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)**:**

Indivior Europe LTD

Name of proposal contact:

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Date and locality:

2019-03-22 Landskrona

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

Buprenorphine depot for the treatment of opioid dependence

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

Buprenorphine in ATRIGEL® delivery system

Biodegradable polymer and solvent create a solid depot of buprenorphine

Prefilled syringe administered subcutaneously

Each 0,5 ml solution for injection in pre-filled syringe contains 100 mg buprenorphine (as buprenorphine base). Each 1,5 ml solution for injection in pre-filled syringe contains 300 mg buprenorphine (as buprenorphine base).

Depot formulation is a common way to administer drugs for several indications and conditions (e.g. schizophrenia, pain, vaccines). Buprenorphine/buprenorphine+naloxone has been on the Norwegian market since many years.
The depot formulation is not a new technology but rather a new administrative form of an established treatment

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 of care (SOC) for treatment of opioid dependence in Norway varies considerably depending on patients' needs and goals, although all treatment has a common objective of reducing the risk of death and ill health due to the opioid dependence. As part of treatment, which typically also involves a framework of medical, social and psychological care, the following opioid substitution medicines may be administrated:

- Sublingual buprenorphine (various products, generic and branded)
- Sublingual buprenorphine (generic and branded)
- Oral methadone (various products, generic and branded)

The proposed technology will represent an alternative to three medicines above. The most relevant comparator is sublingual buprenorphine/naloxone, as this formulation of buprenorphine is recommended by Statens Legemiddelverk for first-line use, to reduce risk of diversion and misuse.

The patient profile for this formulation will be same as for tablets. There will be benefits vs tablets for patients (less stigma, reduce risk of diversion and misuse and no daily supervision of the drug intake). The cost for specialist health services/HF will be reduce due to no daily supervision.

4. This proposal concerns:

	Yes	No
A brand new and innovative health technology	☐	☐
A new 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	☐	☐

The depot formulation is not a new technology but rather a new administrative form of an established treatment

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	☐

The product will be administered by a health care professional

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?	☒	☐

Treatment of opioid dependence is funded through regional hospital healthcare budgets, HF.

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

Yes	No
☒	☐

National guidelines on the treatment of opioid dependence are currently under review. Depot formulation is expected to be part of the new guidelines

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)?)

The health technology is used in addiction medicine, a multidisciplinary field involving psychiatry, social work and pharmacology. The technology has implications for delivery of therapy as, unlike oral and sublingual products, there is no requirement for daily dosing (which in some cases is supervised)

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.

Patient: Patients requiring treatment for opioid drug dependence

Intervention: RBP- 6000 depot buprenorphine

Comparator: Sublingual buprenorphine/naloxone (Suboxone) suggested due to its relevance to the prevention of diversion and misuse

Outcome: Urine samples negative for illicit opioids (i.e. illicit opioids used "on top" of prescribed opioid dependence therapy), overall median cumulative percent negative urine samples, retention in treatment, resource use associated with administration and supervision of consumption of the intervention and comparator.

The depot formulation is not a new technology but rather a new administrative form of an established treatment. The patient profile for this formulation will be the same as for tablets. There will be benefits vs tablets for patients (less stigma, reduce risk of diversion and misuse and no daily supervision of the drug intake). The cost for HF will be reduced due to no daily supervision.

A Cost minimization model and a "forenklet metodevurdering" would be relevant for this depot formulation.

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

RBP- 6000 represents a major innovation in opioid dependence treatment. It has a unique potential to eliminate the potential for buprenorphine diversion and misuse, a major concern for health authorities in Norway.

The Suboxone formulation has potential to deter misuse and thereby reduce its value on the illegal market. However, preventing the misuse and trade of buprenorphine products on the illegal market remain a high priority. Consequently, the administration of sublingual buprenorphine products continues to be frequently supervised.

RBP-6000 is administered monthly by a healthcare professional and cannot be diverted or misused at the point of administration. It also affords potential savings to the healthcare service because unlike sublingual formulations, RBP-6000 does not require daily supervision.

