

Shared care guidelines

GONADORELIN ANALOGUE DEPOTS - for endometriosis and uterine fibroids

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).

It is essential that a transfer or sharing of prescribing responsibilities should not take place without the sharing of information between the Prescriber and the individual GP, and their mutual agreement to this to ensure their full confidence when prescribing.

These are not rigid guidelines. In all cases, Consultants and GPs should clearly communicate regarding the appropriate management of individual patients. As always, the doctor who prescribes the medication has the clinical responsibility for the drug, the consequences of its use.

1.0 Licensed indication:

Management of endometriosis, including pain relief and reduction of endometriotic lesions
Endometrial preparation prior to inter-uterine surgical procedures including endometrial ablation or resection.
Preoperative management of uterine fibroids to reduce their size and associated bleeding.

2.0 Dosage and Administration

Drug	Proprietary Name	Presentation	Administration	Dose	Indication(s)	Maximum treatment duration
Goserelin	Zoladex	3.6mg implant	Subcutaneous (SC) injection into anterior abdominal wall	3.6mg once every 28 days	Endometriosis	6 months
					Endometrial Thinning	8 weeks
					Uterine Fibroids	3 months
Leuprorelin	Prostap SR	3.75mg vial plus pre-filled diluent syringe	SC or intramuscular (IM) injection	3.75mg once every 28 days	Endometriosis	6 months
					Endometrial Thinning	Stat dose
					Uterine Fibroids	6 months
Leuprorelin	Prostap 3 DCS	11.25mg vial plus pre-filled diluent syringe	SC or intramuscular (IM) injection	11.25mg once every 3 months	Endometriosis	6 months
Triptorelin	Decapeptyl SR	11.25mg vial plus pre-filled solvent syringe	SC or deep intramuscular injection	11.25mg once every 3 months	Endometriosis	6 months
Triptorelin	Decapeptyl SR	3 mg vial plus pre-filled solvent syringe	SC or deep intramuscular injection	3mg once every 28 days	Endometriosis	6 months
					Uterine Fibroids	6 months
Triptorelin	Gonapeptyl	3.75mg vial plus pre-filled solvent syringe	SC or deep intramuscular injection	3.75mg once every 28 days	Endometriosis	6 months
					Uterine Fibroids	6 months

3.0 Cautions and Contraindications

3.1 Precautions

Since menstruation should stop with effective doses of Gonadorelin analogues, the patient should notify her physician if regular menstruation persists.

Development or aggravation of diabetes may occur; therefore diabetic patients may require more frequent monitoring of blood glucose during treatment.

Hepatic dysfunction and jaundice with elevated liver enzyme have been reported. Therefore, close observation should be made and appropriate measures taken if necessary.

Spinal fracture, paralysis, hypotension and worsening of depression have been reported.

During the early phase of therapy, sex steroids temporarily rise above baseline because of the physiological effect of the drug. Therefore, an increase in clinical signs and symptoms may be observed during the initial days of therapy, but these will dissipate with continued therapy.

The induced hypo-oestrogenic state results in a small loss in bone density over the course of treatment, some of which may not be reversible. The extent of bone demineralisation due to hypo-oestrogenaemia is proportional to time and, consequently, is the adverse event responsible for limiting the duration of therapy to 6 months. The generally accepted

level of bone loss with Gonadorelin analogues is 5%. During one six-month treatment period, this bone loss should not be important. In patients with major risk factors for decreased bone mineral content such as chronic alcohol and/or tobacco use, strong family history of osteoporosis, or chronic use of drugs that can reduce bone mass such as anticonvulsants or corticosteroids, Gonadorelin analogue therapy may pose an additional risk. In these patients, the risks and benefits must be weighed carefully before therapy is instituted. This is particularly important in women with uterine fibroids where age related bone loss may have already begun to occur.

Therefore, before using Gonadorelin analogues, patients with major risk factors for decreased bone mineral content (see above) who will be receiving Gonadorelin analogues for 6 months should have their bone density measured and where results are below the normal (5th percentile by DEXA scan) range, Gonadorelin analogue therapy should not be started.

Patients should be warned of the possibility of abnormal bleeding or pain as a consequence of the acute degeneration of the fibroids in case earlier surgical intervention is required.

In women receiving Gonadorelin analogues for the treatment of endometriosis, the addition of HRT (an oestrogen and progestogen) has been shown to reduce bone mineral density loss and vasomotor symptoms. If appropriate this could be co administered

3.2 Contra-indications

Hypersensitivity to any of the ingredients or to synthetic Gonadorelin or Gonadorelin derivatives.

