North Cumbria University Hospitals NHS Trust

NHS North Cumbria Clinical Commissioning Group

SHARED CARE GUIDELINE
LHRH analogues for prostate cancer

Drug: Goserelin (Zoladex ®) 3.6mg Implant, Goserelin (Zoladex ®LA) 10.8mg Implant. Leuporelin acetate (Prostap®SR DCS) 3.75mg injection, Leuporelin acetate (Prostap® 3 DCS) 11.25mg injection. Triptorelin (Decapeptyl® SR) 3mg injection, 11.25mg injection or 22.5mg injection.

Introduction	**Licensed indication:** **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.

Background:

The administration of LHRH agonists within primary care for prostate cancer care is designed to be an enhanced service which:

- Patients with an established diagnosis and agreed treatment plan for prostate cancer can undergo part of their treatment safely, effectively and conveniently close to their home.
- Enables greater integration of primary and secondary care services and which recognises the value of providing care closer to the patient in the primary care sector, whist providing the necessary funding of infrastructure to do so.

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.

Dose & Administration

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
Decapeptyl SR	Triptorelin	15mg (includes overage)	11.25mg by IM injection every 12 weeks
Decapeptyl SR	Triptorelin	28mg (includes overage)	22.5mg by IM injection every 6 months

Primary care will always initiate and provide the anti-androgen (e.g. bicalutamide) for 28 days and will arrange for a follow up visit after one week, in order to administer the first dose of a LHRH analogue.* This will be administered by a trained Practice Nurse.

* It is suggested one monthly LHRHa is administered as first dose. If tolerated and no issues patient can switch to 3 monthly administration.

	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. When such problems are anticipated, alternative treatment (e.g. orchidectomy) or concomitant use of an anti-androgen such as cyproterone acetate, flutamide or bicalutamide is recommended. This should be commenced in secondary care before the first dose of LHRH analogue is administered and continued for up to 3 weeks after. 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: **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: 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 care unless directions have been specified in the medical letter to the GP.**
Secondary Care Responsibilities	**List of investigations / monitoring undertaken by secondary care :** Secondary Care are responsible for: • Undertake baseline monitoring. • Ensure no drug interactions with concomitant medicines • Monitor patient's initial reaction to and progress on the drug. • Ensure that the Shared Care agreement has been correctly completed and communicated with the patients GP.

	Baseline monitoring: • Prostate Examination • Radiological Staging Investigations if appropriate. • PSA • Liver Function Test baseline for Leuprorelin • HbA1c • Blood pressure After the appropriate investigation/treatment in secondary care, the consultant looking after the patient will send their GP a letter in preparation of transfer of care. • 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 or investigations, 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. • Any presence of known metastatic disease • 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. • Be available to provide patient specific advice and support to GPs as necessary • Act upon communication from the GP in a timely manner. In addition, the consultant will identify triggers requiring consultant review e.g. increase of PSA above 8, Increase of PSA by greater than 50% over baseline, development of obstructive symptoms, symptoms suggestive of metastatic disease etc. Continue to review, monitor and supervise the patient progress in accordance with this protocol, while the patient remains on this drug, and agree to review the patient promptly if contacted by the GP.
Primary Care Responsibilities	After the appropriate investigation/treatment in secondary care, the consultant looking after the patient will send their GP a letter with the following information in preparation of transfer of care: • Diagnosis • Investigations to date (with summary findings) • Any presence of known metastatic disease • Current PSA & Care Plan • Purpose of monitoring. In addition, the consultant will identify triggers requiring consultant review e.g. increase of PSA above 8, Increase of PSA by greater than 50% over baseline, development of obstructive symptoms, symptoms suggestive of metastatic disease etc. In addition: • The GP will supply and initiate the specified anti-androgen (e.g bicalutamide) for ‘flare’ cover in non-orchidectomised patients. Supply 28 days. Between 1 to 2 weeks after initiation the LHRHa should be administered. The anti-androgen should be continued for at least 2 weeks after administration of the LHRHa. • Initially, a one-monthly LHRHa injection should be administered. If there are no issues and after discussion with patient subsequent injections can be administered as 3-monthly. Continue treatment as directed by the specialist. • Ensure no drug interactions with concomitant medicines

- Provide any support or advice when asked by patients regarding treatment and/or management.
- To monitor and prescribe in collaboration with the specialist according to this protocol, arranging PSA tests for each patient at the required intervals..
- Symptoms or results are appropriately actioned, recorded and communicated to secondary care when necessary.
- The GP will refer to the initial agreement on receipt of any PSA results and, if any of the "triggers" occur, the GP will refer directly back to the original consultant, via a "2 week wait" appointment. The review of results and decisions made are the responsibility of GPs within the patient's practice and will not be delegated to other staff members.

