Nye metoder: Innspill til metoder (forslag/metodevarsler/oppdrag)
Alle har anledning til å komme med tilleggsopplysninger til en metode som er foreslått for nasjonal metodevurdering. Det er ønskelig at innspill kommer inn så tidlig som mulig i prosessen, fortrinnsvis før behandling i Bestillerforum RHF.

Bruk dette skjemaet for å gi innspill til forslag, metodevarsler og oppdrag. På nyemetoder.no vil nye forslag/metodevarsler ha statusen «Forslag mottatt/åpent for innspill» før behandling i

Bestillerforum RHF. Utfylt skjema sendes nyemetoder@helse-sorost.no.

**NB**: **Punkt 1-3 og 11 fylles ut av alle.** Punkt 4-9 fylles ut avhengig av rolle og kjennskap til metoden.

**Jeg er klar over at skjemaet vil bli publisert i sin helhet på nyemetoder.no (kryss av): ☒**

Har du informasjon du mener ikke kan offentliggjøres, ta kontakt med sekretariatet før innsending**.**

**Jeg har fylt ut punkt 11 nedenfor «Interesser og eventuelle interessekonflikter» (kryss av): ☒**

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| 1.Hvilken metode gjelder innspillet?  |
| Metodens ID nummer\*: | ID2020\_097 |
| Metodens tittel: | Buprenorphine implant for substitution treatment of opioid dependence (Sixmo®) |

\*ID-nummer finner du på metodesiden på nyemetoder.no og har formen ID2020\_XXX

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| 2. Opplysninger om den som gir innspill  |
| Navn  | Kajsa Eriksson |
| Eventuell organisasjon/arbeidsplass | Accord Healthcare AB |
| Kontaktinformasjon (e-post / telefon) | kajsa\_eriksson@accord-healthcare.com+46 (0) 70 589 89 98 |

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| 3. Oppsummert innspill til metoden (besvares av alle) |
| Sixmo® is a subcutaneous implant that contains 74.2 mg of buprenorphine free base (equivalent to 80 mg of buprenorphine hydrochloride) as shown on the picture below (size of each implant 26 mm x 2.5 mm). The recommended dose consists of four implants inserted subcutaneously, representing a total of 320 mg of buprenorphine being implanted at once. Sixmo® implants are intended to be in place for 6 months of treatment and provide a sustained delivery of buprenorphine.[[1]](#endnote-1)Probuphine® Medically Assisted Treatment ImplantsBuprenorphine is an opioid partial agonist at the µ opioid receptor and an antagonist at the kappa receptor. Mixed agonist-antagonist activity and slow rates of opioid receptor association and dissociation result in prolonged pharmacodynamic activity and low dependence liability. As a partial µ receptor agonist with low intrinsic activity, buprenorphine exhibits a “ceiling effect” such that the opioid effects of buprenorphine plateau at higher doses.[[2]](#endnote-2)The adoption of the Pro Neura™ drug delivery system in Sixmo® delivers buprenorphine in a continuous release for up to six months, without the peak-and-trough levels that are associated with oral dosing.[[3]](#endnote-3)The Pro Neura™ technology consists in a matchstick sized solid rod made from a mixture of ethylene-vinyl acetate (EVA) and the drug substance.[[4]](#endnote-4) The resulting product is a solid matrix that is implanted subcutaneously, normally in the inner part of the arm with a simple surgical procedure and is removed in a similar way at the end of the treatment period.Sixmo® implants are intended to be in place for 6 months of treatment and provide a sustained delivery of buprenorphine. They are removed by the end of the sixth month. If continued treatment is desired at the end of the first six-month treatment cycle, a new set of 4 Sixmo® implants may be administered following removal of the old implants for one additional treatment cycle of six months.1 |

**Nærmere informasjon om metoden og innspill til PICO\***

\*PICO er et verktøy for å formulere presise problemstillinger i metodevurderingsarbeid. PICO er en forkortelse for Population/Problem – Intervention – Comparison – Outcome. PICO brukes til å presisere hvilken populasjon/problem som skal studeres, hvilke(t) tiltak (metode/behandling) som skal vurderes, hvilket tiltakdet er naturlig å sammenligne med, og hvilke utfall/endepunkter det ~~å~~ er relevant å måle/vurdere. PICO er viktig for planlegging og gjennomføring av en metodevurdering.

