LÄKEMEDELSVERKET
MEDICAL PRODUCTS AGENCY

Notification Form
Clinical Investigation of Medical Devices

This notification form is intended for clinical investigation of non-CE marked medical devices, or medical devices CE-marked for a different purpose than intended in the clinical investigation.

Send the completed form to the National Competent Authority (NCA) for medical devices
The content of fields with blue label will be uploaded into the Eudamed database for Clinical Investigation (CI) of medical devices.

1. Clinical investigation identification and status	
Submission type	NCA registration number (CA Reference), if applicable
First Submission	fill in text
Submission date	EUDAMED identification number, if applicable (CIV-YY-MM-XXXXXX)
2021-02-19	fill in Eudamed identification number (CIV-)
Has an application for clinical investigation of a **medicinal product** linked to this notification been submitted to the NCA or will it be submitted?	EudraCT number, if applicable
Yes	2020-000233-41
Title of the clinical investigation	Clinical investigation plan (CIP) code
OPTION – OutPatienT InductiON: Labour induction in an outpatient setting - a multicenter randomizedcontrolled trial.Labour induction in an outpatient setting - a multicenter randomized controlled trial.	OPTION
	Version and date of the CIP
	V5.0, 2021-02-19

2. Manufacturer		
Name Coloplast A/S		Contact for this Clinical investigation, name Fredrik Folcker
Street/road Kungsparksvägen 2	Number/house/floor fill in text	Phone 0721770825
Postal code 43439	City Kungsbacka	Fax fill in text
State/region fill in text	Country select country	E- mail sefrfo@coloplast.com

3. Authorised Representative within the EEA, if applicable		
Name fill in text		Contact for this Clinical investigation, name fill in text
Street/road fill in text	Number/house/floor fill in text	Phone fill in text

Postal code fill in text	City fill in text	Fax fill in text
State/region fill in text	Country select country	E- mail fill in text

4. Sponsor, according to the EN ISO 14155 definition, if other than manufacturer or authorised representative, if applicable:		
Name Sahlgrenska Universitetssjukhuset		Contact for this Clinical investigation, name Verena Sengpiel
Street/road Diagnosvägen 15	Number/house/floor fill in text	Phone 0046-31-3429242
Postal code 41650	City Gothenburg	Fax fill in text
State/region fill in text	Country Sweden	E- mail Verena.sengpiel@obgyn.gu.se

5. Medical device to be investigated	
Name of the medical device X-FLOW® Prostatectomy short catheter straight tip 3-way 30-50 ml silicone CH FR 22	Model or version AB6H22
Generic name of the medical device (if name not specified above) fill in text	GMDN code fill in text
Name used elsewhere to market same medical device fill in text	Other internationally recognized nomenclature fill in text
Is the medical device CE-marked for other use than intended for this CI? Yes	Class of device IIa - 93/42/EEC
Intended use of the medical device in the CI To induce labour by cervical ripening in women with low-risk pregnancies.	
Description of the medical device The prostatectomy catheters are intended to be placed in the urethra so that their balloon can be inflated (via a first lumen equipped with a non-return valve) in the prostatic cavity and/or the bladder, to stop bleedings at the end of the surgical operation. There is a wide range of prostatic catheters. However, Foley catheters of different kinds have been used for labour induction since the 1970s, the method is recommended by the WHO, several Cochrane reviews and obgyn societies around the world including the Swedish Society for obstetrics and gynecology SFOG. The procedure is used in daily routine in all Swedish delivery units and the X-FLOW® Prostatectomy short catheter straight tip 3-way 30-50 ml silicone CH FR 22 has been in use for the intended indication of labour induction at several Swedish delivery units during the last years.	
6. Additional information of the medical device to be investigated	
Is a medicinal product integrated with the medical device or shall a medicinal product act together with it?	No

Does the medical device incorporate, as an integral part, a human blood derivate?	No
Have tissues of animal origin been used in the manufacturing process?	No

7. Comparator medical device(s) (if applicable)	
Manufacturer Not applicable	GMDN code Not applicable
Name of the medical device, model or version Not applicable	Other nomenclature Not applicable
Product class	select class of device
Is the medical device CE-marked for the intended use in this CI?	select Yes / No
Is a medicinal product integrated with the medical device or shall a medicinal product act together with it?	select Yes / No

