PUBLIC STUDY PROTOCOL

A Comparative Study Between Proctofiz MD and Topical Nifedipine for the Treatment of Chronic Anal Fissure

A single-centre, prospective, randomized, double-blind, parallel-group controlled trial

Protocol number	SMC-0128-23
Public protocol version	1.0
Date of public version	22 July 2026
Original approved protocol	Version 4.0, 6 November 2023
Principal investigator	Professor Edward Ram
Study site	Department of Surgery B / Colorectal Clinic, Sheba Medical Center, Tel Hashomer, Israel
Sponsor type	Investigator-initiated study
Study products	Proctofiz MD and topical nifedipine 0.3% ointment
Planned sample size	100 participants (50 per group)
Trial design	Randomized, double-blind, active-controlled, parallel-group trial
Ethics approval	Sheba Medical Center Institutional Helsinki Committee, SMC-0128-23
Institutional authorization	Director approval dated 1 June 2023

Public disclosure version prepared for trial registration and transparency purposes.

This document does not replace the ethics-approved protocol or subsequent approved amendments.

1. Document control and protocol status

This public protocol consolidates the core study information contained in the ethics-approved protocol, institutional application, informed-consent form and institutional authorization. It is intended for public registration and reporting. Where wording in the source documents was inconsistent, this version uses the description supported most consistently across the approved materials and does not introduce a new intervention, population, visit, or outcome.

Document	Version	Date	Status
Public Study Protocol	1.0	22 July 2026	Prepared for ISRCTN submission
Approved protocol	4.0	6 November 2023	Source document
Hebrew informed-consent form	2.0	14 April 2023	Ethics-approved source document
Institutional director authorization	—	1 June 2023	Approval for conduct of the trial

Important clarification: The trial is active-controlled and does not include a placebo. It is a parallel-group trial and not a crossover trial. References in earlier drafting to “placebo controlled,” “crossover,” hospitalization, surgery-day medication, or postoperative administration are not part of the approved anal-fissure study procedures described in the consent form and visit schedule and are not carried forward into this public version.

2. Protocol synopsis

Scientific title	A Comparative Study Between Proctofiz MD and Topical Nifedipine for the Treatment of Chronic Anal Fissure: a single-centre, prospective, randomized, double-blind, parallel-group controlled trial.
Public title	Proctofiz versus nifedipine ointment for chronic anal fissure.
Condition	Chronic anal fissure.
Rationale	Topical calcium-channel blockers are established conservative therapy for anal fissure. Proctofiz MD is a marketed topical medical-device ointment containing hemp-seed oil and additional botanical ingredients intended to relieve symptoms and support fissure healing. The trial compares both treatments under blinded conditions.
Primary objective	To compare the clinical effectiveness of Proctofiz MD with topical nifedipine in participants with chronic anal fissure.
Primary outcome	Clinical fissure healing at 3 months after initiation of treatment, assessed by a colorectal surgeon.
Key secondary outcomes	Pain severity measured by visual analogue scale; bleeding and other fissure-related symptoms; quality of life using the study fissure questionnaire; referral for surgical intervention; adverse events; treatment adherence.
Design	Single-centre, prospective, randomized, double-blind, active-controlled, parallel-group superiority trial.
Allocation	1:1 allocation; 50 participants per group.

Randomization	Pharmacy-generated allocation in blocks of 10, with five assignments to each treatment within each block.
Blinding	Participants, investigators, treating clinicians and outcome assessors are blinded. The dispensing pharmacy retains the allocation code; emergency unblinding is permitted only when clinically necessary.
Population	Adults aged 18–80 years with clinically diagnosed anal fissure who can provide informed consent and comply with study procedures.
Sample size	100 randomized participants.
Intervention arm	Proctofiz MD topical ointment, applied three times daily for 6 weeks.
Control arm	Topical nifedipine 0.3% ointment, applied three times daily for 6 weeks.
Application method	Approximately 1 cm of ointment is placed on the fingertip, inserted a few millimetres into the anal canal and applied circumferentially to the anal canal and anal verge. After a bowel movement, the perianal area is washed before the first subsequent application; washing is not required before later applications that day.
Follow-up	Baseline; telephone contacts at weeks 1 and 5; clinic visits at weeks 3 and 6 and month 3; telephone follow-up at month 6.
Analysis	Primary analysis by intention to treat. Between-group comparisons will use appropriate parametric or non-parametric tests according to data distribution. Categorical outcomes will be compared using chi-square or Fisher’s exact tests. Two-sided significance level: 0.05.
Study site	Sheba Medical Center, Tel Hashomer, Israel.
Ethics	Approved by the Sheba Medical Center Institutional Helsinki Committee and authorized by the institutional director under protocol SMC-0128-23.

