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Patient Information Leaflet: Medical Management of Endometriosis

What is Endometriosis?

Endometriosis is a chronic condition where tissue similar to the lining of the uterus (endometrium) grows outside the uterus. This can cause inflammation, pain, and the formation of scar tissue. Common sites affected include the ovaries, fallopian tubes, and tissues lining the pelvis. Symptoms vary but often include pelvic pain, painful periods, pain during intercourse, and difficulty conceiving.

Medical Management Options

There are various medical treatments available to help manage symptoms of endometriosis. The choice of treatment depends on symptom severity, patient preferences, and whether pregnancy is currently desired.

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1. Conservative and Lifestyle Measures

Lifestyle modifications and conservative treatments can be used alone or to complement medical therapies and improve overall well-being. We suggest dietary changes and physiotherapy first line.

Stress, poor sleep, and anxiety can make pain feel worse by affecting how your brain processes pain signals. That's why pain management often involves not just treating the body, but also supporting your overall wellbeing—through things like **relaxation techniques, physiotherapy, gentle movement, and sometimes psychological support**.

- **Dietary Changes**: An anti-inflammatory diet rich in omega-3 fatty acids, fruits, vegetables, and whole grains may help reduce pain. Some women find benefit in reducing dairy, gluten, or processed foods. More information can be found in the book "Taking Control of Endometriosis" by Henrietta Norton.
- **Pelvic Floor Physiotherapy**: Targeted therapy can help reduce muscle tension and pelvic pain associated with endometriosis. Physiotherapists trained in pelvic health can help release and relax tight muscles, reduce spasms, and improve pelvic floor coordination, which can ease pelvic pain, bladder, and bowel symptoms.
- **Regular Exercise**: Physical activity, particularly low-impact exercises like yoga and swimming, can help reduce inflammation and improve endorphin release, providing natural pain relief.
- **Stress Reduction Techniques**: Mindfulness, meditation, and acupuncture may help manage stress and pain perception.
- **Heat Therapy**: Applying heat pads to the lower abdomen can provide symptomatic relief during painful episodes.

2. Non-Hormonal Pain Management

For women who prefer not to use hormonal treatments or cannot tolerate them, pain management is essential.

- **Non-Steroidal Anti-Inflammatory Drugs (NSAIDs)**: Medications such as ibuprofen and naproxen help reduce inflammation and alleviate pain associated with endometriosis.
- **Neuromodulators**: In some cases, medications like gabapentin or amitriptyline may be used for chronic pain that does not respond to standard treatment.
- **Pain Management Clinics**: Some women suffer from a mixture of acute and chronic pelvic pain. Long term inflammatory processes in endometriosis can result in chronic pain. Over time, your nervous system can become **more sensitive**, meaning it starts to overreact to signals that wouldn't normally be painful. This is known as **central sensitisation**. Pain clinics specialise in treating people with this kind of complex pain.

3. Hormonal Therapies

Hormonal treatments aim to suppress the growth of endometrial tissue outside the uterus by reducing oestrogen levels. These treatments do not cure endometriosis but can significantly alleviate pain and improve quality of life. They can extend the duration of symptom improvement both alone and following surgery.

- **Combined Oral Contraceptives (COCs)**: These provide symptom relief and help regulate menstrual cycles, reducing pain and heavy bleeding. They work by suppressing ovulation and stabilising hormonal fluctuations. COCs are available in different formulations, and their effectiveness can vary from person to person. While generally well tolerated for long-term use, some women may experience side effects such as nausea, breast tenderness, and an increased risk of blood clots. Symptoms may return once treatment is stopped.
- **Progestins and Progesterone Therapy**: These therapies are more effective in reducing pain compared to COCs and can be administered in various forms such as oral tablets, intrauterine devices, or injections. They work by sometimes suppressing ovulation and by thinning the endometrial lining (and therefore the endometriosis) which reduces inflammation and prevents further lesion growth.

  The intrauterine system (IUS), such as the levonorgestrel-releasing device, provides localized hormone release, minimising systemic side effects while offering long-term symptom control. The most common side effect is unscheduled and erratic bleeding. Other side effects such as bloating and mood changes are more common with oral agents. There is limited evidence that progesterones cause weight gain except those used in the injectable form (depoprovera)

  Most side effects occur particularly in the initial months of use and will settle by 6 months. Long-term safety is generally well-established, making progestins a viable option for women seeking effective, continuous management of endometriosis-related pain.