8. Clinical investigation

Primary objective The primary objective of the study is to show if outpatient induction is as safe and as affective as inpatient induction.	
Inclusion criteria	Exclusion criteria

Based on medical history: - women 18-45 years old - able to communicate with the hospital - uncomplicated live singleton pregnancy - pregnancy week >=37+0 to 41+6 according to crown rump length (CRL) or biparietal diameter (BPD<55 mm) at first or second trimester ultrasound - engaged and stable cephalic presentation Based on clinical examination before start of induction including Leopold´s manoeuvres, digital cervical exam, abdominal ultrasound, temperature, blood pressure and CTG scan: - engaged and stable cephalic presentation with - Bishop score <6 (<5 in parous women) - CTG classified as normal according to the antepartal Swedish Society of Obstetrics and Gynaecology (Svensk Förening för Obstetrik och Gynekologi, SFOG) criteria (www.ctgutbildning.se) Based on observation the first 45 min after start of induction - in case of induction with balloon method: CTG classified as normal according to the antepartal Swedish Society of Obstetrics and Gynaecology (Svensk Förening för Obstetrik och Gynekologi, SFOG) criteria (www.ctgutbildning.se)	Based on medical history: - previous uterine surgery with uterine scar, e.g. caesarean section or myomectomy - pregestational or medically treated gestational diabetes (insulin or metformin) - dietary treated gestational diabetes with large for gestational age foetus - preeclampsia or instable hypertensive disease - multiple pregnancy - intrauterine foetal death (IUFD) in current or previous pregnancy - known foetal malformations or other foetal condition affecting the delivery or immediate care of the new-born - congenital uterine malformation which may affect safety - other condition requiring inpatient care, e.g. delivery within 60 min from arriving at the hospital in previous pregnancy - not able to reach the hospital in a reasonable time, at the discretion of the investigator with a maximum of 60 min as a benchmark - known allergy to any component in the balloon catheter (for balloon catheter method) Based on clinical examination before start of induction including Leopold´s manoeuvres, digital cervical exam, abdominal ultrasound, temperature, blood pressure and CTG scan - Small for gestational age (SGA/IUGR/FGA) Screened for as follows depending on the indication for induction: 1. late term >=41+0 to 41+6 weeks: abdominal ultrasound will be performed and mean abdominal diameter (MAD) needs to be ≥110 mm In case MAD <110 mm, the foetal weight will be estimated to exclude SGA foetus defined as <2 standard deviation according to Marsal et al (32) 2. dietary treated gestational diabetes or stable hypertension: foetal weight estimated by abdominal ultrasound within the last two weeks before induction and showing no SGA defined as <2 standard deviation according to Marsal et al (32) 3. prolonged latent phase, maternal age, mild intrahepatic cholestasis, pelvic girdle pain, PROM, psychosocial: Normal fundal height measurement according to the Swedish reference curves is needed

		In case of not-normal fundal height measurement: foetal weight estimation must be performed and showing no SGA defined as <2 standard deviation according to Marsal et al (32) 4. Other indications: at the discretion of the investigator - Oligohydramniosis: deepest vertical pocket <20 mm or amniotic fluid index <50 mm - polyhydramniosis: if head not engaged or amniotic fluid index >300 mm - maternal pyrexia ≥38 degrees C - known low-lying placenta (less than 20 mm from internal os measured by vaginal ultrasound in week 36) - high head (≥4/5 palpable abdominally) Regarding premature rupture of membranes (PROM) - PROM is exclusion criteria for balloon method - PROM is exclusion criteria for prostaglandin method if: - PROM >30 hours - Known colonisation with group B streptococci or previous pregnancy complication linked to group B streptococci Based on observation the first 45 min after start of induction - any adverse events within the first 45 min after start of induction, e.g. heavy bleeding, pain, PROM in case PROM was not indication for induction of labour - start of contractions	
Planned total number of subjects involved	Planned number of subjects in the NCA state	Planned start date of CI	Planned completion date of CI
8891 (and 2119 women need to be randomized to each arm induced with either balloon catheter or prostaglandin)	8891 (and 2119 women need to be randomized to each arm induced with either balloon catheter or prostaglandin)	2021-04-01	2025-12-31

