North Central London
Joint Formulary Committee

Factsheet

TRIPTORELIN (Decapeptyl® SR) 3mg 11.25mg 22.5mg
LEUPRORELIN (Prostap®) 3.75mg 11.25mg
GOSERELIN (Zoladex®) 3.6mg 10.8mg

Treatment of Prostate Cancer

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FACTSHEET TO FACILITATE PRESCRIBING
PLEASE NOTE THIS IS NOT A SHARED CARE GUIDELINE, NOR IS IT A FULL SUMMARY OF DRUG INFORMATION. ALWAYS REFER TO THE MOST RECENT BNF AND/OR SUMMARY OF PRODUCT CHARACTERISTICS.

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Factsheet – TRIPTORELIN (Decapeptyl® SR) 3mg 11.25mg 22.5mg LEUPRORELIN (Prostap®) 3.75mg 11.25mg GOSERELIN (Zoladex®) 3.6mg 10.8mg for the treatment of Prostate Cancer

Treatment of Prostate Cancer

As per local formulary agreement, triptorelin (Decapeptyl® SR), leuprorelin (Prostap®), goserelin (Zoladex®) for the treatment of prostate cancer should be initiated by a consultant oncologist.

The hospital team will:

1. Provide the patient with initial information regarding the treatment and possible adverse effects. This includes the incidence of depression, and diabetic patients being counselled to increase the frequency of glucose monitoring as appropriate.
2. If no recent blood tests are available (e.g., within the past 3 months), check patient's routine blood tests (including prostate specific antigen, liver function and urea & electrolytes) prior to initiating GnRH analogues.
3. If no recent blood tests for metabolic parameters are available (such as lipids and HbA1C within the past 3 months) and the patient is not already known to have high cholesterol or diabetes, these will be measured prior to initiation. Results do not have to return prior to the first dose. Any irregular metabolic parameters should be referred to the GP for management or onward referral.
4. Check patient's blood pressure prior to initiation (and before switching GnRH analogues)
5. Initiate and optimise (stabilise) treatment and inform GP when patient is stable on that product so that GP can continue prescribing. This will usually be 3 months after initiation.
6. Change preparation if necessary and inform patient and GP of the changes.
7. Clinically supervise patient by routine clinic follow-ups as clinically indicated up to a minimum frequency of every 12 months, to include the relevant tests (such as prostate specific antigen) and assessments to monitor clinical response and toxicity. Inform GP of review and blood results after each monitoring appointment.
8. Provide emergency support for administering GnRH analogues where a practice is unexpectedly unable to provide this within a week of the date the injection is due (e.g., due to unexpected staff absence)

Choice of Preparation

Triptorelin (Decapeptyl® SR) is the preferred 1st line GnRH agonist for new patients across North Central London.

