Guidance for the Prescribing of Goserelin, Leuprorelin & Triptorelin in the treatment of Prostate Cancer (Amber-G)

1.0 Introduction

This document sets out guidance for the assessment and treatment of patients who are prescribed the gonadorelin analogues goserelin, leuprorelin & triptorelin for the treatment of prostate cancer and delineated responsibilities when care for the patient is initiated in Secondary Care and transferred to Primary Care for continuation.

It is intended to provide clear guidance to General Practitioners (GPs) and hospital prescribers regarding the procedures to be adopted when clinical (and therefore prescribing and financial) responsibility for a patient's treatment on goserelin, leuprorelin or triptorelin is shared between secondary and primary care.

The decision to start a patient on treatment of carcinoma of the prostate should be taken by a Consultant Urologist.

	Traffic light system classification			
Drug Class	**Green**	**Amber[A]**	**Amber-G[AG]**	**Red[R]**
Gonadorelin analogues			Goserelin Leuprorelin Triptorelin	

Amber G (AG) – Drug must be initiated and titrated to stable dosage by specialist before GPs take over prescribing responsibility. Once medical condition and drug dosage is stable, there is no specific requirement for ongoing monitoring

This guidance applies only for the indication for which the drugs are stated to be used for. It should not be used for other indications listed on the Doncaster & Bassetlaw APC traffic light system or for unlicensed indications for the drug.

2.0 Background Information

Metastatic cancer of the prostate usually responds to hormonal treatment aimed at androgen depletion. Standard treatments include bilateral subcapsular orchidectomy or use of a gonadorelin analogue (buserelin, goserelin, , leuprorelin, or triptorelin). Response in most patients lasts for 12 to 18 months. No entirely satisfactory therapy exists for disease progression despite this treatment (hormone-refractory prostate cancer) but occasional patients respond to other hormone manipulation e.g. with an anti-androgen.

Gonadorelin analogues are as effective as orchidectomy or diethylstilbestrol but are expensive and required parenteral administration at least initially. They cause initial stimulation then depression of luteinising hormone release by the pituitary.

2.1 National Institute for Health and Clinical Excellence (NICE)

In January 2014, the National Institute for Clinical Excellence (NICE) published a Clinical Guideline on the diagnosis and treatment of prostate cancer. Full guidance can be found at:
https://www.nice.org.uk/guidance/cg175/resources/guidance-prostate-cancer-diagnosis-and-treatment-pdf

2.3 Dosage

Response to gonadorelin agonists in most patients lasts for 12 to 18 months.

2.4 Administration

The goserelin injection is relatively simple to administer. There maybe some discomfort on administration since the instrument used to insert the pellet is a small trocar rather than a needle.

The leuprorelin injection uses a small needle and can be more patient friendly.

Triptorelin is presented as a dry powder for reconstitution (solution provided). It is administered via the needle supplied in the pack and it is an intramuscular injection.

GP's/Practice Nurses are welcome to attend the Urology Clinics at DRI by pre-arrangement for instruction in the technique.

2.5 Adverse Events

Ureteric obstruction/spinal cord compression
Patients at risk of developing ureteric obstruction or spinal cord compression should be considered carefully and the patients monitored closely during the first month of therapy.
Consideration should be given to the initial use of an anti-androgen (e.g. Cyproterone acetate 300mg daily for three days before, and three weeks after commencement of Zoladex) at the start of LHRH (Luteinizing Hormone-Releasing Hormone) agonist therapy since this has been reported to prevent the possible sequelae of the initial rise in serum testosterone.
Should urological/neurological complications occur, these should be treated by appropriate specific measures.

Bone mineral density
The use of LHRH agonists may cause reduction in bone mineral density. In men, preliminary data suggest that the use of a bisphosphonate in combination with an LHRH agonist may reduce bone mineral loss. Particular caution is necessary in patients with additional risk factors for osteoporosis e.g. chronic alcohol abusers, smokers, long-term therapy with anticonvulsants or corticosteroids, family history of osteoporosis).

Blood Sugar
Reduction in glucose tolerance has been observed in patients receiving LHRH agonists. This may manifest as diabetes or loss of glycaemic control in patients with pre-existing diabetes mellitus. Monitoring of blood glucose levels may be considered if appropriate. Development or aggravation of diabetes may also occur; therefore diabetic patients may require more frequent monitoring of blood glucose during treatment.

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

Mood Changes

Mood changes, including depression have been reported. Patients should be informed accordingly and treated as considered appropriate if symptoms occur. Patients with known depression and patients with hypertension should be monitored carefully.

Drug-test Readings
Treatment with Goserelin may lead to positive reactions in anti-doping tests.

Sexual Dysfunction
Impotence and decreased libido will be expected.

General
Side effects similar to the menopause in women and orchidectomy in men and include hot flushes and sweating. Hot flushes are a fairly common side effect and can be managed by the addition of cyproterone in low dose (50mg bd) for about six weeks. Secondary care should initiate this treatment, and subsequent prescriptions maybe obtained from the GP on their agreement.