3. Background and rationale

Anal fissure is a linear tear in the anoderm of the distal anal canal and is commonly associated with severe pain during and after defecation, bleeding, sphincter spasm and impaired quality of life. Chronic fissures generally persist beyond 6–8 weeks and may be associated with exposed internal sphincter fibres, a hypertrophied anal papilla and a sentinel skin tag. The pathophysiology involves local trauma, internal sphincter hypertonicity and impaired anodermal perfusion.

Initial management is usually conservative and aims to achieve atraumatic stool passage, reduce internal sphincter tone, relieve pain and facilitate healing. Typical measures include dietary fibre, stool softening when required, local hygiene and topical vasodilator therapy. Nifedipine is a calcium-channel blocker used topically to reduce sphincter pressure and is a recognized non-operative treatment option.

Proctofiz MD is a topical, over-the-counter medical-device ointment marketed in Israel for anal fissure. The approved study documents describe a formulation including hemp-seed oil, calendula, sweet almond, myrtle, arnica and seaweed extract. The formulation is intended to provide local soothing, anti-inflammatory, analgesic, protective and wound-supporting effects. The present study was designed to compare Proctofiz MD with topical nifedipine under randomized and double-blind conditions.

The comparison is clinically relevant because effective conservative treatment may reduce symptoms, improve quality of life and avoid escalation to botulinum-toxin injection or lateral internal sphincterotomy. Surgical treatment can be highly effective but carries a recognized risk of continence disturbance; therefore, a safe and effective topical alternative would be valuable.

4. Objectives and hypotheses

4.1 Primary objective

To compare the proportion of participants with clinical healing of the anal fissure at 3 months after initiation of treatment between Proctofiz MD and topical nifedipine.

4.2 Secondary objectives

- To compare pain severity during follow-up using a visual analogue scale (VAS).
- To compare anal bleeding, burning, itching and other fissure-related symptoms over time.
- To compare disease-specific quality of life using the study fissure questionnaire.
- To compare the proportion of participants requiring or being referred for surgical intervention.
- To evaluate treatment adherence in both groups.
- To compare the frequency and nature of adverse events and treatment discontinuations.

4.3 Hypothesis

The study is designed as a superiority trial. The working hypothesis is that Proctofiz MD will provide clinical outcomes that are superior to those achieved with topical nifedipine, particularly for pain reduction and fissure healing. The protocol source documents contain different historical descriptions of the single primary endpoint; this public version designates 3-month clinical healing as the primary endpoint and treats 6-week pain change as a key secondary endpoint, thereby preserving both prespecified assessments without creating a new measurement.

5. Trial design

This is a single-centre, prospective, randomized, double-blind, active-controlled, parallel-group clinical trial. Eligible participants are allocated in a 1:1 ratio to Proctofiz MD or topical nifedipine. Treatment is administered for 6 weeks and participants are followed for 6 months from treatment initiation.

- Single centre: Sheba Medical Center.

- Two parallel treatment groups.
- Allocation ratio: 1:1.
- Planned sample: 100 participants.
- Blinding: participants, clinical investigators and outcome assessors.
- Primary time point: 3 months.
- Final follow-up: 6 months.

6. Study setting

Participants are recruited from the colorectal/proctology clinic at Sheba Medical Center, a tertiary referral medical centre in Tel Hashomer, Israel. Screening, consent, randomization, dispensing and clinic assessments are conducted by the authorized study team. Telephone follow-up is performed by the study team or study coordinator.

7. Eligibility criteria

7.1 Inclusion criteria

- Age 18–80 years.
- Anal fissure diagnosed clinically by a board-certified colorectal surgeon.
- Ability to understand the study information and provide written informed consent.
- Ability and willingness to comply with treatment, visits, telephone follow-up and questionnaires.

7.2 Exclusion criteria

- Pregnancy or breastfeeding.
- Diagnosed orthostatic hypotension.
- Previous treatment with either Proctofiz MD or topical nifedipine for the current fissure episode before enrolment, as specified in the approved protocol.
- Known hypersensitivity or contraindication to an ingredient of either study ointment.
- Any medical condition or clinical circumstance that, in the investigator’s judgment, makes participation unsafe or prevents protocol compliance.

