SHARED CARE GUIDELINES

Gonadorelin analogue and gonadotrophin-releasing hormone (GnRH) antagonist depots for treatment of prostate cancer

It is vital for safe and appropriate patient care that there is a clear understanding of where clinical and prescribing responsibility rests between Consultants and General Practitioners (GPs).

It is essential that a transfer or sharing of prescribing responsibilities should not take place without the sharing of information between the Prescriber and the individual GP, and their mutual agreement to this to ensure their full confidence when prescribing.

These are not rigid guidelines. In all cases, Consultants and GPs should clearly communicate regarding the appropriate management of individual patients. As always, the doctor who prescribes the medication has the clinical responsibility for the drug and the consequences of its use.

1.0 Licensed indication, dosage and administration

TRIPTORELIN (Decapeptyl® SR 3mg, 11.25mg and 22.5mg) is first choice gonadorelin analogue for prostate cancer following specialist urologist/oncologist recommendation under shared care agreement.

	Gonadorelin analogues										GnRH antagonist
	Goserelin (Zoladex®)		Leuprorelin (Prostap®)		Leuprorelin (Lutrate®)		Triptorelin (Decapeptyl®)			Triptorelin (Gonapeptyl®)	Degarelix (Firmagon®)
	3.6mg (S/C injection every 28 days)	10.8mg (S/C injection every 12 weeks)	3.75mg (S/C or I/M injection every month)	11.25mg (S/C injection every 3 months)	3.75mg (I/M injection every month)	22.5mg (I/M injection every 3 months)	3mg (I/M injection every 4 weeks)	11.25mg (I/M injection every 3 months)	22.5mg (I/M injection every 6 months)	3.75mg (S/C or I/M injection every 28 days)	240mg (S/C injection (first dose) then 80mg S/C every month)
Metastatic prostate cancer	✓	✓	✓	✓			✓	✓	✓		
Locally advanced prostate cancer, as an alternative to surgical castration	✓	✓	✓	✓			✓	✓	✓		
Adjuvant treatment to radiotherapy in patients with high-risk localised or locally advanced prostate cancer	✓	✓	✓	✓			✓	✓	✓		
Adjuvant treatment to radical prostatectomy in patients with locally advanced prostate cancer at high risk of disease progression	✓	✓	✓	✓			✓	✓	✓		

Neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced prostate cancer	✓	✓	✓	✓			✓	✓	✓		
Palliative treatment of locally advanced or metastatic prostate cancer					✓						
Palliative treatment of hormone dependent advanced prostate cancer						✓					
Hormone dependent locally advanced or metastatic prostate cancer										✓	
Advanced hormone-dependent prostate cancer in people with spinal metastases											✓

3.0 Cautions and contraindications:
3.1 Cautions

Development or aggravation of diabetes may occur; therefore diabetic patients may require more frequent monitoring of blood glucose during treatment.

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

In the initial stages of gonadorelin analogue therapy, a transient rise in serum testosterone is possible with an exacerbation of tumour growth. An anti-androgen (e.g. bicalutamide 50mg daily) for at least three days before and three weeks after commencement of therapy may be administered to prevent this.

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.

The use of gonadorelin analogues may cause reduction in bone mineral density. 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).

There is an increased risk of incident depression in patients undergoing treatment with gonadorelin analogue/GnRH

antagonists. Patients should be informed accordingly, monitored or treated as appropriate if symptoms occur or worsen.

Androgen deprivation therapy may prolong the QT interval. Prior to initiation of therapy, the risk/benefit ratio in patients with risk factors should be assessed.

3.2 Contra-indications
Hypersensitivity to any of the ingredients or to synthetic gonadorelin or gonadorelin derivatives.

4.0 Adverse effects:
Side effects seen with gonadorelin analogue/GnRH antagonists are due mainly to the specific pharmacological action, namely increases and decreases in certain hormone levels.

In cases where a "tumour flare" occurs after gonadorelin analogue (**N.B. not GnRH antagonist therapy**), an exacerbation may occur in any symptoms or signs due to disease, for example, bone pain, urinary obstruction, weakness of the lower extremities and paraesthesia. These symptoms subside on continuation of therapy. (Also see precautions section 3.1)

Adverse events which have been reported include peripheral oedema, pulmonary embolism, blood pressure abnormalities, palpitations, fatigue, QT prolongation, muscle weakness, diarrhoea, nausea, vomiting, anorexia, headache (occasionally severe), fever/chills, hyperhidrosis, arthralgia, myalgia, bone pain, dizziness, insomnia, mood changes, depression, decreased libido, impotence, alopecia, paraesthesia, visual disturbances, weight changes, hepatic dysfunction, jaundice, increases in liver function test values (usually transient), reduction in bone mass, urinary tract obstruction, testicular atrophy, gynaecomastia, breast pain and irritation at the injection site. Changes in blood lipids and alteration of glucose tolerance have also been reported which may affect diabetic control. Thrombocytopenia and leucopenia have been reported rarely. Hypersensitivity reactions including rash, pruritus, urticaria, and rarely, wheezing or interstitial pneumonitis have also been reported. Anaphylactic reactions are rare.