3.0 Drug Treatment Summary

For contraindications or full list of interactions please see the current BNF https://www.medicinescomplete.com/mc/ or summary of product characteristics for the individual drug http://www.medicines.org.uk/

Drug, dose & TLS listing	Adverse effects	Therapeutic monitoring	Consultant / GP	Clinical relevant drug interactions
1. Gonadorelin (LHRH) analogues				
1.1 Goserelin (Amber-G)				
Zoladex LA **Goserelin 10.8mg (as acetate) implant in SafeSystem® syringe applicator** **Treatment:** 10.8mg every 12 weeks **Elderly:** No dosage adjustment required **Renal or hepatic impairment:** No dosage adjustment required **Children:** Not indicated for use To be administered by subcutaneous injection into anterior abdominal wall	**Very Common** • Sexual dysfunction, e.g. impotence, decreased libido • Hot flushes • Sweating **Common** • Reduction in glucose tolerance • Ureteric obstruction/spinal cord compression • Fluctuations in blood pressure • Reduction in bone mineral density • Rash • Injection site reactions **Rare** • Anaphylaxis **Very Rare** • Pituitary tumour/apoplexy • Psychotic disorders **Frequency not known** • Mood changes, e.g. depression	Baseline monitoring: • PSA (Prostate specific antigen) levels • Blood Glucose Every 3 months: • PSA (Prostate specific antigen) levels General: • Injection site reactions • Side effects • Symptom control • Refer to specialist if patient presents with signs of clinical deterioration	Consultant GP	• Drugs which raise prolactin levels, e.g. antipsychotics

1.2 Leuprorelin (Amber-G)			
Lutrate 3 month Depot Leuprorelin acetate 11.25mg vial with 2ml vehicle-filled syringe (microsphere powder for reconstitution) **Treatment:** 11.25mg every 3 months **Elderly:** No dosage adjustment required **Children (under 18 years):** Not recommended for use To be administered by subcutaneous injection every 3 months	• Sexual dysfunction, e.g. impotence, decreased libido • Hot flushes • Sweating • Reduction in glucose tolerance • Ureteric obstruction/spinal cord compression • Fluctuations in blood pressure • Reduction in bone mineral density • Rash • Injection site reactions • Anaphylaxis • Pituitary tumour/apoplexy • Psychotic disorders • Mood changes, e.g. depression • Hair loss	Baseline monitoring: • PSA (Prostate specific antigen) levels • Blood Glucose Every 3 months: • PSA (Prostate specific antigen) levels General: • Injection site reactions • Side effects • Symptom control • Refer to specialist if patient presents with signs of clinical deterioration	
• **Decapeptyl SR Triptorelin 11.25mg powder for suspension, for injection.** **Treatment:** One intramuscular injection should be administered every 3 months. **Elderly:** No dosage adjustment required To be administered by intramuscular injection	**Very Common** • Asthenia • Hyperhidrosis • Back pain • Paraesthesia in lower limbs • Hot flush **Common** • Nausea • Fatigue • Injection site erythema • Injection site inflammation • Injection site pain • Injection site reaction • Oedema	Baseline monitoring: • PSA (Prostate specific antigen levels • Blood Glucose Every 3 months: • PSA (Prostate specific antigen)levels General: • Injection site reactions • Side effects • Symptom control • Refer to specialist if patient presents with	Drugs which raise prolactin levels should not be prescribed concomitantly as they reduce the level of GnRH receptors in the pituitary. When Decapeptyl SR is co-administered with drugs affecting pituitary secretion of gonadotropins, caution should be exercised and it is recommended that the patient's hormonal status be supervised.

• **Decapeptyl SR** **Triptorelin 22.5mg powder for suspension, for injection.** **Treatment:** One intramuscular injection should be administered every 6 months. **Elderly:** No dosage adjustment required To be administered by intramuscular injection	• Musculoskeletal pain • Pain in extremity • Dizziness • Headache • Depression • Mood changes • Erectile dysfunction • Loss of libido	signs of clinical deterioration	

4.0 Arrangements

A series of 3 one-monthly injections of goserelin, leuprorelin or triptorelin will be administered in the urology clinic and then the GP will be asked to take over the responsibility of the physical monitoring, prescribing and administering of the drug. This will be at a three or six-monthly interval depending on which injection is prescribed.

Unless previous use of leuprorelin injections has been problematic, or is in other ways contra-indicated, all patients on goserelin 10.8mg LA injections may be considered for change to leuprorelin 11.25mg SR injections or triptorelin SR 11.25mg.

At the time Secondary Care request Primary Care to take over the prescribing, patients will be on a 3 monthly injection. The Urology department has agreed that Primary Care may use a gonadorelin analogue of their choice. Changes between drugs and/or preparations may be undertaken providing the patient is adequately counselled. There is no requirement for additional monitoring, or for the Urology department to be formally notified by Primary Care.

5.0 References

- British National Formulary 68: September 2014
- Midlands Therapeutic Review and Advisory Committee (MTRAC) Verdict & Summary – Goserelin for the treatment of Prostate Cancer July 2008
- Midlands Therapeutic Review and Advisory Committee (MTRAC) Verdict & Summary – Leuprorelin for the treatment of Prostate Cancer July 2008
- Leicestershire Medicines Strategy Group: Full Shared Care Agreement for Gonadorelin Analogues in the treatment of Prostate Cancer March 2010
- Prostap 3 Leuprorelin Acetate Depot Injection 11.25mg: Summary of Product Characteristics. Last updated 27/07/2009
- Prostap SR: Summary of Product Characteristics. Last Updated 27/07/2009
- Zoladex LA 10.8mg: Summary of Product Characteristics. Last Updated 05/11/2009
- Zoladex 3.6mg Implant: Summary of Product Characteristics. Last Updated 23/11/2009
- Decapeptyl SR 3mg: Summary of Product Characteristics. Last Updated 17/05/13
- Decapeptyl SR 11.25mg: Summary of Product Characteristics. Last Updated 17/05/13
- Decapeptyl SR 22.5mg: Summary of Product Characteristics. Last Updated 17/05/13

6.0 Guidance Development

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