The source documents do not provide a separate detailed list of exclusions for atypical fissures or inflammatory bowel disease. Such conditions should therefore not be added as formal public exclusions unless they were part of an ethics-approved amendment or documented screening practice.

8. Recruitment, consent and enrolment

Potential participants are identified during evaluation in the colorectal clinic. Before any study-specific procedure, an authorized physician explains the study purpose, interventions, randomization, blinding, foreseeable risks, potential benefits, alternatives and the voluntary nature of participation. Participants are given an opportunity to ask questions and to discuss participation with others. Written informed consent is obtained before randomization. A signed copy is provided to the participant and the original is retained in the study file.

Participation is voluntary. Refusal to participate or later withdrawal does not affect the participant’s current or future medical care.

9. Interventions

9.1 Intervention group: Proctofiz MD

Participants allocated to the intervention group receive Proctofiz MD topical ointment. The approved protocol describes the product as a marketed medical-device ointment containing hemp-seed oil and additional botanical components, including calendula, sweet almond, myrtle, arnica and seaweed extract.

9.2 Active-control group: topical nifedipine

Participants allocated to the control group receive topical nifedipine 0.3% ointment. The informed-consent form also refers to the Israeli branded preparation Antrolin. For public reporting, the intervention is described generically as topical nifedipine 0.3%.

9.3 Dose, route and duration

- Route: topical anorectal application.
- Frequency: three times daily.
- Duration: 6 weeks. The original protocol also used the wording “45 days”; the consent form and visit schedule consistently describe 6 weeks, which is used in this public version.
- Both groups receive identical application instructions and equivalent study contact and follow-up.

9.4 Standardized application procedure

1. Place approximately 1 cm of ointment on the fingertip.
2. Insert the fingertip only a few millimetres into the anal canal.
3. Apply the ointment circumferentially around the anal canal and anal verge.
4. After a bowel movement, wash the perianal area before the first subsequent application.
5. Washing is not required before later applications on the same day unless clinically indicated.
6. Wash hands before and after application.
7. Use only the coded study tube supplied by the study team.

9.5 Participant education and support

Every participant receives the same standardized verbal and visual education regarding chronic anal fissure and correct ointment application. Participants receive the study coordinator’s telephone number for questions or concerns. The study team does not provide information that could reveal treatment allocation.

9.6 Concomitant care

Routine conservative measures for anal fissure, including attention to stool consistency, dietary fibre, fluids and stool-softening treatment when clinically indicated, may be provided according to usual care. Any additional fissure-directed topical treatment, botulinum toxin or surgery during the study must be documented because it may affect outcome interpretation.

9.7 Criteria for treatment discontinuation

- Participant request or withdrawal of consent.
- Severe or clinically important adverse reaction attributed to the study ointment.
- Clinically significant hypotension or other cardiovascular symptoms requiring discontinuation.
- Need for urgent alternative medical or surgical treatment.
- Major protocol violation or investigator determination that continuation is unsafe.

10. Randomization, allocation concealment and blinding

10.1 Sequence generation

The dispensing pharmacy generates the randomization sequence using blocks of 10. Within each block, five participants are assigned to Proctofiz MD and five to topical nifedipine. No stratification by demographic or clinical characteristics is specified in the approved protocol.

10.2 Allocation concealment

The pharmacy prepares and labels study ointment tubes using participant codes according to the randomization schedule. Investigators receive coded tubes from the pharmacy and dispense them sequentially to enrolled participants. The allocation sequence is not accessible to recruiting clinicians or participants.

10.3 Blinding

The pharmacy prepares the two ointments in visually uniform containers and packaging to maintain blinding. Participants, investigators, treating clinicians and outcome assessors remain unaware of allocation until completion of the blinded study procedures, unless emergency unblinding is required.

10.4 Emergency unblinding

The pharmacy retains the master allocation code. A sealed emergency code may be held by the principal investigator in a secure location. Unblinding is permitted only when knowledge of the treatment is necessary for urgent clinical management. The reason, date, person requesting unblinding and resulting action must be documented.

