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Open-label, multicenter clinical study to evaluate the safety and efficacy of ULKOX® OLE vs SoC (e.g., cicatridinum ointment, ointment for anal fissures) in adult patients diagnosed with anal fissures

Submission date
17/01/2024

Recruitment status
No longer recruiting

Registration date
31/01/2024

Overall study status
Completed

Last Edited
20/11/2024

Condition category
Digestive System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
An anal fissure is a cut or split in the lining of the anal canal. They are the most common causes of severe anorectal pain. An acute anal fissure typically heals within 6 weeks with conservative treatment. Some disappear when constipation is treated. Anal fissures that last for 6 weeks or more are called chronic anal fissures. Chronic fissures develop ulceration Characteristic symptoms include tearing pain with defecation and blood on toilet paper. It has been estimated that anal fissure afflicts about 10% of patients attending colorectal clinics, with both sexes affected equally. Anal fissures are sometimes confused with haemorrhoids. These are inflamed blood vessels in, or just outside, the anus. Both fissures and haemorrhoids often result from passing hard stool. Fissures result from the stretching of the anal mucosa beyond its normal capacity. This often happens when stools are hard due to constipation. Once the tear happens, it leads to repeated injury. This leads to the development of a chronic anal fissure in about 40% of patients. The aim of this study is to evaluate how well ULKOX® OLE works in comparison with the Standard of Care (SoC), in this case cicatridinum ointment or any other ointment for anal fissures, in the treatment of adult patients diagnosed with anal fissures.
ULKOX®OLE is indicated for wound healing of full- and partial-thickness skin ulcers of different origins such as pressure ulcers, lower limb ulcers (venous ulcers), diabetic foot and anal fissures. For anal fissures It is recommended to make applications after bowel movements and personal grooming; as a rule, apply several times a day.

Who can participate?
Patients aged over 18 years with acute or chronic anal fissures prescribed treatment with ULKOX®OLE or with the standard of care (cicatridinum ointment or any other ointment for anal fissures)

What does the study involve?
Participants are treated with either standard of care (cicatridinum ointment or any other ointment for anal fissures) or with ULKOX®OLE. Each participant administered the prescribed treatment for 6 weeks, three times per day (morning, noon and evening). Each participant attended three visits during product administration to collect information related to the effects of the treatment. At the end of 6 weeks, each patient entered the post-treatment monitoring period until day sixty, which means that for another 18 days each patient was advised not to administer any treatment for anal fissures. The investigator reevaluated each patient on day 60. At the first visit each patient received a journal in which they indicated daily during the treatment their own perception of pain and discomfort. At each visit, each patient was examined to collect information on the following: weight, body mass index (BMI), abdominal girth, temperature, heartbeat, and the presence of bleeding. At the first and the third visit, each patient underwent a survey to evaluate the impact of the condition on the patient's quality of life before and after the treatment.

What are the possible benefits and risks of participating?
This product is expected to be beneficial for relieving anal fissures symptoms. Even if there are no benefits, the results of this study could help in discovering new ways to approach treatment for anal fissures. ULKOX OLE is a medical device with a CE mark used in relieving the clinical symptoms of anal fissures. There are no side effects known in ULKOX OLE administration.

Where is the study run from?
Noventure S.L. (Spain)

When is the study starting and how long is it expected to run for?
February 2022 to October 2022

Who is funding the study?
Noventure S.L. (Spain)

Who is the main contact?
Mrs Alina Iordache, alina.iordache@cebis-int.com

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Protocol serial number
CBSNOV08022022

Study information

Scientific Title
Comparative clinical study to evaluate the safety and utility of ULKOX® OLE in relieving the clinical symptoms of anal fissures in adult patients

Acronym
SECURE

Study objectives
An anal fissure is a cut or split in the epithelial lining of the anal canal distal to the dentate line. They are the most common causes of severe anorectal pain. A chronic anal fissure is usually categorized when the fissure fails to heal within 6 to 8 weeks. Chronic fissures develop ulceration and heaped-up edges with exposure of the internal anal sphincter fiber at the base of the ulcer. Characteristic symptoms include tearing pain with defecation and hematochezia that is usually present as blood on toilet paper. It has been estimated that anal fissure afflicts about 10% of patients attending colorectal clinics, with both sexes affected equally. Lateral internal sphincterotomy, while very effective, can cause faecal incontinence and chemical sphincterotomy by application of cream may have discouraging side effects and/or low efficacy. Anal fissures are sometimes confused with hemorrhoids. These are inflamed blood vessels in, or just outside, the anus. Both fissures and hemorrhoids often result from passing hard stool. Fissures result from the stretching of your anal mucosa beyond its normal capacity. This often happens when stools are hard due to constipation. Once the tear happens, it leads to repeated injury. The exposed internal sphincter muscle beneath the tear goes into spasm. This causes severe pain. The spasm also pulls the edges of the fissure apart, making it difficult for your wound to heal. The spasm then leads to further tearing of the mucosa when you have bowel movements. This cycle leads to the development of a chronic anal fissure in approximately 40% of patients. An acute anal fissure typically heals within 6 weeks with conservative treatment. Some disappear when constipation is treated. Anal fissures that last for 6 weeks or more are called chronic anal fissures. These fail conservative treatment and need a more aggressive, surgical approach. People whose anal fissures don’t heal well may have an imbalance in anal pressure that prevents blood from circulating normally through the blood vessels around the anus. The reduced blood flow prevents healing. Medicine, Botox injections, and even some topical treatments that improve blood flow, may help anal fissures heal.
The aim of this open-label, multicentre clinical study is to evaluate the safety and efficacy of ULKOX® OLE in adult patients diagnosed with anal fissures. ULKOX®OLE is indicated for wound healing of full and partial thickness skin ulcers of different origin such as pressure ulcers, lower limb ulcers (venous ulcers), diabetic foot and anal fissures. ULKOX® OLE can be used throughout the whole healing process. For skin ulcers it is recommended to be used at least three times per week coinciding with the regular cleaning of the ulcer and/or with the change of secondary dressing, if any, aiming to facilitate a favourable environment for the healing. For anal fissures It is recommended to make applications after bowel movements and personal grooming; as a rule, apply several times a day.

