The Pennine Acute Hospitals NHS
NHS Trust

NHS

Greater Manchester Interface Prescribing Group Shared Care Template

Shared Care Guideline for LHRH analogues: Goserelin (Zoladex), Leuprorelin (Prostap) or Triptorelin (Decapeptyl SR) in the treatment of prostate cancer		Reference Number
Author(s)/Originator(s): (please state author name and department) *Updated by: Zahid Hussain Consultant Urologist* *Hafsa Sattar Surgical Pharmacist* *The Pennine Acute Trust*		**To be read in conjunction with the following documents:** Current Summary of Product characteristics (http://www.medicines.org.uk) BNF
Date approved by Commissioners: *08/08/2014*	**Review Date:** *08/08/2017*	

Please complete all sections

1. Licensed Indications	**Goserelin (Zoladex®):** • In the treatment of metastatic prostate cancer where Zoladex has demonstrated comparable survival benefits to surgical castrations. • In the treatment of locally advanced prostate cancer, as an alternative to surgical castration where Zoladex has demonstrated comparable survival benefits to an anti-androgen. • As adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer where Zoladex has demonstrated improved disease-free survival and overall survival. • As neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer where Zoladex has demonstrated improved disease-free survival. • As adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression where Zoladex has demonstrated improved disease-free survival.

	Leuprorelin (Prostap®): • Metastatic prostate cancer. • Locally advanced prostate cancer, as an alternative to surgical castration. • As an adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer. • As an adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression. • As neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer. **Triptorelin (Decapeptyl®)** • Treatment of patients with locally advanced, non-metastatic prostate cancer, as an alternative to surgical castration. • Treatment of metastatic prostate cancer. • As adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer. • As neoadjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer. • As adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression.
2. Therapeutic use & background	Goserelin, Leuprorelin and Triptorelin are synthetic luteinising hormone releasing hormone (LHRH) analogues. LHRH is normally released by the hypothalamus in a pulsatile manner. Chronic administration of these preparations produces an initial rise (hormonal flare) then, within a few weeks, a fall in pituitary derived luteinising hormone secretion. In men, this produces a reduction in testicular testosterone production, the levels of which remain within the castrate range for the duration of treatment. Since most prostate tumours are dependent on testosterone, suppression of its formation can retard or halt tumour growth.
3. Contraindications (please note this does not replace the SPC or BNF and should be read in conjunction with it).	Known severe hypersensitivity to the active substance, any of the excipients of this product or to synthetic gonadotrophin releasing homone (Gn-RH) or Gn-RH derivatives.
4. Prescribing in pregnancy and lactation	N/A

5. Dosage regimen for continuing care

Route of administration	*See below:*

Preparations available:

Preparation	Drug	Strength	Dosage
Zoladex	Goserelin	3.6mg depot	3.6mg by subcutaneous injection every 28 days
Zoladex LA	Goserelin	10.8mg depot	10.8mg by subcutaneous injection every 12 weeks
Prostap SR DCS	Leuprorelin	3.75mg	3.75mg by subcutaneous or IM injection every month
Prostap 3 DCS	Leuprorelin	11.25mg	11.25mg by subcutaneous injection every 3 months
Decapeptyl SR	Triptorelin	4.2mg (includes overage)	3.0mg by IM injection every 4 weeks
	Triptorelin	15mg (includes overage)	11.25mg by IM injection every 12 weeks
	Triptorelin	28mg (includes overage)	22.5mg by IM injection every 6 months

Is titration required		**No**

Secondary care will initiate and provide the anti-androgen bicalutamide for 28 days and will arrange for a repeat hospital visit after one week, in order to administer the first dose of a LHRH analogue. This will be administered by a Urology Nurse. A request to transfer prescribing and administration responsibilities for the LHRH analogue will then be made to the GP in primary care under shared care agreement.

Those GPs willing and competent to administer the first dose of LHRH analogue, and who are already doing so, could continue to do so.