Administration of LHRHa :

- The practitioner must have the necessary experience, skills and training with regard to procedures carried out.
- Nurses must be appropriately trained, competent and be able to discuss any queries with patients e.g. side-effects.

Pharmaceutical aspects :

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 bin.

Monitoring Required in Primary Care

Arrange for the patient to attend for an appropriate PSA blood test at the practice and arrange a clinical assessment at a time when the test results will be available.
Undertake a clinical assessment of the patient including:

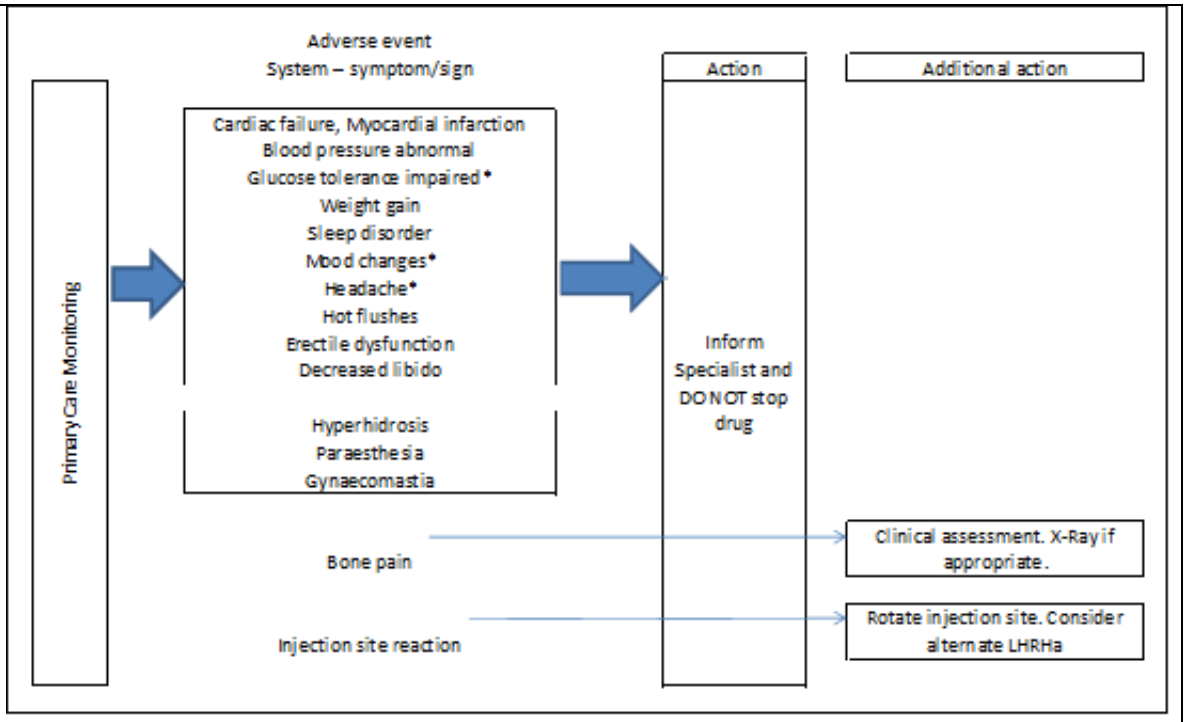
- Review of the PSA blood test results
- Enquire about bone pains and changes in urinary symptoms
- Review care plan

Record the outcome of the follow up.

Is monitoring required?	**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

Refer to ‘Primary Care Responsibilities’ for more information.

Adverse Effects



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.

The patient should be advised to report any of the following signs or symptoms to their GP without delay:

Low mood:
Increased risk of incident depression when undergoing treatment with LHRH analogues. Patient's should be informed accordingly and treated as appropriate if symptoms occur.

Headache/vomiting/visual impairment:
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.

Symptoms of hyperglycaemia:
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.

Worsening Urinary Symptoms/Bone pain:
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.

Common 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 (e.g. antipsychotics, methyldopa, metoclopramide). **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 (e.g. other hormonal therapy, corticosteroids, spironolactone, levodopa, phenothiazines, dopamine antagonists, digoxin).
Contra-indications	**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.
Pregnancy and breast feeding	Not applicable.
This guidance does not replace the SPCs, which should be read in conjunction with this guidance.	

Shared Care Agreement Form

Specialist request

***IMPORTANT: ACTION NEEDED**

Dear Dr *[insert Doctors name here]*

Patient name: *[insert Patients name here]*
Date of birth: *[insert date of birth]*
NHS Number: *[insert NHS Number]*
Diagnosis: *[insert diagnosis here]*

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.
OR
Patient has been started on the following LHRHa _____

Please continue the LHRHa for _____ (duration).

Baseline Tests, 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. Thank you.

Yours

[insert Specialist name]

Shared Care Agreement Form

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