Women who are or may become pregnant while receiving the drug.

Women who are breastfeeding or have undiagnosed abnormal vaginal bleeding.

4.0 Adverse effects:

Side effects seen with Gonadorelin analogues are due mainly to the specific pharmacological action, namely increases and decreases in certain hormone levels.

Adverse events which have been reported infrequently include peripheral oedema, pulmonary embolism, hypertension, palpitations, fatigue, muscle weakness, diarrhoea, nausea, vomiting, anorexia, fever/chills, headache (occasionally severe), hot flushes, arthralgia, myalgia, dizziness, insomnia, depression, paraesthesia, visual disturbances, weight changes, hepatic dysfunction, jaundice, increases in liver function test values (usually transient) and irritation at the injection site. Changes in blood lipids and alteration of glucose tolerance have also been reported which may affect diabetic control. Thrombocytopenia and leucopenia have been reported rarely. Hypersensitivity reactions including rash, pruritus, urticaria, and rarely, wheezing or interstitial pneumonitis have also been reported. Anaphylactic reactions are rare.

Spinal fracture, paralysis, hypotension and worsening of depression have been reported (precautions section 3.1).

Infarction of pre-existing pituitary adenoma has been reported rarely after administration of both short- and long-acting Gonadorelin analogues

Those adverse events occurring most frequently with Gonadorelin analogues are associated with hypo-oestrogenism; the most frequently reported are hot flushes, mood swings including depression (occasionally severe), and vaginal dryness. Oestrogen levels return to normal after treatment is discontinued.

The induced hypo-oestrogenic state results in a small loss in bone density over the course of treatment, some of which may not be reversible (see precautions section 3.1).

Breast tenderness or change in breast size may occur occasionally. Hair loss has also been reported occasionally.

Vaginal haemorrhage may occur during therapy due to acute degeneration of submucous fibroids (see precautions section 3.1

5.0 Monitoring requirements:

Baseline liver function should be determined prior to treatment and repeated during treatment if there is clinical reason for concern.

Diabetic patients should be counselled to increase the frequency with which they monitor blood glucose levels.

A DEXA scan should be performed by secondary care physician in patients with major risk factors for decreased bone mineral content and treatment should not be initiated if result is below normal levels.

See Section 3

6.0 Action to be taken if abnormal results/adverse effects:

Refer back to secondary care specialist (may be specialist nurse or doctor)

7.0 Drug interactions:

Since androgen deprivation treatment may prolong the QT interval, the concomitant use of Zoladex with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes such as class IA (e.g. quinidine, disopyramide) or class III (e.g. amiodarone, sotalol, dofetilide, ibutilide) antiarrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, etc. should be carefully evaluated.

8.0 Specialist responsibilities:

- To initiate therapy and ensure monitoring requirements are met. i.e. To carry out DEXA scan in patients with major risk factors for developing reduced bone mass who will be receiving therapy for greater than 6 months, to carry out baseline LFT levels for patients with previous or current hepatic dysfunction.
- To communicate with primary care colleagues and provide ongoing treatment plan.

9.0 GP responsibilities:

- Ensure review of communication from secondary care on hospital attendances and treatment plan prior to prescribing the continuing supply.
- Prescribe a supply of the most cost effective Gonadorelin analogue injection.
- Liaise with the secondary care gynaecology team regarding any possible adverse effects of treatment. These may include; peripheral oedema, pulmonary embolism, hypertension, palpitations, muscle weakness, fever/chills, arthralgia, myalgia, depression, paraesthesia, visual disturbances, hepatic dysfunction, jaundice, increases in liver function test values, thrombocytopenia and leucopenia, hypersensitivity reactions including rash, pruritis, urticaria, wheezing or interstitial pneumonitis. Persistent regular menstruation must also be reported

10.0 Patient responsibilities:

- Report any adverse effects to their GP and/or specialist whilst undergoing treatment.
- Ensure they have a clear understanding of the indication for treatment and the prescribed dose.

11.0 Secondary care review: To be performed on completion of course of Gonadorelin analogue

- Perform any necessary clinical examination.
- Enquire on any symptoms potentially attributable to treatment.
- Perform biochemical investigations if deemed clinically appropriate.
- Refer for appropriate further investigations based on abnormalities elicited above.

12.0 Availability/Other special considerations

Leuprorelin goserelin or triptorelin may be used for treatment irrespective of which was initiated in secondary care to allow for the most cost effective treatment course.

Back up advice and support	Specialist	Telephone/Fax	E-mail address:
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