NHS
Pan Mersey
Area Prescribing Committee

Prescribing Support Information

Gonadorelin Analogues
(triptorelin, goserelin, leuprorelin)

AMBER patient retained by specialist

These medicines have been categorised as Amber Patient Retained for the indications in this document by the Pan-Mersey Area Prescribing Committee. They have been categorised as Red for infertility and hypersexuality.

Your patient has been identified as being suitable to receive a gonadorelin analogue in accordance with the indications detailed below. The first dose has been administered in secondary care and the patient has been reviewed to assess the efficacy and adverse effects of the treatment by the specialist team. Triptorelin, administered either at 6 monthly (Prostate cancer only), 3 monthly or monthly intervals, is the Pan Mersey first line choice. See table for full list of licensed indications. Where the course of treatment is short, the specialist may wish to continue prescribing until the course is complete.

This medicine has been considered as appropriate for prescribing in primary care and the information contained in this document has been provided to support you to prescribe the medicine for your patient in the community.

Your patient will remain under the care of the specialist team whilst receiving this medicine.

Indication

- Treatment of hormone dependent locally advanced or metastatic prostate cancer:
  - Patients with locally advanced, non-metastatic prostate cancer, as an alternative to surgical castration
  - Metastatic prostate cancer
  - Adjuvant to radiotherapy or radical prostatectomy in high-risk localised or locally advanced prostate cancer
  - Neo-adjuvant prior to radiotherapy in high-risk localised or locally advanced prostate cancer
- Treatment of advanced breast cancer in women suitable for hormonal manipulation and as an alternative to chemotherapy for women with oestrogen receptor- positive early breast cancer.
- 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.
- Treatment of precocious puberty in children.

Drug	Presentation	Administration	Dose	Indication(s)	Recommended treatment duration
Triptorelin	22.5mg vial plus solvent, syringe and needle	Intramuscular injection	22.5mg once every 6 months	Prostate cancer	Long term
				Precocious puberty	Until specified bone maturation age
Triptorelin	11.25mg vial plus pre-filled solvent syringe	Intramuscular injection	11.25mg once every 3 months	Endometriosis	6 months
				Prostate cancer	Long term
				Precocious puberty	Until specified bone maturation age
Triptorelin	3.75mg pre-filled syringe plus prefilled solvent syringe	SC injection or deep IM	3.75mg every 28 days	Endometriosis	6 months
				Uterine fibroids	3-6 months
				Prostate cancer	Long term
				Precocious puberty	Until specified bone maturation age
Triptorelin	3 mg vial plus pre-filled solvent syringe	Intramuscular injection	3mg once every 28 days	Breast cancer	Long term
				Endometriosis	6 months
				Uterine fibroids	3-6 months
				Prostate cancer	Long term
Goserelin	3.6mg implant	SC injection into anterior abdominal wall	3.6mg every 28 days	Breast cancer	Long term
				Endometriosis	6 months
				Uterine fibroids	3 months
				Endometrial thinning	4-8 weeks
				Prostate cancer	Long term
Goserelin	10.8mg implant	SC injection into anterior abdominal wall	10.8mg every 12 weeks	Prostate cancer	Long term
Leuprorelin	3.75mg vial plus pre-filled diluent syringe	SC or intramuscular injection	3.75mg once every 28 days	Breast cancer	Long term
				Endometriosis	6 months
				Uterine Fibroids	3-4 months
				Endometrial Thinning	Stat dose
				Prostate cancer	Long term
				Precocious puberty	Until specified bone maturation age
Leuprorelin	11.25mg vial plus pre-filled diluent syringe	SC or intramuscular injection	11.25mg once every 3 months	Breast cancer	Long term
				Endometriosis	6 months
				Prostate cancer	Long term
				Precocious puberty	Until specified bone maturation age

Monitoring recommendations

Baseline liver function should be determined by specialist team prior to treatment and the GP can repeat this during treatment if there is clinical reason for concern.

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.

Prostate cancer: PSA (prostate specific antigen) levels should be monitored by the specialist team 6 monthly.