11. Study assessments and visit schedule

Assessment	Baseline	Week 1 Phone	Week 3 Clinic	Week 5 Phone	Week 6 Clinic	Month 3 Clinic	Month 6 Phone
Eligibility and consent	X						
Demographics and clinical history	X						
Clinical fissure examination	X		X		X	X	As indicated
Treatment allocation/dispensing	X						
Application education	X						
Pain/VAS assessment	X	X	X	X	X	X	X
Bleeding and fissure symptoms	X	X	X	X	X	X	X
Fissure questionnaire / quality of life	X	As scheduled	X	As scheduled	X	As scheduled	X
Adherence assessment		X	X	X	X		
Tube return/accountability			X		X		
Adverse-event review	X	X	X	X	X	X	X

Assessment	Baseline	Week 1 Phone	Week 3 Clinic	Week 5 Phone	Week 6 Clinic	Month 3 Clinic	Month 6 Phone
Clinical healing outcome						X	
Need/referral for surgery		X	X	X	X	X	X

The approved consent form specifies clinic visits at 3 weeks, 6 weeks and 3 months, with telephone follow-up at 1 week, 5 weeks and 6 months. This schedule governs the public protocol. Any additional symptom contacts may be performed for participant safety or retention but are not treated as mandatory efficacy visits unless documented in the case-report forms.

12. Outcome measures

12.1 Primary outcome

Clinical healing of the anal fissure at 3 months after treatment initiation. Healing is assessed by a board-certified colorectal surgeon and recorded as healed or not healed based on clinical examination.

12.2 Secondary outcomes

- Change in pain severity from baseline, measured using a visual analogue scale, including the key 6-week assessment.
- Pain during defecation and post-defecation pain at scheduled follow-up assessments.
- Presence and frequency of anal bleeding.
- Burning, itching and other fissure-related symptoms.
- Disease-specific quality-of-life responses using the 27-item fissure questionnaire.
- Clinical healing at other assessed time points, where examination data are available.
- Referral for or performance of surgical intervention during follow-up.
- Treatment adherence, based on participant report, contact records and returned study medication packaging when available.
- Adverse events, serious adverse events, treatment-related events and discontinuations.

12.3 Fissure questionnaire

The study questionnaire contains 27 items addressing discomfort during sitting, standing, walking, exercise and defecation; fear of defecation; work, family, social and sexual functioning; body image; pain, burning, itching and bleeding. Responses are recorded on an ordinal frequency scale with a “not relevant” option. The source documents do not provide a validated total-score algorithm; therefore, this public protocol does not invent one. Item-level or prespecified composite analyses should follow the statistical dataset and analysis plan used by the study team.

13. Treatment adherence

Adherence is promoted through standardized education, clear written or visual instructions, access to the study coordinator and scheduled follow-up. At study contacts, participants are asked about the number of daily applications, missed doses, treatment interruptions and problems with administration. Returned tubes or packages are reviewed where available and drug accountability is documented. Missed appointments trigger telephone contact and rescheduling attempts.

A participant is not automatically excluded from the intention-to-treat analysis because of imperfect adherence. Clinically meaningful non-adherence may be considered in a per-protocol sensitivity analysis if defined before database lock.

14. Safety monitoring

14.1 Foreseeable risks

Potential local effects include burning, irritation, itching, discomfort, hyperaemia or localized bleeding. Topical nifedipine may cause headache, dizziness or symptoms related to reduced blood pressure. Hypersensitivity reactions are possible with topical preparations. Participants are instructed to contact the study team if symptoms are severe, persistent or concerning.

14.2 Adverse-event collection

Adverse events are assessed from the time of first study application until the end of follow-up. The study team records onset, duration, severity, seriousness, expectedness, relationship to study treatment, action taken and outcome. Events requiring urgent treatment are managed according to standard clinical practice.

14.3 Serious adverse events

A serious adverse event is any event that results in death, is life-threatening, requires or prolongs hospitalization, results in persistent or significant disability, or is otherwise medically important. Serious adverse events are reported promptly to the principal investigator, sponsor-investigator and ethics committee according to institutional and national requirements.

15. Sample size

The approved study sample is 100 participants, with 50 assigned to each group. The protocol source states that a pain-based calculation using a two-sided alpha of 0.05, 90% power and an assumed 20% attrition rate indicated that at least 72 participants would be required. The approved target of 100 provides additional allowance for attrition and supports analysis of the clinical healing outcome.

The historical calculation refers to an expected difference in pain reduction and cites comparator data described as diltiazem in one section of the draft protocol. This inconsistency is acknowledged; no new retrospective power calculation is introduced into the public version.

16. Statistical analysis

16.1 Analysis populations

- Intention-to-treat population: all randomized participants, analysed according to assigned treatment.
- Safety population: all randomized participants who applied at least one dose of study ointment, analysed according to treatment received.
- Per-protocol population: participants without major protocol deviations who completed the required treatment exposure and key assessments.