The administration of gonadorelin analogue/GnRH antagonists is often associated with hot flushes and sometimes sweating.

Rarely, treatment with gonadorelin analogues may reveal the presence of a previously unknown gonadotroph cell pituitary adenoma.

5.0 Monitoring requirements:

Baseline Monitoring: (Secondary care)

- FBC, U&Es, LFTs and PSA
- PSA at start of treatment and then on further visits to secondary care. When patients are discharged to primary care they will be advised a PSA value above which to refer back patients to secondary care.

A DEXA scan should be performed by secondary care physician in patients **with major risk** factors for decreased bone mineral content and treatment should not be initiated if result is below normal levels.

Ongoing Monitoring: (Primary care)

- Monitor LFTs every 3 months, if ALT > 2 x UNL (upper normal limit) or total bilirubin > 1.5 x UNL, repeat LFTs after 7 days. If the LFTs have not normalised, re-test after 2-3 weeks. If LFTs have still not normalised refer back to secondary care.
- Monitor U&Es and FBC every 6 months. Contact the hospital specialist if potassium or serum creatinine (unless known to have chronic renal failure) are significantly raised.
- Monitor PSA every 3-6 months, refer patients back if the PSA rises above the value specified at discharge from secondary care (see above).

Diabetic patients should be counselled to increase the frequency with which they monitor blood glucose levels.

6.0 Action to be taken if abnormal results/adverse effects:
Refer back to secondary care specialist (may be specialist nurse or doctor)

7.0 Drug interactions:

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

When gonadorelin analogues are 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.

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

8.0 Specialist responsibilities:

- To assess the patient's appropriateness for gonadorelin analogue/GnRH antagonist treatment.
- To review patient's current medications to check for drug-drug interactions and to review if the patient is currently taking any medications which may prolong the QT interval.
- To ensure that the patient/carer has received counselling and understands the therapy, its benefits, limitations, continued monitoring (where applicable), adverse effects, and is aware of actions to take if adverse effects are suspected
- Perform baseline monitoring as detailed in section 5.0.
- Initiate an anti-androgen therapy (e.g. bicalutamide 50mg daily) at least three days before initiation of gonadorelin analogue therapy (and continue for three weeks after commencement).
- Initiation and administration of at least the first gonadorelin analogue/GnRH antagonist dose.
- To contact the patient's GP regarding the commencement of gonadorelin analogue/GnRH antagonist and to request shared care.
- To include in the letter a copy of this protocol and the following information:
  – Diagnosis of the condition with relevant clinical details
  – Details of patient's treatment to date and the date when the first injection to be administered by the GP is due
  – Frequency of review by the consultant
- To review the patient at agreed intervals and copy all relevant results to the GP.
- Monitor for therapeutic effect by clinical parameters and PSA during treatment. Initiate any dose changes as appropriate including discontinuation of treatment.
- Provide advice to the GP if they have any clinical queries relating to the patient's condition or the use of gonadorelin analogue/GnRH antagonist.
- Review patients promptly if required by the GP concerned within an agreed time frame.
- Report adverse events to the MHRA and GP www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm

9.0 GP responsibilities:

- Ensure consultant has provided the appropriate information regarding the therapeutic issues relating to the patient's clinical condition.
- Review communication from secondary care and treatment plan prior to prescribing the continuing supply.
- Prescribe gonadorelin analogue/GnRH antagonist therapy at a dose advised by the consultant (following administration of at least the first dose by secondary care).
- Arrange for administration of gonadorelin analogue/GnRH antagonist by district nurse, clinic or practice as appropriate.
- Monitor patient's overall health and wellbeing, observing for any adverse effects of treatment and highlighting this to the consultant.
- Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment
- Inform the consultant of any relevant change in the patient's circumstances.
- Perform ongoing monitoring as detailed in section 5.0.

- For diabetic patients check HbA1c after 3 months to ensure diabetes control has not been altered and make any appropriate adjustment to management of diabetes if necessary.
- Report adverse events to specialist and MHRA. www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/index.htm

10.0 Patient responsibilities:

- Discuss potential benefits and side effects of treatment with the specialist and GP, to identify whether they have a clear picture of these from the specialist and to raise any outstanding queries.
- Share any concerns they have in relation to treatment with gonadorelin analogue/GnRH antagonist.
- Report any adverse effects to their specialist or GP.
- Report to the specialist or GP if they do not have a clear understanding of their treatment.
- Participate in the monitoring of therapy and the assessment of outcomes, to assist health professionals to provide safe, appropriate treatment.

11.0 Secondary care review:
Patients will be reviewed one month after first injection and most would be discharged back to primary care with clear advice about PSA value that would trigger a referral back to secondary care. Some may be reviewed at a frequency determined by the clinical need by the consultant clinic or if requested to review by the GP.

12.0 Availability/Other special considerations
Gonadorelin analogues may be used for treatment irrespective of which gonadorelin analogue was initiated in secondary care (in line with licensed indications) to allow for the most cost effective treatment course. **Triptorelin (Decapeptyl® SR 3mg, 11.25mg and 22.5mg)** is the Wirral gonadorelin analogue of choice.

Back up advice and support:	**Telephone/Fax**
Contact patient's consultant	Via switchboard:0151 6785111
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