CLINICAL GUIDELINE

Medical management of endometriosis (suspected and confirmed)

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

Version Number:	4
Does this version include changes to clinical advice:	Yes
Date Approved:	6th August 2025
Date of Next Review:	31st July 2030
Lead Author:	Claire Higgins
Approval Group:	Gynaecology Governance Group
Guideline ID number:	638

Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Medical management of endometriosis (suspected and confirmed) (638)

Objectives:
To describe options for the medical management of symptoms related to endometriosis

Scope:
Audience: All healthcare professionals working in GG&C involved in the care of women with endometriosis

The diagnosis of endometriosis based on symptoms is difficult. Women can experience various symptoms including cyclical or chronic pelvic pain, heavy menstrual bleeding (HMB), deep dyspareunia, infertility, dyschezia or bladder pain.

Examination and investigations

Abdominal and vaginal examination

This is not diagnostic and may be normal in those with endometriosis.

Abdominal examination should be offered as it may identify areas of pain or the presence of any abdominal masses.

Vaginal examination can be useful in assessing pelvic organ size and motility, adnexal masses, or the presence of nodules on the rectovaginal wall.

Full blood count (FBC)

This should be performed in women with associated heavy menstrual bleeding (HMB). (see Menstrual disorders guideline id-621-menstrual-disorders-fp-added.pdf (scot.nhs.uk))

CA125
This should not routinely be performed for the diagnosis of endometriosis.

Pelvic Imaging
The possibility of endometriosis should not be excluded if clinical suspicion remains high, even in the presence of a normal examination, normal ultrasound or normal MRI.

Pelvic ultrasound
NICE [1] suggests a transvaginal ultrasound scan (TVUS) should be offered to all women with suspected endometriosis, even if pelvic or abdominal examination is normal. If TVUS is declined, a transabdominal scan can be undertaken. These investigations can be organized by the patients GP in primary care.

The Pelvic ultrasound imaging is not diagnostic of endometriosis, but is useful to identify any associated endometrioma. A typical appearance is characteristically ground glass echogenicity and one to four compartments with no papillary structures with detectable blood flow. Additionally, it can suggest deep endometriosis, including that involving the bowel, bladder or ureter.

It may also be useful in the assessment of other pathology which may be causing symptoms and can help guide ongoing management options.

Magnetic Resonance Imaging
This should not be used as a primary investigation to diagnose endometriosis. It may be considered to assess the extent of deep endometriosis involving the bowel, bladder or ureter. It is recommended that the scans are interpreted by a health care professional with specialist expertise in gynaecological imaging.

Diagnostic laparoscopy
Diagnostic laparoscopy with biopsy is considered the 'gold standard' for diagnosis of endometriosis. However, in many cases the visualisation of endometriotic implants can be regarded as sufficient evidence.

Laparoscopy should not be performed prior to a trial of medical management.

Laparoscopy should be performed by a clinician with skills and equipment to surgically treat mild/moderate disease if visualised at that time.

A biopsy can be useful in the diagnosis of endometriosis, and should be undertaken if an endometrioma is treated but not excised.

If assessment of fertility is a consideration, it may be appropriate to consider tubal patency testing during diagnostic laparoscopy.

Treatment
Medical treatment includes analgesia and hormonal therapies.

The needs and preferences of the woman should be considered. This will include wishes for future fertility, experience of previous treatments, co-morbidities, and any potential contraindications to treatment.

In those without a definitive diagnosis, it is reasonable to start a trial of empirical treatment with analgesia +/- hormonal treatment. If there is not a favourable response following a trial of at least 3- 6 months, of medical management, a diagnosis can be confirmed by laparoscopy after discussion of patient wishes.

Referral to the assisted conception service (ACS) should be considered as per current national ACS referral guidance. Referral Acceptance Criteria - NHSGGC

Analgesia
Simple analgesia is appropriate for women wishing to avoid hormones or actively trying to conceive. Suggested regimes include NSAIDS, Paracetamol and neuromodulators. Of note, dosing regimes suggested below may need to be altered based on weight and patient age.

Nonsteroidal anti-inflammatory drug (NSAIDs)
NSAIDs can help with the management of pain associated with endometriosis. Added benefits include reduction in menstrual flow by 20-50%.

