Farmaceutisk bedömning/*Pharmaceutical assessment*

A. Väsentliga invändningar/*Major objections* Ja/*Yes* ☐ Nej/*No* ☐

Ej aktuellt

B. Kommentarer/*Comments* Ja/Yes ☐ Nej/No ☐

Ej aktuellt

Preklinisk bedömning/*Non-clinical assessment*

A. Väsentliga invändningar/*Major objections* Ja/*Yes* ☒ Nej/*No* ☐

1. In ”00 Notification form clinical investigation of medical devices_210219_3” the medical device to be investigated is “X-FLOW® Prostatectomy short catheter straight tip 3-way 30-50 ml silicone CH FR 2” from manufacturer Coloplast. However, in for example ” 04_Investigators_Brochure_Coloplast_balloon_catheter_modifiedID16FEB2021” (IB) and “02_OPTION_LMV_MPT_studieprotokoll_v5_210219” (CIP), it appears that the clinical investigation is also going to include Foley Catheter (general name for urinary catheters) and Cook® Cervical Ripening Balloon. These names are used interchangeable, which makes it difficult to follow when and how X-FLOW, Foley (potentially any urinary catheter) and or Cook catheter are going to be used. Please, clarify and update to make documentation coherent regarding the investigational product/products.

2. The IFU in Annex 1 IB do not comply with requirements in point 13.6 Annex 1 LVFS 2002:11. The IFU in Annex 1 does for example lack information about manufacturer. In addition, the IFU is about Foley catheter in general, there is no information about “X-FLOW® Prostatectomy short catheter straight tip 3-way 30-50 ml silicone CH FR 2”. Please provide updated IFU for X-FLOW® Prostatectomy short catheter straight tip 3-way 30-50 ml silicone CH FR 2.

3. The Swedish IFU (Bruksanvisning Svenska _210226) does not comply with point 13.6 Annex 1 LVFS 2003:11. The IFU does for example lack information about sponsor or manufacturer and their contact details. Please update the IFU according to point 13.6 Annex LVFS 2003:11.

4. To confirm CE-marking of “X-FLOW® Prostatectomy short catheter straight tip 3-way 30-50 ml silicone CH FR 2”, please provide copy of declaration of conformity.

B. Kommentarer/*Comments* Ja/*Yes* ☒ Nej/*No* ☐

1. There appear to be no planned tests and follow up studies on the actual product. To facilitate future CE-marking of device for the intended purpose of Labour induction in an outpatient setting, we highly recommend that sponsor communicate with manufacturer to add appropriate tests in this study on the investigational product. For example, data can be collected to mitigate suggested action for hazard number 10404 and 10405 “Simulation of product use” in risk analysis, Annex 4 IB.

2. It is unclear which new product specifications are required to meet new intended purpose. The documentation would gain by a summary of this and how these new specifications have been verified and validated. The documentation would also benefit by a summary table on how each applicable requirement in Annex I LVFS 2003:11 has been addressed.

Statistisk bedömning/*Statistical assessment*

A. Väsentliga invändningar/*Major objections* Ja/*Yes* ☐ Nej/*No* ☒

B. Kommentarer/*Comments* Ja/*Yes* ☐ Nej/*No* ☒

Klinisk bedömning / *Clinical assessment*

A. Väsentliga invändningar/*Major objections* Ja/*Yes* ☐ Nej/*No* ☒

B. Kommentarer/*Comments* Ja/*Yes* ☐ Nej/*No* ☒

Medicinteknisk bedöming / *Medical Technical assessment*

A. Väsentliga invändningar/*Major objections* Ja/*Yes* ☒ Nej/*No* ☐

The Medical Device Unit of the Medical Products Agency (MPA) has assessed sponsor´s notification documentation in accordance with Läkemedelsverkets föreskrifter (LVFS 2003:11) om medicintekniska produkter, SS-EN ISO 14155:2011 Clinical investigation of medical devices for human subjects – Good clinical practice, other relevant standards, relevant guidelines, and the Declaration of Helsinki.
The Medical Device Unit have identified the following issues, which need to be addressed:

