

## Guideline on Prescribing of Gonadorelin (GnRH) Analogues in treatment of Endometriosis, Uterine Fibroids (including pre-op use) or prior to Endometrial Resection

### 1. BACKGROUND

Endometriosis is a chronic condition characterised by growth of endometrial tissue in sites other than the uterine cavity. The commonest symptom of endometriosis is pain, usually manifesting as dysmenorrhoea or dyspareunia and non-cyclic pelvic pain and sub-fertility. Gonadorelin analogues, also known as Gonadotrophin Releasing Hormone (GnRH) analogues are used in the treatment of endometriosis. Administration of these agents produces an initial phase of stimulation; continued administration is followed by a down regulation of gonadotrophin releasing hormone receptors thereby reducing the release of gonadotrophins (FSH and LH). This in turn leads to inhibition of androgen and oestrogen production.

Endometrial ablation is a modern surgical treatment for menorrhagia after medical methods have failed to control symptoms. There are many methods by which the endometrium can be ablated or resected. Patients having resection benefit from the endometrium being as thin as possible prior to surgery. Gonadorelin analogues give excellent endometrial suppression with a single dose administered prior to menstruation a month before surgery.

Uterine fibroids are the most common benign tumours in women of reproductive age. Common symptoms include menorrhagia and anaemia, but uterine fibroids can also cause pelvic pain, dysmenorrhoea and pressure effects, which can affect quality of life and fertility. Gonadorelin analogues can be used pre-operatively to reduce volume of fibroids and suspend menstruation, or as an intermittent treatment in patients in who wish to avoid surgery or are unsuitable for surgery.

Other unlicensed indications: Gonadorelin analogues are also used for treatment of other conditions either whilst waiting surgery or where surgery is not an option. These include chronic pelvic pain; premenstrual syndrome where other treatments have failed; severe menstrual disorders in the peri-menopausal period. Where treatment is continued for more than six months, add back hormonal therapy (e.g. combined HRT or tibolone) should be prescribed to reduce risk of trabecular bone density loss.

This document provides guidance on prescribing and of gonadorelin analogues and progesterone receptor modulators for these indications.

**Treatment will be initiated by specialist and continued by GP following assessment and recommendation from specialist.**

## 2. INDICATION

See sections 1 & 3

## 3. DOSE / DURATION

### Treatment with Gonadorelin analogues:

Patients should be prescribed a licensed treatment, where available, with the lowest acquisition cost.

Drug Name	Trade name	Dose for: Endometriosis, chronic pelvic pain*, PMS, severe menstrual disorders*	Endometrial ablation dose	Uterine fibroids dose
Goserelin	Zoladex®	3.6mg every 28 days	3.6mg single dose	3.6mg every 28 days**
Leuporelin	Prostap SR DCS® Prostap 3 DCS®	3.75 mg every 28 days OR 11.25 every 3 months	3.75mg single dose	3.75mg every 28 days**
Triptorelin	Decapeptyl SR®	3mg every 28 days OR 11.25mg every 3 months	Not licensed	3mg every 28 days
	Gonapeptyl Depot®	3.75mg every 28 days	Not licensed	3.75mg every 28 days**

\* unlicensed indications \*\* licensed for pre-op treatment of uterine fibroids only

Injection sites should be changed each time.

No dosage adjustments are required for renal or hepatic impairment or in the elderly.

### Duration of Treatment with Gonadorelin analogues:

- Endometriosis: Continue every 4 weeks or 3 months for up to 6 months. Repeat courses should not be administered due to the concern of reduced bone mineral density. Initial dose can be given at any time of the menstrual cycle but some manufacturers advise first dose to be given within first 5 days of cycle for optimal effect.
- Endometrial resection: Given as a single dose in the week before a period, 5-6 weeks prior to resection surgery.
- Uterine fibroids: Continue every 4 weeks for a minimum of 3 months. Treatment can be continued for up to 6 months if advised by specialist. Initial dose can be given at any time of the menstrual cycle but some manufacturers advise first dose to be given within first 5 days of cycle for optimal effect.
- Chronic pelvic pain: Continue every 4 weeks or 3 monthly until surgery, or where surgery is not an option - duration and supplementary treatment to be advised by specialist
- Severe menstrual disorders in perimenopausal period, PMS: Duration and supplementary treatment to be advised by specialist

## 5. DRUG INTERACTIONS

### Interactions for Gonadorelin analogues:

Drugs which raise the prolactin levels should not be used at the same time as they may reduce the level of LHRH receptors in the pituitary.

## 6. ADVERSE EFFECTS

### Gonadorelin analogues

Skin rashes have been reported but are generally mild and occasionally local reactions such as mild bruising at the injection site can occur.

Pharmacological effects include hot flushes, sweating and loss of libido: headaches, mood changes including depression, vaginal dryness and change in breast size have also been noted, although this is highly unlikely to occur with the single dose used prior to endometrial ablation. During early treatment, some women may experience vaginal bleeding of variable duration and intensity. This occurs usually in the first month after starting treatment and probably represents oestrogen withdrawal bleeding and is expected to stop spontaneously. Serum oestradiol concentrations will be initially enhanced if the first injection is administered during the follicular phase of the menstrual cycle but levels become suppressed approximately 21 days after the first depot injection if it is given immediately prior to menstruation. This produces endometrial thinning and will result in amenorrhoea in the vast majority of patients.

Rarely some women may enter the menopause during treatment and do not resume menses on cessation of treatment.

Prolonged use of more than 6 months may cause a loss in bone mineral density in women and should be used with caution in women with known metabolic bone disease

**Details of contraindications, cautions, drug interactions and adverse effects listed for all drugs above are not exhaustive. For further information always check with BNF [www.bnf.org.uk](http://www.bnf.org.uk) or SPC ([www.medicines.org.uk](http://www.medicines.org.uk)).**

## 7. MONITORING

Diabetic patients - when the drug is initiated, the specialist will counsel the patient that this may affect their diabetes control. The GP would then monitor the patient as usual as part of their ongoing care.

## 8. INFORMATION TO PATIENT

### Patients should be informed of risks and benefits of treatment, including

- Common adverse effect
- Need for non hormonal contraceptive
- Importance of compliance for successful surgery
- For unlicensed indications, patients should be informed that treatment is unlicensed and given sufficient information to allow them to make an informed decision, as per GMC guidance.

## APPROVAL PROCESS

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