NSAIDS are not suitable for patient who are sensitive to their effects e.g. gastric ulcers, NSAID sensitive asthma. Consider addition of proton pump inhibitor for gastric protection in long term use. Suggested regimes are outlined below and should be taken at time of menstruation:

- **Ibuprofen** 200–400mg oral, 3–4 times a day oral

- **Naproxen** 500mg oral initially, followed by 250mg 6-8 hourly (max 1.25g/day)

- **Diclofenac** 50 mgs suppositories 2-3 times per day, 6-8 hourly

Paracetamol:
This can be used where NSAIDS are contraindicated, not tolerated, or in addition to an NSAID.

Neuromodulators and neuropathic pain treatments:
Where this type of medication is considered, involvement of endometriosis specialists and pain management teams should be considered.

Suggested treatments for pelvic pain include

- **Duloxetine** 30mg od at night. This can be increased to 60mg as needed after 3-6 months.

GG&C Patient information is available drugs-duloxetine.pdf (paindata.org)

Hormonal Treatments
These preparations can reduce pain and menstrual flow. Consider a 3 - 6 month trial of therapy. It should be explained to the woman that early hormonal treatment for endometriosis can reduce pain and is not associated with a permanent negative effect on subsequent fertility.

Combined Hormonal Contraception
This type of contraception is highly effective in reducing menstrual blood loss and associated menstrual pain.

There are currently three methods of CHC available in the UK:

- Combined oral contraceptive pill (COC)
- Combined transdermal patch (CTP) that releases an average of 33.9 µg EE and 203 µg norelgestromin per 24 hours.10
- Combined vaginal ring (CVR) that releases EE and etonogestrel at daily rates of 15 µg and 120 µg, respectively.

Monophasic combined oral contraception is usually first choice as all pills in the packet contain the same dose of estrogen and progestogen.

Tailored regimes with shorter hormone free intervals (HFI) have shown a greater improvement in symptoms of HMB and endometriosis associated pain. Examples of tailored regimens are shown in the table below (from FSRH Guideline Combined Hormonal Contraception). Flexible extended usage and Continuous use regimes are associated with improved contraceptive efficacy.

There are a number of common contraindications see UK Medical Eligibility Criteria for Contraceptive Use (UKMEC)] at www.ffprhc.org.uk for further information.

Table 1: Standard and tailored regimens for use of combined hormonal contraception (CHC)

Type of regimen	Period of CHC use	HFI
Standard use	21 days (21 active pills or 1 ring, or 3 patches)	7 days
Tailored use		
Shortened hormone-free interval (HFI)	21 days (21 active pills or 1 ring, or 3 patches)	4 days
Extended use (tricycling)	9 weeks (3 x 21 active pills or 3 rings, or 9 patches used consecutively)	4 or 7 days
Flexible extended use	Continuous use (≥21 days) of active pills, patches or rings until breakthrough bleeding occurs for 3–4 days	4 days
Continuous use	Continuous use of active pills, patches or rings	None

Progestogens
Levonorgestrel Intra-Uterine System (LNG-IUS 52mg)
- Treatment is particularly useful following surgery for endometriosis with reduction in dysmenorrhoea at 12 months compared with expectant management
- Reduces menstrual loss by up to 90% after 6 months of use
- Erratic vaginal bleeding is common in the first 4-6 months of use but rarely heavy or painful
- There are very few contraindications to LNG-IUS
- Systemic effects are uncommon and often improve after the first 2-3 months
- LNG-IUS is a highly effective contraceptive and can also be used as the progestogen component of Hormone replacement therapy (Currently only Mirena® 52mg IUS has this license)
- Expulsion is higher where there are fibroids >3cm

Progesterone only oral preparations

These are useful where oestrogen is contra-indicated, however, irregular bleeding is common.

- **Desogestrel** 75 micrograms daily, appears to be more effective in reducing menstrual loss and for contraceptive protection than other progesterone only preparations.

- **Dienogest** 2 mgs daily tablet is an oral progestin licensed for the treatment of endometriosis. It is a nortestosterone derivative that has a progestogenic effect in the uterus, reducing the production of estradiol and thereby suppressing endometriotic lesions. It is usually initiated within the secondary care setting.

While acting to reduce endometriotic implants Dienogest provides similar symptomatic relief to gonadotrophin-releasing hormone (GnRH) agonists, with better quality-of-life scores. Clinical studies have shown that dienogest has improved compliance with less side effects in patients. 3- 4 months of treatment may be required to see the full effect.