- **Dienogest**: is another progestin that has shown high efficacy in controlling endometriosis-related pain while being well tolerated over long-term use. It is currently licensed in the Uk for treatment of disease and has been shown to be as effective as medications that induce menopause without some of their side effects. Dienogest can affect your menstrual cycle, and you may have irregular bleeding or no periods at all while taking it. However, it is **not licensed as a contraceptive**, so it's important to use barrier contraception to avoid becoming pregnant. Dienogest is **not considered safe during pregnancy**, so you should avoid getting pregnant while taking it.
- **GnRH Agonists and Antagonists**: These drugs have been considered the medical gold standard and offer strong symptom relief by significantly suppressing oestrogen levels, which helps reduce the growth of endometrial lesions and alleviate pain. However, they induce a hypoestrogenic state, leading to side effects such as hot flashes, mood changes, vaginal dryness, and bone loss, which limits their duration of use. To mitigate these side effects, they are typically prescribed with hormone replacement therapy (HRT) add-back, which involves small doses of oestrogen and/or progestogen to protect bone density and alleviate menopausal symptoms while maintaining therapeutic effectiveness against endometriosis.
    - **GnRH Agonists (Leuprorelin, Goserelin):** These initially cause a temporary increase in oestrogen levels (flare effect) before downregulating the pituitary gland to suppress oestrogen production. They are highly effective for symptom relief but can cause significant bone mineral density (BMD) loss (approximately 3-5% over six months), requiring the use of add-back therapy (low-dose oestrogen or progestogen) to mitigate adverse effects. They are currently Licensed for 6-12 months in the UK, however in some cases use may be extended with bone scans every 24 months.
    - **GnRH Antagonists (Relugolix with oestradiol/norethisterone):** These directly block GnRH receptors, leading to a rapid reduction in oestrogen without the initial flare effect seen in agonists. They have a comparable efficacy to agonists but cause **less BMD loss** (approximately 1-3% over six months). The combination with add-back therapy helps reduce menopausal symptoms and bone loss, making them suitable for longer-term use. Licensed for up to 24 months in the UK, however in some cases use may be extended with bone scans every 24 months.

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Comparison of Hormonal Treatments

Type of Hormone Treatment	Examples	Efficacy	Benefits	Side Effects	Risks	Length of Use (UK)
Combined Oral Contraceptives (COCs)	Ethinylestradiol + progestogen	Moderate symptom relief, slows disease progression	Regulates menstrual cycles, reduces bleeding and pain	Nausea, breast tenderness, breakthrough bleeding	Increased risk of blood clots, may not fully prevent progression	Long-term
Progestins and Progesterone Therapy	Norethisterone, medroxyprogesterone, levonorgestrel IUS	Effective for pain relief and disease suppression	Reduces inflammation, suppresses endometrial growth	Irregular bleeding, weight gain, mood changes	May cause bone loss with long-term use (injection forms)	Long-term
Dienogest	Dienogest 2mg daily	Highly effective for pain, slows progression better than COCs	Specific for endometriosis, well-tolerated, does not act as contraception	Irregular bleeding, headache, decreased libido	Long-term safety data limited, but generally well tolerated	Long-term
GnRH Agonists	Leuprorelin, goserelin	Very effective at pain relief and lesion suppression	Strongest suppression of estrogen, reduces lesion size	Hot flashes, mood swings, vaginal dryness	Significant bone loss (~3-5% BMD loss per 6 months)	6-12 months*
GnRH Antagonists	Relugolix with estradiol/norethisterone	Comparable efficacy to GnRH agonists, faster onset	Rapid suppression of estrogen, add-back therapy reduces bone loss	Headache, fatigue, nausea	Less bone loss than agonists (~1-3% BMD loss per 6 months)	Licensed for up to 24 months in the UK *

4. Fertility Considerations

For women trying to conceive, medical management must be tailored accordingly. All hormonal treatments must be avoided whilst trying to conceive as they will significantly reduce the likelihood of pregnancy. Alternative approaches such as non-hormonal treatment and sometimes assisted reproductive technologies (ART) may be considered. In cases where endometriosis impacts fertility, surgical intervention may be an option to improve reproductive outcomes.

5. More Information

For additional support, advice, and the latest information on endometriosis, the following resources may be helpful:

- **Endometriosis UK** (www.endometriosis-uk.org): A leading UK charity offering patient support, educational resources, and advocacy for those affected by endometriosis.
- **NHS Endometriosis Information** (www.nhs.uk): Provides reliable medical information on symptoms, diagnosis, and treatments available in the UK.
- **British Society for Gynaecological Endoscopy (BSGE)** (www.bsge.org.uk): Offers professional guidance and information on surgical and medical management options for endometriosis.

References:

- National Institute for Health and Care Excellence (NICE). Endometriosis: diagnosis and management. NICE Guideline NG73. 2017.
- Taylor HS, Kotlyar AM, Flores VA. Endometriosis-associated pain: mechanisms and management. *Nat Rev Endocrinol.* 2021;17(11):654-670.
- Surrey ES, Taylor HS, Levy B, et al. Long-term effects of GnRH analogues on bone mineral density in women with endometriosis. *J Clin Endocrinol Metab.* 2021;106(10):e3943-e3953.
- SPIRIT Phase 3 Trial: Evaluating the efficacy and safety of relugolix combination therapy for the management of endometriosis-related pain.
- LIBERTY Trials: Investigating the safety and efficacy of relugolix in women with moderate to severe endometriosis and fibroid-associated pain.