Adjunctive treatment regime:

During the first 1-2 weeks of treatment in non-orchidectomised patients, the increased production of testosterone may be associated with progression of prostate cancer. In susceptible individuals this 'flare up' may cause spinal cord compression, ureteric obstruction or increased bone pain. Therefore concomitant use of an anti-androgen such as cyproterone acetate, flutamide or bicalutamide is recommended in all patients. This should be commenced in secondary care for 1 week before the first dose of LHRH analogue is administered and continued for up to 3 weeks after (total 4 weeks).

The use of LHRH agonists may cause reduction in bone mineral density. Particular caution is necessary in patients with additional risk factors for osteoporosis.

Conditions requiring dose reduction

e.g. impaired renal/ liver function

Goserelin - No dose reduction in renal/liver impairment or the elderly.

Triptorelin – No dose reduction in the elderly.

Leuprorelin – No dose reduction in the elderly. Hepatic dysfunction and jaundice with elevated liver enzyme reported. Close observation recommended and appropriate measures taken if necessary.

Usual response time:

Response itself is variable and will be monitored by secondary care.

Response time in those that do respond is also variable – usually several weeks to months.

Duration of treatment:

Neo-adjuvant patients suitable for radical radiotherapy: 3 to 6 months treatment to reduce tumour burden and prostate size prior to radiotherapy.

Adjuvant treatment after radiotherapy (in selected higher risk patients with adverse histological features): up to 3 years treatment; lifelong if particularly high risk.

Metastatic prostate cancer: treatment may continue lifelong. Can be used intermittently if treatment supervised by Urologist/Oncologist.

Treatment to be terminated as per advice of individual clinician on a case by case basis.

NB. All dose adjustments will be the responsibility of the initiating specialist unless directions have been specified in the medical letter to the GP.

6.Drug Interactions

For a comprehensive list consult the BNF or Summary of Product Characteristics

The following drugs must not be prescribed without consultation with the specialist:

Goserelin - Not known

Triptorelin - Drugs which raise prolactin levels should not prescribed concomitantly as they reduce the level of GnRH receptors in the pituitary.

Leuprorelin – No interaction studies performed

The following drugs may be prescribed with caution:

Triptorelin – When co-administered with drugs affecting pituitary secretion of gonadotrophins, caution should be exercised and it is recommended that the patient's hormonal status is supervised.

7. Adverse drug reactions

For a comprehensive list (including rare and very rare adverse effects), or if significance of possible adverse event uncertain, consult Summary of Product Characteristics or BNF

Specialist to detail below the action to be taken upon occurrence of a particular adverse event as appropriate. Most serious toxicity is seen with long-term use and may therefore present first to GPs.

Adverse event System – symptom/sign	**Action to be taken** Include whether drug should be stopped prior to contacting secondary care specialist	**By whom**
Cardiac failure, Myocardial infarction	Standard 1ry & 2ndry care management Inform Specialist. Do not stop drug.	GP
Glucose tolerance impaired	Standard primary care management. Inform Specialist. Do not stop drug.	GP
Blood pressure abnormal	Standard primary care management. Inform Specialist. Do not stop drug.	GP
Weight gain	Standard primary care management. Inform Specialist. Do not stop drug.	GP
Sleep disorder	Standard primary care management. Inform Specialist. Do not stop drug.	GP
Mood changes	Standard primary care management. Inform Specialist. Do not stop drug.	GP
Erectile dysfunction	Standard primary care management. Inform Specialist. Do not stop drug.	GP
Decreased libido	Standard primary care management. Inform Specialist. Do not stop drug.	GP
Injection site reaction	Rotate injection site. Consider alternate LHRH analogue. Inform Specialist. Do not stop drug.	GP
Bone pain	Clinical assessment. X-Ray if appropriate. Inform Specialist. Do not stop drug.	GP
Headache	Standard primary care management. Inform Specialist. Do not stop drug.	GP

	Hot flushes	Inform Specialist. Do not stop drug.	GP
	Hyperhidrosis	Inform Specialist. Do not stop drug.	GP
	Paraesthesia	Inform Specialist. Do not stop drug.	GP
	Gynaecomastia	Inform Specialist. Do not stop drug.	GP

The patient should be advised to report any of the following signs or symptoms to their GP without delay:
Increased risk of incident depression when undergoing treatment with LHRH analogues. Patient's should be informed accordingly and treated as appropriate if symptoms occur.