Ethics approval required

Ethics approval required

Ethics approval(s)
1. Approved 30/03/2022, National Bioethics Committee for Medicines and Medical Devices (19-20 Stefan cel Mare Street, Sector 2, Bucharest, 020125, Romania; +40 (0)21/210.28.80; comisia.bioetica@gmail.com), ref: 4DM

2. Approved 21/09/2022, The Ethics Committee for Clinical Trials (8, Damyan Gruev Street, Sofia, 1303, Bulgaria; +359 (0)2 8903435; delovodstvo@mh.government.bg), ref: ЕКК*И*/СТ-0858/21.09.2022

Primary study design
Interventional

Study design
Open-label multicenter comparative clinical study

Study type(s)
Safety, Efficacy

Health condition(s) or problem(s) studied
Anal fissures

Interventions
Participants fulfilling the inclusion criteria will be recruited by GP doctors or gastroenterologists. After signing the Informed Consent Form each participant will be evaluated for inclusion /exclusion criteria and assigned randomly to one of the study groups (Group A/Group B). Participants from one group will receive ULKOX® OLE and participants from the second group will receive SoC (e.g., cicatridinum ointment, ointment for anal fissures). The dosage schedule for the treatments will be according to the dosage and administration scheme. ULKOX® OLE and SoC will be administrated by topical route every day for 42 consecutive days. Each patient will attend four visits during product administration to collect information related to clinical efficacy and safety and will attend a follow-up visit on Day 60.

Intervention Type
Device

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
ULKOX® OLE

Primary outcome(s)
Efficacy of ULKOX® OLE will be evaluated by measuring time to complete healing – subjective evaluation through the patient journal on a daily basis for the first 7 days of the treatment phase (Bleeding Present/Absent), and then on a weekly basis until treatment end.

Key secondary outcome(s)
Effectiveness will be evaluated through:
1. Proportion of patients that experienced bleeding disappearance from Baseline to EOT (Day

42)
2. Time to pain reduction evaluated by a VAS scale from 1-10 - through the patient journal on a daily basis for the first 7 days of the treatment phase, and then on a weekly basis until treatment end.
3. Time to discomfort level reduction evaluated by a daily 7-point Likert scale (1 – Totally unacceptable, 2 – Unacceptable, 3 – Slightly unacceptable, 4 – Neutral, 5 – Slightly acceptable, 6 – Acceptable, 7 – Perfectly Acceptable) - through the patient journal on a weekly basis during the treatment phase (day 42)
4. Patient quality of life evaluated using SF-36 from baseline to visit 3 - EOT (Day 42)

Safety will be evaluated by:
1. Proportion of patients that experience adverse events (AEs) during the study period
2. Patients' participation withdrawal due to AE occurrence during the study period

Completion date
23/10/2022

Eligibility

Key inclusion criteria
1. Adult patients (aged >18 years)
2. Patients diagnosed with acute anal fissures or chronic anal fissures, with an acute episode
3. Treatment prescription decision (ULKOX® OLE or SoC) before participation invitation into the study
4. Willing to sign the Informed Consent form for data collecting and processing

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
60 Years

Sex
All

Key exclusion criteria
1. Unwillingness to provide signed Informed Consent for data collecting
2. Other medical condition that does not allow participation in this study (e.g., immunodeficiency patients, patients that are administering blood pressure medication that can determine relax the anal sphincter – e.g., calcium channel blockers)
3. Patients that receive as Standard of Care a drug treatment

4. Pregnancy and breastfeeding patients
5. Administration of medication/treatments that could have the same effect as the study proposed treatment (e.g., nitroglycerin, lidocaine hydrochloride, botulinum toxin, nifedipine, diltiazem)
6. Hypersensitivity or individual allergy to one or more components of the product

Date of first enrolment
15/06/2022

Date of final enrolment
23/10/2022

Locations

Countries of recruitment
Bulgaria

Romania

Study participating centre
Ambulatory Practice for Primary Medical Care Dr. Elenski EOOD
23 Petko D. Petkov Street
Plovdiv
Bulgaria
4000

Study participating centre
Medical center Prolet EOOD
25 Olimpi Panov Street, fl. 2
Ruse
Bulgaria
7000

Study participating centre
Ambulatory Practice for Primary Outpatient Medical Care SANA OOD
8 Akademic Stefan Mladenov Street
Sofia
Bulgaria
1700

Study participating centre
Medical center Prolet EOOD
25 Olimpi Panov Street, fl. 2

Ruse
Bulgaria
7000

Study participating centre
Clinica Medicala Endodigest
5, Olimpiadei Street
Bucharest
Romania
410151

Sponsor information

Organisation
Noventure S.L.

Funder(s)

Funder type
Industry

Funder Name
Noventure S.L.

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		11/03/2024	20/11/2024	Yes	No