It is not licensed for contraception in the UK, and manufacturer advises that if contraception is required, females of child-bearing potential should use non-hormonal contraception during treatment. See BNF for cautions and contraindications including consideration of bone density and VTE risk during surgery/immobility, breast feeding/pregnancy/diabetes.

Progestogen-only injectable: depot medroxyprogesterone acetate (DMPA)

- Many women are rendered amenorrhoeic by DMPA (e.g. Depo Provera® 150mg, 12 weekly as an intramuscular injection)
- Erratic bleeding is common in the first few months of use however often improves with time
- May be associated with a delay in menses return
- Osteoporosis risk should be checked for all women, particularly when under 18 or over 45 years of age. (see UKMEC). This should be re-evaluated every 2 years.

Etonogestrel Subdermal Implant (Nexplanon®)

- Implant inserted during first 5 days of menstrual cycle and removed within 3 years
- Highly effective in the prevention of pregnancy
- Acts to thin endometrium and prevent ovulation
- Suggestion that after 6 month of use there is a reduction in pain in >60% of users
- Can be associated with erratic bleeding initially. Some women may wish a trial of an additional POP e.g. Desogestrel for 3-6 months to improve bleeding pattern.

Continuing treatments and future options

Treatment can be continued for as long as it remains effective and the woman is experiencing no adverse effects.

If there is no improvement with above medical treatments, consider

- **Laparoscopy and surgical treatment of lesions**

For women wishing to consider surgical management, please refer to a consultant who can perform treatment or specialist treatment if required.

- **Gonadotrophin Releasing Hormone (GnRH) analogue injections +/- add-back HRT**

This option can be considered under consultant supervision (refer to BNF).

- **Gonadotrphin Releasing Hormone Antagonist oral tablet with add back HRT**

Ryeco® is an oral tablet preparation containing GnRH-receptor antagonist combined with add-back HRT therapy (Relugolix 40mg, Estradiol 1mg and Norethisterone Acetate 0.5mg). It is licensed for use in adult women of reproductive age for symptomatic treatment of endometriosis with a history of previous medical or surgical treatment for their endometriosis. (for fibroids see Uterine Fibroids, Gynaecology (512) | Right Decisions (scot.nhs.uk))

Currently, use is restricted to specialist initiation for use in patients who have failed or are unsuitable for conventional therapies described above.

It is reasonable to assess symptomatic benefit at 6 months and assess need for continued therapy. Discontinuation of therapy should be considered when the patient enters menopause.

Benefits include significant reduction in menstrual blood loss (50% reduction at 4 weeks), Amenorrhoea (50% at 6months and 71% at 12 months), reduction in anaemia and pelvic pain, and a small non-significant reduction in fibroid volume (up to 14%)
Common side effects include hot flushes, headaches and abnormal uterine bleeding. Additionally, bone loss occurs in 3-8% women (average of 0.04% at 1 year)

Menstruation and ovulation return quickly after treatment and no associated endometrial changes have been reported.

Advice on use

- One tablet should be taken daily at the same time each day
- Treatment should be commenced during the first 5 days of menstrual cycle
- Pregnancy should be excluded prior to commencing treatment.
- Hormonal contraception should be stopped prior to starting treatment. Of note, Ryeco® will inhibit ovulation after at least 1month of correct treatment. Barrier contraception is recommended for the first month of use.
- If two or more consecutive tablets are missed, barrier contraception is advised for 7 days.
- Start contraception immediately after stopping treatment, if required.
- Owing to the small risk of bone loss, a DEXA scan is advised pre-treatment IF at high risk of osteoporosis. Otherwise, a DEXA scan is advised 52 weeks after treatment.

The clinician initiating treatment is responsible for organising the DEXA scan investigation.

Contraindications: current or previous venous thromboembolism, arterial thromboembolic cardiovascular disease, (e.g. myocardial infarction, cerebrovascular accident, ischemic heart disease), osteoporosis, known thrombophilic disorders, migraine with aura, pregnancy, severe liver problems, hormone-related malignancy.

Gonadotrphin Releasing Hormone Antagonist oral tablet

Yselty® (Linzagolix 200mg) is an oral GnRH receptor antagonist. Unlike Ryeco®, it does not contain add back HRT so may be more suitable as an alternative for women where they do not wish to take oral HRT, or are not suitable for oral HRT preparations.

