Shared Care Guideline for advanced hormone-dependent prostate cancer

Degarelix acetate (Firmagon®) (Gonadotrophin-releasing hormone antagonist)

Executive Summary/ Critical Information.

Indication	Route & Dose	Key aims of treatment in the long term	Monitoring undertaken by specialist before requesting shared care	Ongoing monitoring to be undertaken by GP	Duration of treatment	Stopping criteria	Follow up (weeks/months)
To treat advanced hormone-dependent prostate cancer in adult male patients with spinal metastases. In whom a rapid lowering of testosterone is required and an initial tumour flare would be of significant clinical	Initiation dose (administered by specialist in secondary care): 240mg SC once only (administered as two injections of 120mg each) Maintenance dose (administered by GP surgery in primary care): 80mg SC once a month.	To reduce PSA levels To reduce tumour size	The following baseline monitoring will be undertaken by the urology specialist prior to initiating shared care: <u>Baseline</u> Serum PSA Testosterone level U&Es Bone profile Liver profile Full blood count Renal function (in patients with known or suspected poor renal function)	After the first month the following monitoring will be undertaken by the GP: <u>Follow-up</u> PSA to be reviewed annually as a minimum The patient will remain under close follow up by urology who will support ongoing management	Indefinite	Hypersensitivity and/or anaphylactic reactions The urology team will provide ongoing regular 3-4 monthly follow up and make any decisions around stopping treatment.	**Specialist -** **The urology team will provide ongoing follow up every 3-4 months.** **GP-** **Frequency of any additional follow up will be agreed on an individual patient basis if required in addition to urology follow up.**

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importance that prevents the patient from receiving an LHRH agonist. In accordance with NICE TA 404 and NICE CG 75	The first maintenance dose must be given one month after the initiation dose. The urology specialist team will communicate this date in a letter to the GP.						
Key Safety Notice (for instance: notification if prescribing must be brand specific or BNF cautionary and advisory warnings).							
Not applicable							
Other							
Not applicable							

1. Background

Prostate cancer is one of the most common cancers in men in the UK. Most prostate cancers are diagnosed in the local stage and are asymptomatic; however, patients may present with non-specific urinary symptoms, haematuria, or hematospermia.

In patients with advanced, metastatic prostate cancer the following signs and symptoms can occur: Bone pain, weight loss, weakness or pain due to spinal cord compression, pain due to pathologic fractures, fatigue caused by anaemia, or renal/urinary symptoms (e.g. haematuria, inability to void, incontinence, or symptoms associated with chronic renal failure).

Prostate cancer is dependent on testosterone for growth. Therefore, treatment for advanced hormone-dependent prostate cancer involves reducing testosterone levels to prevent tumour growth. Common pharmacological agents include anti-androgens (e.g. bicalutamide), abiraterone, luteinizing hormone-releasing hormone agonists (LHRH) (e.g. leuprorelin and goserelin) and gonadotrophin-releasing hormone (GnRH) antagonist (e.g. degarelix).

2. Important information

Degarelix (Firmagon®) is a GnRH antagonist. It is licensed for treatment of adult male patients with advanced hormone-dependent prostate cancer. Unlike LHRH agonists GnRH antagonists do not produce a surge in luteinising hormone at the start of treatment. Consequently, there is no initial testosterone surge or tumour stimulation and therefore no potential for symptomatic flares. Patients therefore do not require concurrent treatment with anti-androgens when commencing therapy.

For the purpose of this Shared Care Guideline, degarelix is indicated for patients with advanced hormone dependent prostate cancer in adult male patients with spinal metastases. In whom a rapid lowering of testosterone is required and an initial tumour flare would be of significant clinical importance that prevents the patient from receiving an LHRH agonist.

Degarelix will be prescribed for patients who present with signs or symptoms of spinal cord compression as per NICE TA 404 and NICE CG 75.