Rarely, treatment with LHRH analogues may reveal the presence of a previously unknown gonadotroph cell pituitary adenoma. These patients may present with sudden headache, vomiting, visual impairment and ophthalmoplegia.

Reduction of glucose tolerance may occur and manifest as diabetes or loss of glycaemic control in patients with pre-existing diabetes who are receiving LHRH agonists. Monitoring of blood glucose should be considered.

Patients may experience a temporary worsening of their prostate cancer (tumour flare), usually manifested by an increase in urinary symptoms and metastatic pain which can be managed symptomatically. These symptoms are usually transient and usually disappear in 1-2 weeks.

Any adverse reaction to a black triangle drug or serious reaction to an established drug should be reported to the MHRA via the "Yellow Card" scheme.

8.Baseline Investigations

Prostate Examination
Radiological Staging Investigations if appropriate.
PSA

9. Ongoing monitoring requirements to be undertaken by GP

Is monitoring required?	**Yes or No (if yes complete following section)** *Yes*

Monitoring	**Frequency**	**Results**	**Action**	**By whom**
Blood pressure	Every 3 months		As above	GP
Blood tests including PSA	Variable			to be requested by specialist

10. Pharmaceutical aspects

e.g. special storage requirements, washout periods Or where there are "no special considerations"

The injection site should be varied periodically.

Goserelin

1. Do not store above 25°C
2. Use only if pouch is undamaged. Use immediately after opening pouch.

Leuprorelin

1. Do not store above 25°C. Store in the original container to protect from light
2. The pre-filled syringe of PROSTAP 3, PROSTAP SR microsphere powder should be reconstituted immediately prior to administration by subcutaneous or intramuscular injection.
3. To prepare for injection, screw the plunger rod into the end stopper until the end stopper begins to turn.
4. Remember to check if the needle is tight by twisting the needle cap clockwise. Do not overtighten.
5. Holding the syringe upright, release the diluents by SLOWLY PUSHING the plunger until the middle stopper is at the blue line in the middle of the barrel. NOTE: Pushing the plunger rod quickly or over the blue line will cause leakage of the suspension from the needle.
6. Gently tap the syringe on the palm keeping the syringe upright to thoroughly mix the particles to form a uniform suspension. The suspension will appear milky. NOTE: Avoid hard tapping to prevent the generation of bubbles.
7. Remove the needle cap and advance the plunger to expel the air from the syringe.
8. At the time of injection, check the direction of the safety device (with round mark face up) and inject the entire contents of the syringe. Inject the entire contents of the syringe subcutaneously or intramuscularly as you would for a normal injection.
9. Withdraw the needle from the patient. Immediately activate the safety device by pushing the arrow forward with the thumb or finger until the device is fully extended and a CLICK is heard or felt. NOTE: The suspension settles out very quickly following reconstitution and therefore the product should be mixed and used immediately.

Triptorelin

1. Do not store above 25°C. Keep container in outer carton.
2. The suspension for injection must be reconstituted using an aseptic technique and only using the ampoule of mannitol solution 0.8% for injection that is provided as the suspension vehicle for Decapeptyl SR 3mg, Decapeptyl SR 11.25mg, Decapeptyl SR 22.5mg.
3. The suspension vehicle should be drawn into the syringe provided using one of the injection needles and transferred to the vial containing the powder for injection.
4. The vial should be shaken from side to side until a homogeneous suspension is formed and the mixture then drawn back into the syringe without inverting the vial.
5. The injection needle should then be changed and the second needle used to

	administer the injection. 6. As the product is a suspension, the injection should be administered immediately after reconstitution to prevent sedimentation. The suspension should be discarded if it is not administered immediately after reconstitution. 7. To ensure patients receive the correct dose, each vial of Decapeptyl contains a small overage to allow for predictable losses on reconstitution and injection. 8. The vial is intended for single use only and any remaining product should be discarded. Used injection needles should be disposed of in a designated sharps container.
11. Secondary care contact information	**If stopping medication or needing advice please contact:**
	Dr: Appropriate secondary care specialist (Urologist or Oncologist)
	Contact number: As documented in correspondence
	Hospital: As documented in correspondence
12. Criteria for shared care	Prescribing responsibility will only be transferred when ▪ Treatment is for a specified indication and duration. ▪ Treatment has been initiated by the secondary care specialist. ▪ The patient's initial reaction to and progress on the drug is satisfactory. ▪ The GP has agreed in writing in each individual case that shared care is appropriate. ▪ The patient's general physical, mental and social circumstances are such that he/she would benefit from shared care arrangements