16.2 General principles

- Two-sided statistical tests with alpha = 0.05.
- Descriptive statistics presented as mean and standard deviation or median and interquartile range for continuous variables, and count and percentage for categorical variables.
- Normality assessed using distributional plots and an appropriate normality test, including the Kolmogorov-Smirnov test where used in the source protocol.
- Categorical outcomes compared using chi-square or Fisher’s exact test.
- Continuous outcomes compared using an independent-samples test appropriate to distribution, including the Mann-Whitney U test for non-normally distributed variables.

- Repeated symptom measurements may be analysed using a longitudinal method appropriate to the final dataset, provided the method is prespecified before unblinding.

16.3 Primary analysis

The primary outcome is the proportion of participants with clinical fissure healing at 3 months. The treatment groups will be compared using a risk difference and/or relative risk with a 95% confidence interval, together with a chi-square or Fisher's exact test as appropriate.

16.4 Secondary analyses

Pain, bleeding, quality-of-life items, need for surgery and adverse events will be summarized by treatment group and time point. Change from baseline in VAS pain at 6 weeks is a key secondary comparison. Time-specific analyses will be interpreted as secondary and exploratory unless otherwise prespecified.

16.5 Missing data

Every reasonable effort will be made to obtain key follow-up data after treatment discontinuation or missed visits, provided consent has not been withdrawn. The number and pattern of missing observations will be reported. The primary intention-to-treat analysis will use the prespecified approach applied in the final statistical analysis plan; sensitivity analyses may test plausible assumptions regarding missing healing outcomes.

17. Data collection and management

Clinical and questionnaire data are recorded using participant study codes. Identifying information and the code key are stored separately with access limited to authorized study personnel. No directly identifying information is transferred outside the hospital network except where permitted by law, ethics approval and institutional policy.

Study records, approvals and collected documents are retained for at least 15 years after study completion, in accordance with the institutional authorization. Data-quality checks include review for completeness, internal consistency, visit timing and protocol deviations. Corrections are traceable and do not obscure the original entry.

The final dataset used for analysis should contain only the minimum information needed for the research questions. Public reports will present aggregated or de-identified data.

18. Confidentiality

Participant confidentiality is protected throughout the study. Access to identifiable records is restricted to the study team, authorized monitors, the ethics committee and regulatory authorities when required. Publications and registry entries will not identify individual participants.

19. Protocol deviations and amendments

Any change to the approved protocol that affects participant safety, rights, scientific validity, study procedures or data interpretation requires prior written approval from the institutional ethics committee and, where applicable, the Ministry of Health. Urgent safety measures may be implemented before approval when necessary to eliminate an immediate hazard, with prompt notification thereafter.

Protocol deviations are documented, assessed for impact and reported according to institutional requirements. Major deviations are considered in the per-protocol analysis and study interpretation.

20. Monitoring and quality assurance

The investigator is responsible for ensuring that the study is conducted according to the approved protocol, informed-consent requirements, institutional procedures and applicable regulations. Study-product receipt, storage, dispensing and return are documented. Access to source records for authorized review is permitted subject to confidentiality safeguards.

21. Ethics and regulatory considerations

The trial received approval from the Sheba Medical Center Institutional Helsinki Committee and authorization from the institutional director under application SMC-0128-23. The director's authorization, dated 1 June 2023, permitted recruitment of up to 100 participants and required informed consent to be obtained by a licensed physician serving as an investigator or sub-investigator.

The study is conducted in accordance with the principles of the Declaration of Helsinki, applicable Israeli Public Health Regulations for medical research in humans, institutional requirements and accepted principles of Good Clinical Practice.

The institutional authorization initially remained valid through 31 May 2024. Continued conduct beyond that date requires documented renewal or subsequent ethics authorization. This public protocol does not represent evidence of renewal; the investigator should retain and provide the current approval documentation if requested by the registry.

22. Participant withdrawal

Participants may withdraw consent at any time without giving a reason and without affecting their medical care. When a participant stops the study ointment but permits follow-up, the study team may continue to collect outcome and safety information. When consent for further data collection is withdrawn, no new data are collected except as required for safety or legal obligations. Data already collected may be retained and analysed as permitted by the consent form, ethics approval and applicable law.

