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)**:**

Camurus AB

Name of proposal contact:

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Date and locality:

Cambridge, 18/9/2018

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:

Prolonged-release solution for subcutaneous injection in a pre-filled syringe (PFS) with a 12.5mm, 23G needle. The BD UltraSafe Plus™ Passive Needle Guard is a single-use cover intended to be extended over a used needle (attached to a prefilled syringe) to prevent accidental needle sticks. Please see Figure below.

Pictured are q1w PFS syringes in following dose strengths (left to right):

- 8 mg buprenorphine/0.16 ml
- 16 mg buprenorphine/0.32 ml
- 24 mg buprenorphine 0.48 ml
- 32 mg buprenorphine/0.64 ml

List of all strengths and durations available:

CAM2038 50 mg/mL q1w SC BPN FluidCrystal® injection depot PFS:

- 8 mg buprenorphine/0.16 ml
- 16 mg buprenorphine/0.32 ml
- 24 mg buprenorphine 0.48 ml
- 32 mg buprenorphine/0.64 ml

CAM2038 356 mg/mL q4w SC BPN FluidCrystal® injection depot PFS:

- 64 mg buprenorphine/0.18 ml
- 96 mg buprenorphine/0.27 ml
- 128 mg buprenorphine/0.36 ml

NOTES: SC, subcutaneous; BPN, buprenorphine; q1w, administered weekly; q4w, administered monthly;

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 the treatment, which typically also involves a framework of medical, social and psychological care, the following opioid substitution medicines may be administered:

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

The proposed technology will represent an alternative to the 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.

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	☐	☐

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

Pharmaceutical	☒
Medical device/IVD medical device that is CE-marked*	☐
Medical device/IVD medical device that is not CE-marked	☐

Procedure	☐
Screening	☐
Highly specialized services / national offers	☐
Organization of the health services	☐
Other (describe)	☐

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.

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.

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

Yes	No
☐	☒

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 addiction.

Intervention: CAM2038 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.

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

CAM2038 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.

Following a call from Bivirkningsnemnda to withdraw mono-buprenorphine from the Norwegian market, Statens Legemiddelsverket decided in 2014 to keep mono-buprenorphine on the market (in part to ensure access for pregnant and breastfeeding women) but recommended that Suboxone® (sublingual buprenorphine/naloxone) be used as the first-line buprenorphine formulation.

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.

CAM2038 is administered weekly or 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, CAM2038 does not require daily supervision. Furthermore, CAM2038 has demonstrated superiority in median cumulative percent of negative urine samples compared to sublingual buprenorphine/naloxone (Suboxone®) in a 24 week randomised controlled trial.

The potential impact of CAM2038 on the effectiveness, safety and cost-efficiency of opioid dependence treatment make this an important product for evaluation by the Decision Forum.

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 healthcare sector, families and the community. The impact on wider society is also severe, due to drug-related crime, in particular acquisitive crimes committed to fund the drug use.

Expected effect

The CAM2038 depot formulation will deliver clinically superior efficacy compared to Suboxone® in terms of urine samples negative for illicit opioids (see Lofwall 2018). It will have marked benefits for the LAR clinic sector, due to its potential to generate resource savings and free up resources to treat more patients, for example.

For patients, CAM2038 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 also 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. Furthermore, successful management of opioid dependence will reduce patients' future morbidity and their burden on the public sector including healthcare.

Safety

Safety profile is detailed in the CHMP assessment (published 21 September 2018).

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

The licensed indication for CAM2038 does not limit usage to any one subpopulation of patients with opioid dependence.

Consequences for resource use in the public health service

The CAM2038 product would result in an increase to medicine acquisition costs, but this would be offset by savings in supervision costs (which would otherwise be spent when supervising the dispensation and administration of Suboxone®).

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

National guidelines for opioid dependence treatment are currently under revision and Camurus will ensure that appropriate clinical evidence is submitted to the guideline development group.

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):

Albayaty M, Linden M, Olsson H, Johnsson M, Strandgården K, Tiberg F. Pharmacokinetic Evaluation of Once-Weekly and Once-Monthly Buprenorphine Subcutaneous Injection Depots (CAM2038) Versus Intravenous and Sublingual Buprenorphine in Healthy Volunteers Under Naltrexone Blockade: An Open-Label Phase 1 Study. Adv Ther. 2017 Feb;34(2):560-575. doi: 10.1007/s12325-016-0472-9. Epub 2017 Jan 9. PubMed PMID: 28070862.

Haasen C, Linden M, Tiberg F. Pharmacokinetics and pharmacodynamics of a buprenorphine subcutaneous depot formulation (CAM2038) for once-weekly dosing in patients with opioid use disorder. J Subst Abuse Treat. 2017 Jul;78:22-29. doi: 10.1016/j.jsat.2017.04.008. Epub 2017 Apr 14. PubMed PMID: 28554599.Walsh 2017

Lofwall MR, Walsh SL, Nunes EV, Bailey GL, Sigmon SC, Kampman KM, Frost M, Tiberg F, Linden M, Sheldon B, Oosman S, Peterson S, Chen M, Kim S. Weekly and Monthly Subcutaneous Buprenorphine Depot Formulations vs Daily Sublingual Buprenorphine With Naloxone for Treatment of Opioid Use Disorder: A Randomized Clinical Trial. JAMA Intern Med. 2018 Jun 1;178(6):764-773. doi: 10.1001/jamainternmed.2018.1052. PubMed PMID: 29799968.

Strang J, Dunlop A, Frost M, Lintzeris N, Nunes E, Bailey G, Billeskov Jansen J, Chemnitz Frey L, Weber B, Kim S, Tiberg F. Poster presentation. SSA (Society for the Study of Addiction): November 9-10, Newcastle, UK

Walsh SL, Comer SD, Lofwall MR, Vince B, Levy-Cooperman N, Kelsh D, Coe MA, Jones JD, Nuzzo PA, Tiberg F, Sheldon B, Kim S. Effect of Buprenorphine Weekly Depot (CAM2038) and Hydromorphone Blockade in Individuals With Opioid Use Disorder: A Randomized Clinical Trial. JAMA Psychiatry. 2017 Sep 1;74(9):894-902. doi: 10.1001/jamapsychiatry.2017.1874. PubMed PMID: 28655025; PubMed Central PMCID: PMC5710238

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

Camurus AB

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

EMA Marketing Authorisation has been applied for.

CHMP positive opinion granted 21/09/2018

Marketing Authorisation expected late November 2018

Product launch is expected in Q1 2019

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)

Camurus AB is the marketing authorization holder of the CAM2308 depot buprenorphine product.