13. Responsibilities of initiating specialist	Initiate and supply initial treatment and agree shared care with GP Undertake baseline monitoring. Dose adjustments. Monitor patient's initial reaction to and progress on the drug. Ensure that the patient has an adequate supply of medication until GP supply can be arranged. Continue to monitor and supervise the patient according to this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP Provide GP with diagnosis, relevant clinical information and baseline results, treatment to date and treatment plan, duration of treatment before consultant review. Provide GP with details of outpatient consultations, ideally within 14 days of seeing the patient *or* inform GP if the patient does not attend appointment Provide GP with advice on when to stop this drug. Provide patient with relevant drug information to enable Informed consent to therapy Provide patient with relevant drug information to enable understanding of potential side effects and appropriate action Provide patient with relevant drug information to enable understanding of the role of monitoring. Provide patient with monitoring booklet where appropriate.
14. Responsibilities of the GP	Initiate treatment as directed by the specialist Ensure no drug interactions with concomitant medicines To monitor and prescribe in collaboration with the specialist according to this protocol To ensure that the monitoring and dosage record is kept up to date To undertake vaccination as directed by the initiating consultant, the BNF or Green Book Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary.
15. Responsibilities of the patient	To take medication as directed by the prescriber, or to contact the GP if not taking medication To attend hospital and GP clinic appointments, bring monitoring booklet (if issued) Failure to attend will result in medication being stopped (on specialist advice). To report adverse effects to their Specialist or GP.

16.Additional Responsibilities	**List any special considerations**	**Action required**	**By whom**	**Date**
	[insert]	***[insert]***	***[insert]***	***[insert]***
	[insert]	***[insert]***	***[insert]***	***[insert]***
17. Supporting documentation	The SCG must be accompanied by a patient information leaflet.			
18. Patient monitoring booklet				
19. Shared care agreement form	Attached below			

Shared Care Agreement Form

LHRH Analogue

IMPORTANT: ACTION NEEDED

Name:	Date: _____
D.O.B:	Consultant: _____
Hospital No:	Hospital: _____

Dear Dr

Your patient has been seen in clinic today and started Androgen Deprivation Therapy (Hormone Therapy) for Prostate Cancer.

He has been given ..... for 28 days and asked to start on .....

See table below for specific indication.

Please tick	Indication for LHRH Analogue (LHRHa)	LHRHa UK Drug Licence		
		Decapeptyl®	Prostap DCS®	Zoladex®
	Metastatic Prostate Cancer	✓	✓	✓
	Locally Advanced Prostate Cancer	✓	✓	✓
	Neoadjuvant **before** Radiotherapy	✓	✓	✓
	Adjuvant **after** Radiotherapy	✓	✓	✓
	Adjuvant after Radical Prostatectomy	✓	✓	✓

Please can you start the appropriate LHRHa (of your choice) in _____ days.

Please continue the LHRHa for _____ (duration).

Baseline Tests, Monitoring and Follow-Up will be undertaken in secondary care.

You will receive a written summary / clinic letter within 14 days.

Please use the attached form to reply as soon as possible.

Yours sincerely,

Signature: _____

Name: _____

Shared Care Agreement Form

LHRH Analogue

GP RESPONSE

Dear Dr

RE: Patient: _____

Identifier: _____

_____

_____

I have received your request for shared care of this patient.

Decision	Please tick
• I agree to undertake shared care as per guideline	
• I do not agree to undertake shared care as per guideline	
Reason for not agreeing to shared care:	

GP Signature: _____ Date: _____

GP Name: _____