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

Opioid dependence is a potentially fatal condition which has profound impacts for the patient and the society in which they live. Aside from the risk of fatal overdose, long-term addiction to opioids can increase an individual´s risk of comorbidities, greatly increasing their likelihood of premature death (e.g. due to respiratory or liver diseases) as well as their burden to the health care sector, families and the community. The impact on wider society is also severe, due to drug-related crime, acquisitive crimes committed to fund the drug use.

Expected effect

RBP-6000 has a potential to generate resource savings and free up health services capacity and therefore will have benefits for the LAR clinic sector.

For patients, RBP-6000 represents an opportunity to stop having daily (usually supervised) opioid maintenance treatment. This has potential to remove the psychological impact, stigma and disruption of visiting addiction clinics on a regular basis and would remove the daily reminder to patients of their condition and risk of returning to use illicit opioids.

For wider society, sustained treatment retention and reduced levels of “on-top” illicit opioid use have a proven impact on the level of crime committed. Further, successful management of opioid dependence will reduce patients ‘future morbidity and their burden on the public sector including healthcare.

Safety

Summary of the safety profile The most common side effects reported during the pivotal clinical studies with RBP-6000 were those related to withdrawal symptoms (eg insomnia, headache, nausea and hyperhidrosis) and injection site pain. The frequency of adverse reactions observed during the pivotal clinical studies with RBP-6000 was consistent with those reported with SUBUTEX, except for injection site reactions (eg erythema, induration, pain and pruritus）.

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

Relevant for the existing patients in “LAR” treatment. The licensed indication for RBP-6000 does not limit usage to any one subpopulation of patients with opioid dependence.

Consequences for resource use in the public health service

The RBP-6000 product is expected to result in savings in supervision costs.

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

National guidelines for opioid dependence treatment are currently under revision. A new guideline is expected to include depot formulation as this is requested by the LAR services to reduce administration costs and improve patient satisfaction.

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):

Height B, Learned S, Laffont C, Fudala P, Zhao Y, Garofalo A. Efficay and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicenter, randomized, double-blind, placebo-controlled, phase 3 trial. Lancet 2019 Feb:778-90.

Nasser AF, Greenwald MK, Vince B, Fudala PJ, Twumasi-Ankrah P, Liu Y, Jones JP 3rd, Heidbreder C.Sustained-Release Buprenorphine (RBP-6000) Blocks the Effects of Opioid Challenge With Hydromorphone in Subjects With Opioid Use Disorder. J Clin Psychopharmacol. 2016 Feb;36(1):18-26.

Laffont CM[1], Gomeni R[2], Heidbreder C[1], Jones JP 3rd[1], Nasser AF.Population Pharmacokinetic Modeling After Repeated Administrations of RBP-6000, a New, Subcutaneously Injectable, Long-Acting, Sustained-Release Formulation of Buprenorphine, for the Treatment of Opioid Use Disorder. J Clin Pharmacol. 2016 Jul;56(7):806-15

Ling W1, Nadipelli VR, Solem CT, Ronquest NA, Yeh YC, Learned SM, Mehra V, Heidbreder C. Patient-centered Outcomes in Participants of a Buprenorphine Monthly Depot (BUP-XR) Double-blind, Placebo-controlled, Multicenter, Phase 3 Study. J Addict Med. 2019 Mar 4. doi: 10.1097/ADM.0000000000000517. [Epub ahead of print]

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

Indivior Europe LTD

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

If the application for MA is approved and a license issued, the MA numbers will be as follows:

18 -12593 (100mg) – approx. (25/03/2020)

19-12682 (300mg) - approx. (25/03/2020)

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

The depot formulation is not a new technology but rather a new administrative form of an established treatment. The patient profile for this formulation will be the same as for tablets. There will be benefits vs tablets for patients (less stigma, reduce risk of diversion and misuse and no daily supervision of the drug intake). The cost for HF will be reduced due to no daily supervision.

A Cost minimization model and a “forenklet metodevurdering” would be relevant for this depot formulation.

We have established a dialog with Sykehusinnkjop and it is our understanding that they are both positive to the introduction of depot formulation in Norway and that a Cost minimization model/BIM and a “forenklet metodevurdering is sufficient.

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)

Indivior Europe LTD will be the marketing authorization holder of the RBP-6000 depot buprenorphine product.