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)**:**

Unimedic Pharma AB

Name of proposal contact:

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Date and locality:

2023-04-05 Solna

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

"Espranor (buprenorphine) freeze dried tablet for opioid maintenance therapy.

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

Espranor oral lyophilisate is a freeze-dried buprenorphine wafer which disperses very rapidly - 15 to 30 seconds - on the tongue. It is indicated as a substitution treatment for opioid drug dependence within a framework of medical, social and psychological treatment. It is intended for use in adults and adolescents aged 15 years and above.

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?

An opioid maintenance treatment (OMT) programme represents an opportunity for opioid dependent individuals to minimize the many negative health and societal outcomes associated with opioid use through meeting the physiological need of their bodies for opioids. In Norway, substitution treatment for opioid addiction was implemented in 1998, and has existed in its current form since 2001 (Granerud and Toft 2015).

OMT in Norway is a cooperation between the three parties – municipal social services, the patient's physician, and the specialist healthcare. When the patient is stabilized and is functioning well, most of the responsibility should be at the municipal level. The regional health authorities are responsible for providing interdisciplinary specialized treatment (IST). In 2019 treatment was mainly anchored in the IST (69,6%), and municipalities had the responsibility of the follow up of 29,4% of the patients, and for 1% the responsibility was anchored elsewhere.

31.December 2021, there were 8 198 persons in OMT programs in Norway. That is an increase of 99 patients from 2020 (Bech et al 2022).

Patients on OMT from the eastern part of Norway is primarily treated with methadone, whereas the remainder of the country is treated with primarily buprenorphine or combination treatment of buprenorphine/naloxone. This is partly explained from a historic perspective, as the areas which initiated treatment in the 1990s began treatment with methadone will still have a considerable portion of the population on methadone, whereas buprenorphine or combination treatment first became available in 2002 (Lobmaier et al. 2020).

Buprenorphine mono products' share of the market is steadily increasing. In 2015 buprenorphine's share of the market was 35% while it was 45% in 2020. It's share of the market for mono products (buprenorphine and methadone) increased from 46%, to 54% in the same period of time. Buprenorphine combination products is steadily declining, it's market share is reduced from 25% in 2015 to 14% in 2020 according to numbers from the Norwegian Prescription Database.

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	☐	☒

Any comments on the use of the method:

Buprenorhpine is a well-known compound used in OMT. However, in patients who require supervised consumption of buprenorphine, the oral lyophilisate formulation has the advantage of a faster dissolution time compared to other available buprenorphine preparations, and thereby reduced potential for misuse or leakage (Lyseng-Williamson 2017). Strang et al (2017) compared the oral lyophilisate formulation with sublingual buprenorphine and reported that the median time for tablets to completely disintegrate was 2.0 min for the lyophilizate formulation versus 10 min for sublingual buprenorphine ($p < 0.0001$). Furthermore, partial or complete disintegration at 15 s happened in 96,3% of lyophilizate formulations versus 71,8% in sublingual formulations.

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	☒

OMT in Norway is a cooperation between the three parties – municipal social services, the patient's physician, and the specialist healthcare.

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?	☒	☐

OMT is financed by specialized health services in Norway.

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

Yes	No
☒	☐

Nasjonal faglig retningslinje: Legemiddelassistert rehabilitering (LAR) ved opioidavhengighet.

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)?)

OMT in Norway is a cooperation between the three parties – municipal social services, the patient's physician, and the specialist healthcare. When the patient is stabilized and is functioning well, most of the responsibility should be at the municipal level. The regional health authorities are responsible for providing interdisciplinary specialized treatment (IST). In 2021 treatment was mainly anchored in the IST (73%), and municipalities had the responsibility of the follow up of 26% of the patients, and for 1% the responsibility was anchored elsewhere (Bech et al 2022). Also pharmacies in Norway are supporting supervised administration of addiction drugs.

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: Patients with opioid addiction who are treated with buprenorphine or methadone, exceptionally levomethadone or long-acting morphine as a drug in substitution treatment.

I: Fixed or flexible maintenance dose determined after individual assessment with the oral lyophilisate formulation.

C: Fixed or flexible maintenance dose determined after individual assessment with the sublingual formulation and implant and depot formulations.

O: Reduced misuse potential.

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

Approximately 40% of all persons in OMT-programs in Norway use ibuprofen monoproducts. The abuse potential of oral buprehorphin monoproducts is so high that they were suggested to be prohibited by the "side effect board" (bivirkningsnemda) in 2014 (Aftenposten, November 8th 2018) . An oral formulation with less abuse potential will therefore mitigate abuse potential.

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:

Severity has not been calculated in previous buprenorphine submissions.

Expected effect

Less abuse of oral buprenorphine. Wider use of oral buprenorphine.

Safety

The safety profile of Espranor is consistent with the safety profiles of that of other formulations of buprenorphine. The most common side effects are insomnia, headache, constipation, nausea, hyperhidrosis and drug withdrawal symptoms.

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

It is very difficult to foresee how many patients will be using Espranor. In the Buvidal report it was assumed that approximately 1/3 of those using oral buprenorphine, mono and in combination with Naloxone would be using Buvidal. Unimedic Pharma assumes that as many as 1/3 of patients will be using Espranor in year 5 after launch. The sales since 2017 on non-licensed Espranor indicates an established medical need.

Consequences for resource use in the public health service

Less abuse, wider use of oral buprenorphine, easier control, less time for supervised administration.

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

It is not assumed that national guidelines need to be revised because of Espranor.

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):

Lyseng-Williamson, K. A. (2017). Buprenorphine oral lyophilisate (Espranor®) in the substitution treatment of opioid dependence: a profile of its use. *Drugs & Therapy Perspectives*, *33*(6), 241-248.

Strang, John, et al. "Randomised Comparison of a Novel Buprenorphine Oral Lyophilisate versus Existing Buprenorphine Sublingual Tablets in Opioid-Dependent Patients: A First-in-Patient Phase II Randomised Open Label Safety Study." *European Addiction Research*, vol. 23, no. 2, 2017, pp. 61–70.

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

Unimedic Pharma AB will market the drug in Norway as local representative.

Marketing authorization holder is Ethypharm France

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

The consolidated dossiers for the update of the Assessment Report of Espranor 2mg and 8mg oral lyophilizate (PA22617/001/002-3), prior to the start of the Repeat Use Procedure (repeat DCP), was submitted to Health Products Regulatory Authority Dublin, Ireland on February 23rd this year.
Proposed Concerned Member State: Norway.

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

Other publications referenced in this document.

- Granerud, A., & Toft, H. (2015). *Opioid dependency rehabilitation with the opioid maintenance treatment programme - a qualitative study from the clients' perspective.* Substance abuse treatment, prevention, and policy, 10, 35
- Legemiddelverket 2018. *ID2018_108 Buprenorfin depotinjeksjon (Buvidal) til behandling av opioidavhengighet*
- Bech et al 2022. *SERAF RAPPORT 2/2022*
- Lobmaier, P., Skeie, I., Waal, H., et al. (2020*). SERAF Rapport 1/2020. Statusrapport 2019*.

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)

Magnus Ivarsson is Head of Market Access and Governmental affairs in Unimedic Pharma who has a commercial interest in marketing the product in Norway.