Nomenclature

1. Good clinical practice assumes stringent instructions, for patient safety and to avoid unnecessary study deviations. The investigational product is called Coloplast (as in p.13), Coloplast (AB6H22) (as in p.17), Coloplast X-FLOW® Prostatectomy short catheter straight tip 3-way 30-50 ml silicone CH FR 22 REF. AB6H22. (as in p.36), X-FLOW® Prostatectomy short catheter straight tip 3-way 30-50 ml silicone CH FR 22 (REF. AB6H22) (as in p.33), Balloon (as in p.47) and Foley catheter (as in p.49).
   The Cook device have five variant names, but they all start with "Cook" and therefore may be acceptable.
   The word "balloon" is used for the investigational product (as in p.47), the balloon part of the catheter (as in p.22) and for balloon catheter (as in p.22).
   Sponsor is expected to revise the study protocol to achieve a better consensus in naming the investigational product.

Concerning labelling (section 5.10 in ISO 14155:2011 and LVFS 2003:11)

2. In section 7.1, under the headline "Märkningstext på svenska", there is a picture of a labelling sticker in English.
   In section 7.3 there is also a picture of a labelling sticker, with a different shape and another sponsor than in 7.1.
   Since the study is conducted in Sweden solely, the text "Endast för klinisk prövning" shall be used.
   Sponsor is requested to label the investigational product correct and harmonize the information in section 7.1 and 7.3.

Concerning amendments (section 6.5.1 in ISO 14155:2011)

3. In the study protocol, section 13, sponsor states the following:" A change that concerns a new site, new investigator or a new study patient information sheet shall only be approved by EPM". In Sweden, such amendments to clinical investigations of medical devices need approval from the Medical Products Agency. Sponsor is expected to change section 13 concerning this.

Concerning reporting Serious Adverse Events (section 9.8 in ISO 14155:2011 and LVFS 2003:11)

4. In section 9 sponsor states "SAEs for the Foley catheter will be reported at:".
   In section 9.3.1 the correct and inclusive wording is used: "This is only for the events experienced by subjects induced by balloon catheter."

Sponsor is requested to change section 9 in the study protocol accordingly.

5. The hyperlink for reporting SAEs for the balloon catheter group in section 9 does not work.
   Sponsor is expected to update the hyperlink.

B. Kommentarer/*Comments* Ja/*Yes* ☒ Nej/*No* ☐

1. In section 7.1 sponsor states: “Angusta® will be ordered from the pharmacy and stickers will be attached by the pharmacy prior to distribution.” In section 7.3 sponsor states:”Angusta® will be ordered from the Pharmacy and stored according to the manufacturer. No sticker will be applied.”
   Will there be a sticker to Angusta?

2. In the Synopsis, page 17 sponsor states: “Up to eight doses of 25microgram misoprostol tablets taken orally no closer than 2 hours apart/24 hours, for a maximum of 2 days. Intake can be paused during the night. Intake can also start with 24 hours of Angusta® and then a switch to Foley catheter might be applicable.” Almost the same text is in section 7.1, but “Foley” is changed to “balloon”. The latter can also include the Cook device. A clarification or correction is suggested.

3. Consider adding IFU for Cook Cervical Ripening Balloon to section 9.7 in study protocol.

4. Consider harmonization naming of the investigational product in Bruksanvisning svenska_210226.

Regulatorisk bedömning/*Regulatory assessment*

A. Väsentliga invändningar/*Major objections* Ja/*Yes* ☒ Nej/*No* ☐

1. Försökspersonen behöver uttryckligen samtycka till att monitor och myndighetsrepresentanter får tillgång till journaluppgifter, vänligen uppdatera samtyckesformuläret (sidan 5) i ”Deltagarinformation till kvinnan, RCT” avseende detta.

B. Kommentarer/*Comments* Ja/*Yes* ☐ Nej/*No* ☒