidegib in patients with advanced basal cell carcinoma. J Am Acad Dermatol. 2016 Jul;75(1):113-125.e5. doi: 10.1016/j.jaad.2016.02.1226. Epub 2016 Apr 7. PMID: 27067394.

Lear JT, Migden MR, Lewis KD, Chang ALS, Guminski A, Gutzmer R, Dirix L, Combemale P, Stratigos A, Plummer R, Castro H, Yi T, Mone M, Zhou J, Trefzer U, Kaatz M, Loquai C, Kudchadkar R, Sellami D, Dummer R. Long-term efficacy and safety of sonidegib in patients with locally advanced and metastatic basal cell carcinoma: 30-month analysis of the randomized phase 2 BOLT study. J Eur Acad Dermatol Venereol. 2018 Mar;32(3):372-381. doi: 10.1111/jdv.14542. Epub 2017 Nov 6.

Dummer R, Guminski A, Gutzmer R, Lear JT, Lewis KD, Chang ALS, Combemale P, Dirix L,Kaatz M, Kudchadkar R, Loquai C, Plummer R, Schulze HJ, Stratigos AJ, Trefzer U, Squittieri N, Migden MR. Long-term efficacy and safety of sonidegib in patients with advanced basal cell carcinoma: 42-month analysis of the phase II randomized, double-blind BOLT study. BJD. Volume 182, issue 6, June 2019

ERIVANCE

Sekulic A, Migden MR, Oro AE, Dirix L, Lewis KD, Hainsworth JD, et al. Efficacy and safety of vismodegib in advanced basal-cell carcinoma. N Engl J Med. 2012a;366(23):2171-9.

Sekulic A, Migden MR, Lewis K, Hainsworth JD, Solomon JA, Yoo S, Arron ST, Friedlander PA, Marmur E, Rudin CM, Chang AL, Dirix L, Hou J, Yue H, Hauschild A; ERIVANCE BCC investigators. Pivotal ERIVANCE basal cell carcinoma (BCC) study: 12-month update of efficacy and safety of vismodegib in advanced BCC. J Am Acad Dermatol. 2015 Jun;72(6):1021-6.e8. doi: 10.1016/j.jaad.2015.03.021. PMID: 25981002.

Sekulic, A., Migden, M. R., Basset-Seguin, N., Garbe, C., Gesierich, A., Lao. Long-term safety and efficacy of vismodegib in patients with advanced basal cell carcinoma: final update of the pivotal ERIVANCE BCC study. BMC Cancer, 17(1), 332.

Indirect comparisons

Odom D, Mladsi D, Purser M and Kaye J. A Matching-Adjusted Indirect Comparison of Sonidegib and Vismodegib in Advanced Basal Cell Carcinoma. Journal of Skin Cancer 2017(5, article ab137):1-7. 9, 53, 55, 103

Dummer R, Ascierto PA, Basset-Seguin N, Dreno B, Garbe C, Gutzmer R, et al. Sonidegib and vismodegib in the treatment of patients with locally advanced basal cell carcinoma: a joint expert opinion. J Eur Acad Dermatol Venereol (2020)

European treatment guidelines

Peris K, Fargnoli MC, Garbe C, Kaufmann R, Bastholt L, Seguin NB, Bataille V, Marmol VD, Dummer R, Harwood CA, Hauschild A, Höller C, Haedersdal M, Malvehy J, Middleton MR, Morton CA, Nagore E, Stratigos AJ, Szeimies RM, Tagliaferri L, Trakatelli M, Zalaudek I, Eggermont A, Grob JJ; European Dermatology Forum (EDF), the European Association of Dermato-Oncology (EADO) and the European Organization for Research and Treatment of Cancer (EORTC). Diagnosis and treatme,t of basal cell carcinoma. European consensus-based interdisciplinary guidelines. Eur J Cancer. 2019 Sep;118:10-34.

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

Sun pharma

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

Marketing Authorization was granted 2015-08-17

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

Despite the approval and launch of vismodegib, unmet treatment needs remain for patients with laBCC. Vismodegib demonstrated an Objective Response Rate (ORR) of 47.6% in patients with laBCC. In addition, there are safety concerns associated with the use of vismodegib. The efficacy profile of sonidegib is at least non-inferior to vismodegib with significantly improved safety. Sonidegib also is the first HHI to report QoL data, with over 80% of patients showing maintenance or improvement in QoL via EORTC QLQ-C30 as well as EORTC-H&N35 criteria. Because of the longer response duration of treatment with sonedigib vs. vismodegib, and because the benefits of the treatment may last longer after treatment discontinuation, the sonedigib label provides the opportunity to reduce the frequency of administration from once daily to once every two weeks. This can help physicians better manage the side effect associated with the HHI treatment and lower the overall treatment cost. Therefore, sonedigib provides an additional treatment option for HCPs and patients with a strong efficacy/safety profile and improved QoL.

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)

None