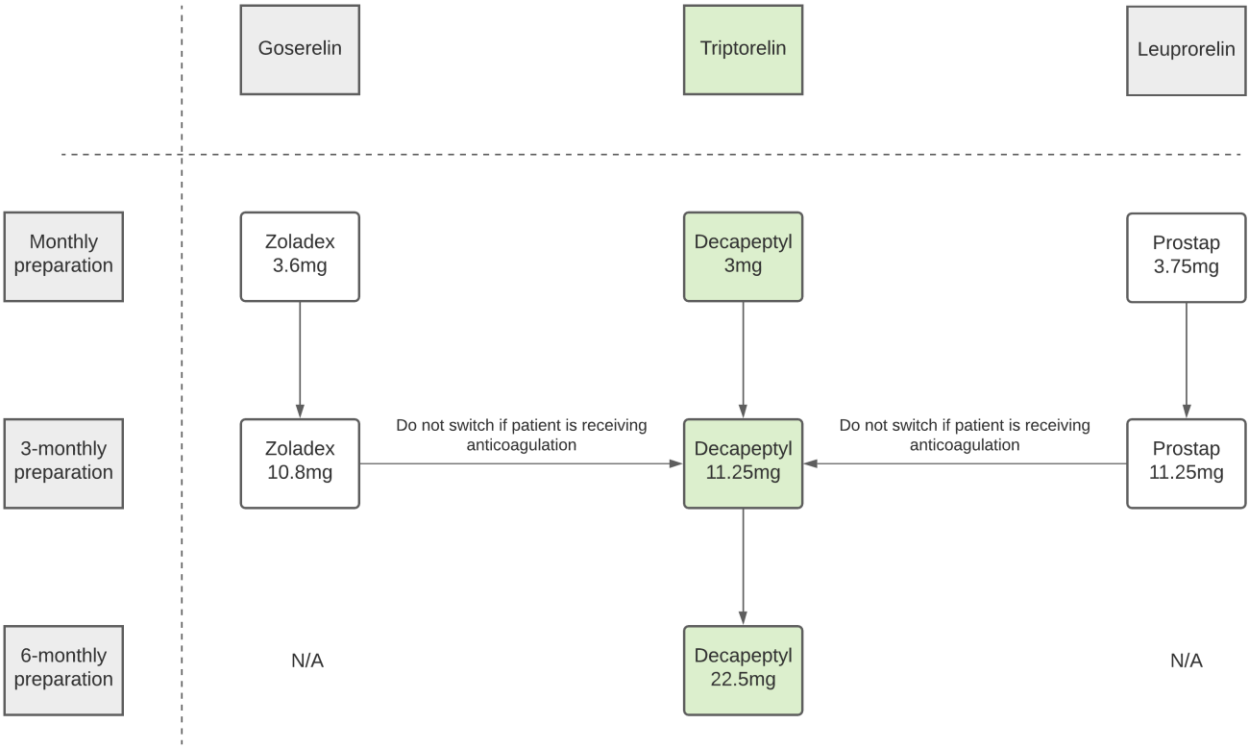
Switching Between Preparations

- All switches can be undertaken in primary care following specialist advice, which will be communicated to the GP.
- The letter from the consultant will detail information on which product the patient should be switched to, the relevant timepoint(s), relevant blood test results, and any other relevant specific requirements; it should also signpost to the Factsheet for further advice and will provide contact details if different to those provided in this factsheet.
- Switches are undertaken in accordance with Figure 1 below.
    - Existing patients receiving leuprorelin or goserelin should be escalated to the three-monthly preparation of their respective GnRH analogue before considering a switch to the three-monthly preparation of triptorelin (Decapeptyl® SR 11.25mg).
    - At least one dose of the three-monthly triptorelin preparation MUST be given before a

switch is made to triptorelin (Decapeptyl® SR) 22.5mg six-monthly preparation.

- In order to determine continued efficacy, PSA and testosterone will be checked prior to receiving the second dose (i.e., at 3 months if switched to a 3-month formulation, or at 6 months if switched to a 6-month formulation).
- The specialist will then review up to a minimum of every 12 months (as per box above).
- No routine drug-specific monitoring is required in general practice following switching of preparations (though please see section below on "clinical monitoring in primary care").
- Please note that triptorelin is only administered via intramuscular injection; switches should only be made where this method of administration is suitable.

Figure 1 – Preferred switching algorithm employed in North Central London



The preferred option (triptorelin) is highlighted in green. Arrows represent switches, which can be undertaken by a GP based upon a patient-specific request from the specialist team after discussion between the specialist team and patient. At least one dose of a product is administered before a further switch is conducted. Switches are only conducted upon the advice of a consultant.

Dose and Administration

Table 1 – Table of available GnRH analogue products in NCL with associated licensing information

Drug and Dose	Goserelin 3.6mg	Leuprorelin 3.75mg	Triptorelin 3mg*	Goserelin 10.8mg	Leuprorelin 11.25mg	Triptorelin 11.25mg*	Triptorelin 22.5mg*
Brand name (click link for SPC)	Zoladex® 3.6mg Implant	Prostap® SR DCS	Decapeptyl® SR 3mg	Zoladex® LA 10.8mg	Prostap® 3 DCS	Decapeptyl® SR 11.25mg	Decapeptyl® SR 22.5mg
Form	Implant in prefilled syringe/ needle size can be a problem	Powder plus solvent in prefilled syringe	Powder for suspension with diluent	Implant in prefilled syringe/ needle size can be a problem	Powder plus solvent in prefilled syringe	Powder for suspension with diluent	Powder for suspension with diluent
Injection Frequency	28 days	Monthly	4-weekly	12-weekly	3-monthly	3-monthly	6-monthly
Licenced Uses							
Metastatic Prostate Ca	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Locally advanced Prostate cancer - alternative to castration	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Prostate cancer - Adjuvant treatment post radiotherapy	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Prostate cancer - Neo-adjuvant treatment prior to radiotherapy	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Prostate cancer - Adjuvant treatment post radical prostatectomy	Yes	Yes	Yes	Yes	Yes	Yes	Yes

*Triptorelin is the preferred choice for newly initiated patients in NCL, with the potential to titrate to a six-monthly formulation

Refer to the summary of product characteristics for more information on method of administration

***Renal impairment**:* No dose reduction is required in renal impairment

***Hepatic impairment**:* No dose reduction is required in hepatic impairment

Elderly patients: No dose reduction is required in the elderly

Discontinuing treatment: If prescribed for metastatic disease treatment is usually prescribed life-long although breaks in treatment may be undertaken in specific circumstances and only under the guidance of a consultant oncologist. In recurrent non-metastatic prostate cancer, hormonal treatment may be given on a life-long or intermittent basis at the discretion of the treating consultant oncologist.