23. Dissemination and transparency

The trial will be registered in a publicly accessible clinical-trial registry. Results will be submitted for peer-reviewed publication and may be presented at scientific meetings. Reporting will follow applicable randomized-trial reporting guidance. Trial registration and publications will be updated with the study status and results when available.

Authorship will reflect substantial scientific contributions. No participant-identifiable information will be disclosed. Where feasible and permitted, de-identified aggregate data or supporting materials may be shared under controlled conditions.

24. Roles and responsibilities

Role	Responsibility
Principal investigator	Overall scientific and regulatory responsibility; participant safety; protocol compliance; oversight of enrolment, treatment and reporting.
Study investigators	Eligibility assessment, informed consent, clinical examinations, adverse-event assessment and protocol-compliant follow-up.
Study coordinator	Scheduling, participant contact, questionnaire administration, adherence support and

	documentation.
Dispensing pharmacy	Randomization sequence, preparation of visually uniform coded tubes, allocation concealment, code retention and study-product accountability.
Sheba Medical Center	Institutional oversight, ethics governance, secure data environment and regulatory record retention.

25. Public protocol limitations and source-document reconciliation

This public version was prepared from documents created at different stages of the study and therefore explicitly resolves the following drafting inconsistencies without altering the approved clinical study:

- The study is active-controlled; no placebo is used.
- The design is parallel-group; no crossover occurs.
- Treatment duration is presented as 6 weeks, consistent with the informed-consent form and follow-up schedule; “45 days” in the source protocol is treated as an approximate description.
- The primary endpoint is designated as clinical healing at 3 months, while 6-week change in pain is retained as a key secondary endpoint because both were specified in source documents.
- Surgical-day, inpatient and postoperative-administration wording in the source protocol is unrelated residual template text and is excluded.
- The study is described by design rather than assigning a pharmaceutical “Phase III” label, because one product is documented as a marketed medical device and the comparator is topical nifedipine.
- The public protocol does not add unsupported scoring algorithms, exclusion criteria, laboratory tests or biological sampling.

26. References

The approved protocol includes a numbered reference list supporting the background on anal fissure, conservative treatment, topical calcium-channel blockers, botulinum toxin and sphincterotomy. For the registry public version, the scientific content is retained without reproducing unverified bibliographic details from the partially formatted source document. The full reference list should be taken directly from the approved protocol or final manuscript when submitted as a publication supplement.

Appendix 1. Standardized patient application instructions

8. Use the coded study ointment three times each day for 6 weeks.
9. Wash your hands before application.
10. Place approximately 1 cm of ointment on the fingertip.
11. Insert the fingertip only a few millimetres into the anal canal.
12. Spread the ointment gently around the anal canal and anal verge.
13. After a bowel movement, wash the anal area before the first subsequent application.
14. You do not need to wash again before later applications that day unless the area is soiled.
15. Wash your hands after application.
16. Do not use another fissure ointment unless instructed by the study physician.
17. Contact the study coordinator or physician if you develop severe burning, rash, dizziness, faintness, severe headache, bleeding that concerns you or any other unexpected symptom.
18. Bring the study tube or packaging to clinic visits when requested.

Appendix 2. Schedule summary for participants

Time	Contact	Main procedures

Baseline	Clinic	Consent, eligibility, clinical examination, questionnaires, randomization, ointment and application instructions
Week 1	Telephone	Symptoms, pain, adherence and adverse events
Week 3	Clinic	Clinical examination, questionnaires, adherence and adverse events
Week 5	Telephone	Symptoms, pain, adherence and adverse events
Week 6	Clinic	Clinical examination, pain, symptoms, quality of life, adherence, adverse events and treatment completion
Month 3	Clinic	Primary healing assessment, symptoms, quality of life and need for further treatment
Month 6	Telephone	Longer-term symptoms, quality of life, adverse events and need for surgery

Appendix 3. Registration-ready trial description

A single-centre randomized double-blind trial comparing Proctofiz MD with topical nifedipine 0.3% in 100 adults with clinically diagnosed chronic anal fissure. Participants are allocated 1:1 by a pharmacy-generated blocked randomization sequence. Both ointments are supplied in coded, visually uniform packaging and applied topically three times daily for 6 weeks. Participants are followed by telephone at weeks 1 and 5, in clinic at weeks 3 and 6 and month 3, and by telephone at month 6. The primary outcome is clinical fissure healing at 3 months. Secondary outcomes include pain, bleeding, other fissure symptoms, disease-specific quality of life, adherence, adverse events and referral for surgery.