Planned states within EEA, Switzerland and Turkey for the CI

☐ Austria	☐ Greece	☐ Norway
☐ Belgium	☐ Hungary	☐ Poland
☐ Bulgaria	☐ Iceland	☐ Portugal
☐ Croatia	☐ Ireland	☐ Romania
☐ Cyprus	☐ Italy	☐ Slovakia
☐ Czech Republic	☐ Latvia	☐ Slovenia
☐ Denmark	☐ Liechtenstein	☐ Spain
☐ Estonia	☐ Lithuania	☒ Sweden
☐ Finland	☐ Luxembourg	☐ Switzerland
☐ France	☐ Malta	☐ Turkey
☐ Germany	☐ Netherlands	☐ United Kingdom

9. Clinical investigation – Design and additional information

Area of investigation

☐ Cardiology ☐ Surgery ☐ Orthopaedics ☐ Oncology ☐ Radiology ☒ Other

Secondary objective(s)
Summary of clinical investigation plan

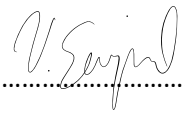
Objective: To evaluate if induction of labour in an outpatient setting is non-inferior to induction in hospital in a low-risk population regarding safety for the child as well as regarding efficacy, defined as proportion of women with vaginal delivery. Further pregnancy outcomes, the acceptability and experience of the woman, her partner and the staff, as well as future pregnancy outcome and health economic consequences will also be studied. Our hypothesis is that outpatient induction regardless of method (balloon catheter or oral misoprostol) is non-inferior to inpatient induction in low-risk women regarding the primary outcomes neonatal safety and efficacy.
Background: The recently published SWEdish Post term Induction Study (SWEPIS) (1) showed increased perinatal mortality when late term pregnancies were induced at 42+0 weeks – current routine in Sweden – instead of at 41+0 weeks. The Swedish Society for Obstetrics and Gynaecology now recommends that women should be allowed to choose themselves whether they want to be induced at 41+0 weeks (https://www.sfog.se/start/om-sfog/aktuellt/nya-sfog-raad-om-induktion-paa-grund-av-graviditetslaengd/). As 22% of all women are still undelivered at week 41+0, few delivery units are able to offer this change of routine within the current organization. When labour starts spontaneously, women usually stay at home during the phase of cervical ripening and are admitted to the hospital upon entering active labour. How to induce labour depends on the status of the cervix. When the cervix is ripe, labour can be induced by artificial rupture of the membranes. Otherwise induction needs to start with cervical ripening, either by inserting a balloon catheter or by the use of prostaglandins. Few and small studies have investigated if induction by cervical ripening could be performed in an outpatient setting. None of these studies were powered to study safety aspects of the rare outcome of perinatal or maternal death or severe morbidity. Nor were the studies sufficiently large or homogenous to allow for a meta-analysis of safety outcomes. Nevertheless, some hospitals in other Scandinavian countries have introduced outpatient induction in clinical routine during recent years, with balloon catheter as well as with prostaglandins. At these hospitals, 42-75% of all inductions begin as outpatient induction. As a consequence of the result from the SWEPIS trial, many clinics in Sweden are now turning to outpatient induction as a solution to the demand of extra inductions at 41+0 weeks. However, as studies published on outpatient induction are underpowered for efficacy and especially the rare outcome of maternal and perinatal death or severe morbidity, the number needed to treat by induction in week 41+0 could be in the same range as the number needed to harm by outpatient induction. Therefore, outpatient induction should only be introduced in Sweden in the context of a clinical multicentre study. Studies on women´s experiences of outpatient induction described that the home environment resulted in physical and emotional comfort, which improved their birth experiences. Sense of security in pregnancy, childbirth and the postnatal period can depend on multiple internal and external factors, which can differ between mothers and fathers. Midwives in Australia experienced the introduction of outpatient induction as feasible. To our knowledge, there are no studies of the partner's experiences of outpatient induction and no studies describing women's or healthcare staff experiences of outpatient induction in a Swedish setting.
Method: A national multicentre register-based parallel group randomized controlled trial (R-RCT) performed within the Swedish Network for clinical studies in Obstetrics and Gynaecology (SNAKS, www.snaks.se). The study will be run as an Register Randomised Controlled Trial (R-RCT) with randomization by the Swedish Pregnancy Register (SPR, www.graviditetsregistret.se) and data collection from SPR, the Swedish Neonatal Quality Register (SNQ, Svenskt neonatalt kvalitetsregister), the Swedish Ambulance Register, the Swedish Inpatient Register, the Cause of Death Register and Statistics Sweden (SCB). Secondary outcomes will also be collected from patient charts and in form of questionnaires based on validated instruments as well as interviews. The trial will be conducted according to Good Clinical Practice (GCP) and the International Conference on Harmonization (ICH) guidelines. Approval from the Swedish Medical Products Agency and the Swedish Ethical Review Authority will be in place before trial start. The trial will be reported according to the CONSORT guidelines. Eligible participants are healthy