Add back therapy should be initiated separately at clinician discretion. This can include any combination suitable for the patient.

Linzagolix has been accepted by NICE for use in adult women of reproductive age for symptomatic treatment of endometriosis in women with a history of previous medical or surgical treatment for their endometriosis'. Currently, use is restricted to specialist initiation for use in patients who have failed or are unsuitable for conventional therapies described above in this guideline.

It is reasonable to assess symptomatic benefit at 6 months and assess need for continued therapy. Discontinuation of therapy should be considered when the patient enters menopause.

• **Treatment regimes**
The suggested treatment regime for endometriosis is Linzagolix 200 mg daily with add back HRT.

• **Benefits**
This regime demonstrated statistically significant reductions in both reported dysmenorrhea and non-menstrual pelvic pain with a stable or decreased use of analgesics.

• **Advice on use**
Children under 18 years of age
The safety and efficacy of Linzgolix in children aged under 18 years for the indication of treatment of endometriosis has not been established.

Contraception and exclusion of pregnancy
Linzagolix with or without concomitant add back HRT has not been demonstrated to provide contraception. Based on current data, manufacturer suggests women of childbearing potential at risk of pregnancy should use effective contraception while on treatment with Linzagolix.

Use of hormonal contraceptive options (for contraception or add back hormone therapy) is off label.

Current data suggests return of menstruation around 30 days after stopping therapy.

Pregnancy must be excluded prior to initiation of treatment with Linzagolix and is usually started within the first week of the menstrual cycle.

Bone Density Assessment
Owing to the small risk of bone loss, a DEXA scan is advised pre-treatment IF at high risk of osteoporosis. Otherwise, a DEXA scan is advised 52 weeks after treatment.

The clinician initiating treatment is responsible for organising the DEXA scan investigation.

• **Contraindications**: Known osteoporosis, pregnancy or breastfeeding, hormone-related malignancy, undiagnosed vaginal bleeding, severe hepatic impairment.

• **Cautions:** consider recognised contraindications to add back HRT therapy.

Additional Therapies

Consideration can be given to other non-medical therapies such as

- Lifestyle modifications (exercise, yoga, diet, sleep)
- Pelvic Floor Physiotherapy
- Cognitive Behavior Therapy (CBT) Computerised Cognitive Behavioural Therapy (cCBT) - NHSGGC

Information and Support

It is important that women understand the diagnosis and treatment options available. Information and support groups can be helpful, in addition to Patient Decision Aids. Useful resources are included below.

- Endometriosis UK (www.endo.org.uk)

- NHS inform (Endometriosis | NHS inform)

- RCOG patient information leaflet (www.rcog.org.uk/globalassets/documents/patients/patient- information-leaflets/gynaecology/pi-endometriosis.pdf)

- NICE Patient Decision Aid, Hormone treatment for endometriosis symptoms – what are my options? patient-decision-aid-on-hormone-treatment-for-endometriosis-symptoms-what-are-my-options-pdf-4595573197.pdf (nice.org.uk)

References :

Endometriosis: diagnosis and management (2017) NICE guideline NG73 last updated November 2024 Overview | Endometriosis: diagnosis and management | Guidance | NICE

Endometriosis. Guideline of the European Society of Human Reproduction and Embryology. 2022. www.eshre.eu/guidelines

NICE Clinical Knowledge Summaries, Endometriosis, May 2014, https://cks.nice.org.uk/endometriosis

FSRH Guideline (January 2019, amended October 2023) Combined Hormonal Contraception https://doi.org/10.1136/bmjsrh-2018-CHC

Pain Management for the West of Scotland weblink- Pain Management Home (paindata.org)

https://www.medicines.org.uk/emc/product/100021/smpc

NICE Linzagolix for treating symptoms of endometriosis, Technology appraisal guidance Reference number:TA1067 Overview | Linzagolix for treating symptoms of endometriosis | Guidance | NICE

Author:
Claire Higgins, Consultant O&G, QEUH

Co-Authors:
Rosie McLuskey, Specialist Endometriosis Nurse, QEUH
Frances Lowrie, W&C Pharmacist, QEUH
Robert Hawthorne, Consultant endometriosis specialist, QEUH

Authorised by:
Dr Vanessa Mackay, Clinical Director, Gynaecology GG&C

Last reviewed date: July 2025

Date of next review: July 2030

Key words: endometriosis, medical management, hormones, analgesia, pain,