If prescribed for early prostate cancer in the neo-adjuvant or adjuvant setting, treatment will last for between 6 months and 3 years depending on risk factors determined by the consultant oncologist

Effects on ability to drive and operate machinery: GnRH agonists can influence the ability to drive and use machines due to visual disturbances and dizziness.

Pregnancy and Breastfeeding: Not applicable

Adverse Effects
See Clinical Monitoring in Primary Care" section below

Contraindications
Hypersensitivity to the active substance or to any of the excipients.
There are no other contraindications in men.

Special Warnings and Precautions for Use
Triptorelin can only be administered by intramuscular injection. For this reason, goserelin or leuprorelin (given via subcutaneous administration) may be preferable in anticoagulated patients.

Development or aggravation of diabetes mellitus may occur and so diabetic patients should be informed to increase the frequency of monitoring of blood glucose during treatment if appropriate.

Epidemiological data have shown that during androgen deprivation therapy, changes in the metabolic condition, as well as an increased risk for cardiovascular diseases, may occur. However, prospective data has not confirmed the link between treatment with GnRH analogues and an increase in cardiovascular mortality. Patients at high risk for metabolic disease (which can manifest as high blood pressure, high blood sugar, excess body fat around the waist, abnormal cholesterol or abnormal triglyceride levels) or cardiovascular diseases should be appropriately monitored. Specialists will check the patient's blood pressure prior to initiation or switching of GnRH analogue.

Hepatic dysfunction and jaundice with elevated liver enzymes has been reported. Therefore, liver function tests should be monitored as below and appropriate measures taken if necessary.

There is an increased risk of incidence of depression (which may be severe) in patients undergoing treatment with GnRH agonists. Patients should be informed accordingly at the start of treatment and treated as appropriate if symptoms occur.

Post-marketing reports of seizures have been observed in patients treated with GnRH agonists and these events have been reported in adults with or without a history of epilepsy, seizure disorders or risk disorders for seizures.

Long-term androgen deprivation, either by bilateral orchiectomy or administration of GnRH analogues is associated with increased risk of loss of bone density which, in patients with additional risk factors, may lead to osteoporosis and increased risk of bone fracture.

Androgen deprivation therapy may prolong the QT interval. In patients with a history of, or risk factors for, QT prolongation and in patients receiving concomitant medicinal products that might prolong the QT interval, physicians should assess the benefit-risk ratio, including the potential for Torsade de pointes prior to initiating a GnRH agonist.

Patients at risk of ureteric obstruction or spinal cord compression should be considered carefully and closely supervised in the first few weeks of treatment. These patients should be considered for prophylactic treatment with anti-androgens. Should urological/neurological complications occur, these should be treated by appropriate specific measures.

In the initial stages of therapy, a transient rise in levels of testosterone, dihydrotestosterone and acid phosphatase may occur. This may be associated with a "tumour flare" or exacerbation of the tumour growth, resulting in temporary deterioration of the patient's condition. These symptoms usually subside on continuation of therapy. "Tumour Flare" may manifest itself as systemic or neurological symptoms in some cases.

Bicalutamide MUST be administered for at least three days and up to 2 weeks prior to initiation of GnRH therapy and should continue for up to one month in total. In these circumstances, bicalutamide is supplied by the specialist centre and should not be continued by the GP.
This prevents the sequelae of an initial rise in serum testosterone.

Drug Interactions
No interaction studies have been performed.

Since androgen deprivation treatment may prolong the QT interval, the concomitant use of GnRH agonists 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) antiarrhythmic medicinal products, methadone, moxifloxacin, antipsychotics, etc. should be carefully evaluated.

Drugs which raise prolactin levels (e.g., metoclopramide, domperidone, anti-psychotics) should not be prescribed concomitantly as they reduce the level of GnRH receptors in the pituitary.

Clinical Monitoring in Primary Care

- ALL blood tests including prostate specific antigen levels and their interpretation are carried out in secondary care; reviews are communicated to the GP following clinic attendance.
- Observe for any adverse effects of treatment (listed above in the adverse effects section). Mild to moderate adverse effects can generally be managed in primary care. The management of severe adverse effects may require referral directly to another specialist service for additional support (e.g., diabetes specialist nurse for blood glucose control, mental health specialist for severe depression etc).
- If referring to another specialist to manage a potential adverse effect, inform the initiating specialist.
- Advice on common adverse effects and when to refer back to the initiating specialist is below. GPs can contact the oncology specialist if any concerns arise with the ongoing prescribing and administration of the GnRH agonist.
- If there is a risk that the next dose cannot be administered within a week of the due date, contact the specialist team (using the contact details below) to discuss whether they can help by administering the injection in hospital on this occasion.
    - Where the specialist team agree to provide ad hoc support to administer the GnRH analogue, the primary care team should contact the patient in the first instance to advise them that they will need to go to secondary care on this occasion.
- If the primary care clinician is not receiving communication from the hospital team, or there is concern that monitoring tests are not being conducted, please contact the specialist team (using the contact details below).
- A full list of suggested management by a GP is in **Table 2**.