Prevention of tumour flare

In prostate cancer, during the initial stage of treatment increased production of testosterone may be associated with progression of prostate cancer. In susceptible patients this tumour 'flare' may cause spinal cord compression,

ureteric obstruction or increased bone pain. Men at risk of tumour 'flare' should be monitored closely during the first month of therapy.

To prevent the tumour 'flare', patients are usually provided with a 2-4-week course of an antiandrogen such as bicalutamide or cyproterone at the time of their first injection. This will be prescribed and supplied by the specialist team.

Prevention of osteoporosis

The NICE Clinical Knowledge Summary for the management of endometriosis (2014) recommends that add-back hormone replacement therapy (HRT) or tibolone 2.5mg daily is initiated in secondary care for women who are taking GnRH analogues, to reduce the risk of adverse effects such as osteoporosis or menopausal symptoms. Specialist advice should be sought if the symptoms of endometriosis are reactivated. Prescribing will be for the duration of GnRH analogue therapy and the first month will be supplied by the specialist.

How long the medicine should be prescribed for

The specialist team is responsible for adjusting or stopping treatment. See table for recommended treatment duration.

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.

Adverse effects

Side effects seen with gonadorelin analogues are due mainly to the specific pharmacological action, namely increases and decreases in certain hormone levels, such as impotence and decreased libido, hot flushes, mood swings, vaginal dryness, sweating and, rarely, orchiatrophy or gynaecomastia

Signs and symptoms of prostate cancer may worsen initially if measures are not taken to prevent tumour 'flare' (as detailed above).

Women should be warned of the possibility of abnormal bleeding or pain due to the acute degeneration of the fibroids and this should be reported to the specialist if it occurs.

Other side-effects include hypersensitivity reactions (rashes, pruritus, asthma, and rarely anaphylaxis), injection site reactions, headache (rarely migraine), visual disturbances, dizziness, arthralgia and possibly myalgia, hair loss, peripheral oedema, gastro-intestinal disturbances, weight changes, sleep disorders, breast tenderness or hair loss.

Caution is required in patients with metabolic bone disease because reduced bone mineral density can occur.

Please note this list is not exhaustive – refer to SPC for complete list.

Special warnings/cautions

Long-term androgen deprivation is associated with increased risk of bone mineral loss. 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 and dexa scans may be performed initially by the specialist team.

Patients developing signs of ureteric obstruction or spinal cord compression during treatment should be referred immediately to the specialist team or emergency department.

Interaction with other medicines

Drugs which raise prolactin levels (e.g. anti-psychotics, metoclopramide, domperidone) should not be prescribed concomitantly as they reduce the level of GnRH receptors in the pituitary. When co-administered with drugs affecting pituitary secretion of gonadotropins, caution should be exercised.

Since androgen deprivation treatment may prolong the QT interval, the concomitant use of with medicinal products known to prolong the QT interval or medicinal products able to induce Torsade de pointes should be carefully evaluated.

Please refer to SPC for full list of drug interactions.

Referral back to specialist

Referral back to the specialist should be considered if any adverse effects are reported by the patient. Any deterioration in symptoms should be reported.

Administration information

Rotate injection sites to prevent atrophy and nodule formation. For product specific information, please contact the pharmaceutical company who provide training or advice for administration of their product.

Missed/Delayed dose advice

When the dose has been missed or delayed it is important to administer at the earliest opportunity.
Triptorelin: dose may be administered 7-10 days before or after the due date.
Goserelin: dose may be administered 3-7 days before or after the due date.
Leuprorelin: dose may be administered 3 days before or after the due date.
For patients with prostate cancer, if the period of time since the dose was due is over 3 months it should be discussed with the specialist team and prescribing an antiandrogen (as per management of tumour flare above) should be considered. An in-house incident form should be completed.

Contact details for advice

Please refer to the contact details included in the clinic letter issued by the specialist.

Signposting

Prostate Cancer UK produce a booklet ‘Living with hormone therapy’ along with a factsheet which can be downloaded/ordered via their website.

https://prostatecanceruk.org/