women between greater than or equal to 37+0 and 41+6 gestational weeks with Bishop score <6 (<5 in parous women) planned for induction at one of the participating hospitals. Each centre will have a unique randomization list at a ratio of 1:1 with random permuted blocks. Randomization will be stratified for parity, indication for induction, and induction method. Women will have an abdominal palpation and ultrasound scan to exclude malpresentation and oligo- or polyhydramniosis, a cardiotocography (CTG), and a digital cervical exam to establish Bishop score prior to inclusion (as per clinical practice). Randomization will be performed by the attending physician, midwife or study coordinator. Randomization takes place in the hospital after examination of maternal and foetal well-being and screening of inclusion and exclusion criteria (establishment of eligibility). Randomization is not dependent of the method, which is decided upon clinical basis, but only affects outpatient or inpatient care. Blinding is not deemed feasible neither for the patient nor the investigator due to the character of the intervention (inpatient or outpatient care). During statistical analyses allocation will be blinded. Two primary outcomes have been defined: a composite outcome for neonatal morbidity and mortality as well as an efficacy outcome defined as proportion of women with a vaginal delivery. Further pregnancy outcomes, the acceptability and experience of the woman, her partner and the staff, as well as future pregnancy outcome and health care economics will also be studied. Non-inferiority will be tested with a two-sided 95% confidence interval and 80% power. Given 2.8% in outpatients and 2.3% in inpatients for the primary composite variable and a 5% drop-out rate, we need to randomize 8891 women in order to achieve a probability of greater than or equal to0.80 that the upper limit of a two-sided 95.7% confidence interval (CI) for the difference in primary outcome will be less than the non-inferiority margin 1.5%.

Controlled study?				Yes
If controlled	☒ Parallel groups		☐ Cross over	☐ Other
Randomization?				Yes
Masking	☒ Open	☐ Single blinded	☐ Double blinded	☒ Blinded evaluation
Gender				Women
Subjects <18 yrs?				Yes
If yes, which ages?				Unborn
Countries outside EEA, Switzerland and Turkey participating in the CI?				No
If yes, which?	fill in text			

10. Mandatory attachments	
Invoice documentation	Yes
Clinical Investigation Plan, CIP	Yes
Investigator's Brochure, IB	Yes
Copy of clinical investigation insurance policy covering the participating subjects	Yes
Subject information and consent form (in national language)	Yes
Copy of the opinion of the Ethics Committee if available	No
List of National investigations site(s), Clinical Investigator (s)	Yes
Qualifications of the principal investigator and one investigator per site	Yes
Declaration of conformity with Essential Requirements	Yes
11. Attachments, if not included in the IB, as applicable	
Results of risk analysis	select Yes / No

List of applied standards: Standards applied in full and description of deviations from applicable harmonised European standards.	No
Documentation on tissues of animal origin in the investigational device	No
Documentation on human blood derivate in the investigational device	No
Documentation on medicinal substances in the investigational device	No
Documentation of products/drugs/substances which the device under investigation will be used together / co-act / be compared with	No
Intended device labelling	No
Instructions for use to subjects (in national language) or professional users	Yes
Case Report Form (CRF)	No
Evaluation forms to be filled in by subjects or staff (in national language)	No
Copy of the application to the Ethics Committee	Yes

12. Signature	
Sponsor / Manufacturer / Authorized representative (if applicable)	I hereby certify that information provided in this notification is correct and I will see to that the investigation is carried out in accordance with the Declaration of Helsinki, applicable medical device directives, national regulations, EN ISO 14155 and the attached investigation plan. I keep available upon request documentation mentioned in annex 8 of directive 93/42/EEC and/or annex 6 of directive 90/385/EEC. Date and signature 2021-02-19  …… Name Verena Sengpiel