Table 2 – Possible adverse effects, suggested management and when to refer

Adverse effect	Frequency	Suggested management by GP
Decreased libido	Very common	If an intolerable adverse effect, refer back to specialist to discuss alternative treatment options
Hot flushes	Very common	Consider treatment as per NICE CKS; If severe/intractable, refer back to initiating specialist
Erectile dysfunction	Very common	Consider treatment as per NICE CKS and local pathway. If severe/refractory/intolerable, refer back to initiating specialist
Hyperhidrosis	Very common	Offer advice/treatment as per NICE CKS; if resistant consider referral to dermatologist
Weight fluctuation	Very common	Consider referral to dietitian; if severe/intolerable refer back to initiating specialist
Fatigue	Very common	Consider therapy as per NICE CKS; If severe/intractable, refer back to initiating specialist
Impaired glucose tolerance	Common	Management of diabetes will remain the responsibility of the patient's routine supervising specialist (e.g., GP, diabetes specialist nurse etc)
Mood changes leading to depression	Common	Refer back to initiating specialist if depression develops
Paraesthesia	Common	Refer back to initiating specialist if paraesthesia develops
Bone pain	Common	Refer back to initiating specialist if bony pain develops
Hypertension	Common	Consider treatment as per local/NICE guidance; refer back to initiating specialist if persistent
Rash	Common	Treat as appropriate; If thought to be an allergy, stop immediately and refer back to the specialist for advice
Gynaecomastia	Common	Refer back to initiating specialist if gynaecomastia develops
Reduction in bone mass	Common	Consider guidance in NICE CKS; if resistant consider referral to rheumatologist
Injection site reactions	Common	Treat as appropriate; If thought to be an allergy, stop immediately and refer back to the specialist for advice
Nausea	Common	Treat as appropriate; If thought to be an allergy, stop immediately and refer back to the specialist for advice
Serious adverse effects		
QT prolongation is caused by androgen deprivation therapy.	Unknown	The risk/benefit ratio in patients with risk factors will be assessed prior to initiation of therapy. If suspected, refer for immediate assessment.
Pulmonary embolism	Unknown	If suspected, refer to A&E for immediate assessment
Thrombocytopenia and Leucopaenia	Unknown/ Uncommon	Should be identified by secondary care blood tests; incidental findings should be referred back to specialist.
GnRH agonists may reveal the presence of a previously unknown gonadotroph cell pituitary adenoma.	Rare	If suspected, refer back to specialist.
Jaundice and hepatic enzyme elevation	Unknown	Should be identified by secondary care blood tests; incidental findings should be referred back to specialist.

Contact Details

Royal Free London NHS Foundation Trust
Department of Oncology
Please see individual consultant secretaries below

Dr Mark Prentice	AngieFisher@nhs.net
Dr Sarah Needleman	For Royal Free Hospital patients wasamunu.sitali@nhs.net For Barnet Hospital patients clare.besset3@nhs.net
Dr Soosaipillai	For Royal Free Hospital patients AngieFisher@nhs.net For Barnet Hospital patients clare.besset3@nhs.net
Prostate Cancer Clinical Nurse Specialists	020 8216 4367
Oncology admin mailbox	rf.oncologyadmin@nhs.net

Other specialist contact – **Royal Free Hospital Patients**-Angie Fisher 0207 830 2169,
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Uro-Oncology CNS team	0203 447 7151 (bleep via main switch: 1050) uclh.oncology.urology.admin@nhs.net

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Dr George Imseeh	linda.payne1@nhs.net 020 8887 3061

Whittington Health NHS Trust
Department of Oncology
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Dr Mark Prentice	AngieFisher@nhs.net (0207 830 2169) Or oncology admin mailbox for RFL (for the attention of Mark Prentice: rf.oncologyadmin@nhs.net)

References

1. Summary of Product Characteristics Prostap SR DCS and Prostap 3 DCS accessed on 21st December 2020 https://www.medicines.org.uk/emc/product/4650/smpc and https://www.medicines.org.uk/emc/product/4651
2. Summary of Product Characteristics Zoladex 3.6mg Implant and Zoladex LA 10.8mg accessed on 21st December 2020 https://www.medicines.org.uk/emc/product/1543 and https://www.medicines.org.uk/emc/product/1567/smpc
3. Summary of Product Characteristics Decapeptyl SR 3mg, Decapeptyl SR 11.25mg (triptorelin pamoate) and Decapeptyl SR 22.5mg accessed on 21st December 2020 https://www.medicines.org.uk/emc/product/963/smpc https://www.medicines.org.uk/emc/product/780/smpc and https://www.medicines.org.uk/emc/product/5906/smpc