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| 4. Kjenner du til om metoden er i bruk i Norge i dag?  |
| Er metoden i bruk utenom kliniske studier i dag: NoFra hvilket tidspunkt har den vært i bruk: not applicableHvor er eventuelt metoden i bruk: Licensed in the USA and Canada |

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| 5. Hvilken pasientgruppe i den norske spesialisthelsetjenesten er metoden aktuell for? (PICO) |
| Beskriv kortfattet: Sixmo® is indicated for the substitution treatment for opioid dependence in clinically stable adult patients who require no more than 8 mg/day of sublingual buprenorphine, within a framework of medical, social and psychological treatment.1 |

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| 6. Er du kjent med behandlingsalternativer til denne metoden og hvordan disse fungerer for pasientgruppen i dag? (PICO) |
| Beskriv kortfattet:As part of the treatment, along with a framework of medical, social and psychological care, the following opioid substitution medicines may be administered for treatment of opioid use disorder: * Sublingual buprenorphine tablets
* Sublingual buprenorphine/naloxone tablets
* Oral methadone
* Subcutaneous buprenorphine depot injection

Treatment with sublingual buprenorphine or buprenorphine/naloxone can be associated with the following:* administration by the sublingual route requires good patient adherance, however patients who are having difficulty adhering to their buprenorphine can have their medication provided under directly observed therapy.[[5]](#endnote-5)
* Poor medication adherence is the leading cause of relapse and treatment failure[[6]](#endnote-6),[[7]](#endnote-7)
* poor medication adherence resulting in craving and withdrawal symptoms increased the likelyhood of a relapse[[8]](#endnote-8)
* the patient is in control of his/her dosing, and a conscious decision to discontinue buprenorphine treatment for the short term in anticipation of exposure to illicit drugs can easily occur (i.e., a “drug holiday”);7
* Buprenorphine plasma concentrations initially peak sharply and then decrease to the trough levels within 12-24 hours with each dose, potetially leading some patients to experience withdrawal symptoms between doses.3.
* Frequent visits to the clinic or pharmacy limit patients quality of life and opportunites to do normal things such as work, go to college, travel.[[9]](#endnote-9)
* Buprenorphine sublingual tablets can be diverted for illicit use or accidentally ingested after misidentification, leading to a growing public health issue.[[10]](#endnote-10). Accidental poisoning with available sublingual formulations of buprenorphine has occurred in adults and children.[[11]](#endnote-11),[[12]](#endnote-12)

These concerns highlight some of the limitations associated with oral buprenorphine preparations, and the opportunity for long-acting buprenorphine implants.  |

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| 7. Har du innspill til hva som vil være viktig for pasienter som er aktuelle for behandling med metoden? (PICO) |
| Hva kan oppfattes som en fordel for pasienter og brukere med denne metoden sammenlignet med aktuelle alternativer? Hvilke endepunkter/resultater av behandlingen er det aktuelt å måle? Beskriv kortfattet:Sixmo® represents a new therapeutic option that could address the limitations associted with current alternatives: * The 6-month treatment cycle will allow for long-term uninterrupted therapy.1
* The gradual release profile over time offers a lower degree of exposure to buprenorphine and substantially less variability in plasma levels of buprenorphine compared to sublingual buprenorphine.3
* The 6-month implant reduces the number of visits for patient and healthcare professional which are cumbersome.
* Implant formulation reduces the risk of diversion and misuse.
* Reduces the need for the patients to attend multicple clinic visits in a pandemic situation
* Implants are considered as the least stigmatising of all the given opioid substitution treatments considering they would be invisible to others once they have been admistered.8

**It is relevant to measure following outcomes:** evidence of illicit opioid use using self-reported outcomes and/or urine samples, retention in treatment, withdrawal symptoms or opioid cravings, resource use associated with administration and supervision of consumption of the intervention and comparator, quality of life due to reduced need to attend clinics on a daily basis. |

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| 8. Spesielt for medisinsk utstyr (besvares av leverandør): CE-merking |
| Foreligger det CE-merking for bruksområdet som beskrives i metoden? I så fall angi type og tidspunkt: Yes, Sixmo implants come with an applicator which is a class IIa device |

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| 9. Spesielt for legemidler (besvares av leverandør): Markedsføringstillatelse (MT) |
| Har legemiddelet MT for indikasjonen som omfattes av metoden? Angi i så fall tidspunkt eller ventet tidspunkt for MT:Marketing authorisation was granted by EMA on July 2019MA (EU) number: EU/1/19/1369/001 |

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| 10. Andre kommentarer |
| Additional risk minimisation measures (ARMM) requested in the EMA RMP will be implemented before Sixmo is launched. E.g. Live insertion and removal training technique will be provided before an HCP can administer Sixmo.All ARMM measures will be approved by the Norwegian medicines agency before it is launched in Norway.PASS (post-authorisation safety study) – mandatory data collection for safety aspects with regards to insertion and removal of implant, sponsored by marketing authorisation holder Molteni. |

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| **11. Interesser og eventuelle interessekonflikter**Beskriv dine relasjoner eller aktiviteter som kan påvirke, påvirkes av eller oppfattes av andre å ha betydning for den videre håndteringen av metoden som det gis innspill på (for eksempel: økonomiske interesser i saken, oppdrag eller andre bindinger). |
| Beskriv kortfattet: Accord Healthcare AB is the marketing and distribution partner for L. Molteni & C. dei Fratelli Alitti Società di Esercizio S.p.A., a marketing authorisation holder of Sixmo®.  |

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