3. Drug name, form, and licensed indications (unlicensed/off-label)

Drug name and form:
Degarelix acetate (Firmagon®) 80mg powder and solvent for solution for injection
Degarelix acetate (Firmagon®) 120mg powder and solvent for solution for injection

Licensed indications:
Adult male patients with advanced hormone-dependent prostate cancer

4. Dose and Administration

Initiation dose: 240mg SC once only.

Maintenance dose (to start one month after the initiation dose): 80mg SC once a month

5. Contraindications/Cautions

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Contraindications:

- Hypersensitivity/allergy to degarelix or any of the excipients

Cautions:

- Diabetes
- Susceptibility to QT prolongation
- Hepatic impairment
- Renal impairment
- Cardiovascular disease

For complete list of contraindications and cautions, please refer to the SPC: https://www.medicines.org.uk/emc.

6. Drug interactions

Drug-drug interactions:
Anti-androgen treatment may prolong the QTc interval. Consequently, concomitant use of degarelix with medicinal products known to prolong the QTc interval or drugs which can induce torsades de pointes such as class IA (e.g. quinidine or disopyramide) or class III (e.g. amiodarone or sotalol) antiarrhythmics, methadone, moxifloxacin and antipsychotics must be carefully evaluated.

Degarelix is not a substrate for the human CYP450 system and has not been shown to induce or inhibit CYP1A2, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1, or CYP3A4/5 to any great extent *in vitro*. Therefore, clinically significant pharmacokinetic drug-drug interactions in metabolism related to these isoenzymes are unlikely.

Drug-disease interactions:

- Diabetes mellitus: Development or worsening of diabetes may occur with the use of degarelix
- Cardiovascular disease: Myocardial infarction or stroke have been reported in those patients on anti-androgen therapy.
- Bone density: Long term testosterone suppression can reduce bone density in men.

For complete list of drug interactions, please refer to the SPC: https://www.medicines.org.uk/emc.

7. Side effects which require managing

In the event that an adverse effect to degarelix is suspected or has occurred in a patient, the urology team will make appropriate referrals to the relevant clinical specialties.

Adverse effects	Symptoms/signs	Actions
Physiological consequence of testosterone suppression (common)	Gynaecomastia, testicular atrophy, erectile dysfunction, decreased libido, hyperhidrosis (including night sweats), fatigue, hot flush, weight increase and anaemia.	Specialist review of treatment if patient intolerant of adverse effects.
Cardiac disorders (uncommon)	Cardiac arrhythmia (including atrial fibrillation), palpitations, QT prolongation.	Benefit/risk ratio must be thoroughly appraised and documented in patients with a history of a corrected QT interval over 450 msec, a history of or risk factors for torsades de pointes and in patients

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		receiving concomitant medicines that might prolong the QT interval.
Hepatobiliary disorders (common)	Liver transaminases increased.	Monitor liver function in patients with known or suspected hepatic disorder during treatment.
Renal impairment (uncommon)	Increased urinary frequency, micturition urgency, dysuria, nocturia and incontinence	Monitor renal function in patients with known or suspected poor renal function during treatment.
Metabolism and nutrition disorders (uncommon)	Hyperglycemia/diabetes mellitus, cholesterol increased, weight gain (common), appetite decreased, changes in blood calcium.	Diabetic patients may require more frequent monitoring of blood glucose
Musculokeletal and bone disorders (uncommon)	Reduced bone density (osteoporosis/osteopenia), joint swelling/stiffness, muscular weakness	Specialist review of treatment if patient intolerant of this adverse effect or at risk of falls (to avoid bone fracture).
General disorders and administration site conditions (common)	Injection site reactions, chills, fever, fatigue and flu-like symptoms	Specialist review of treatment if patient intolerant of adverse effects

For complete list of side effects, please refer to the SPC: https://www.medicines.org.uk/emc.

8. Process for Referral Back to Secondary Care

The urology team will continue to provide close follow up of patients and closely support ongoing monitoring
Referral criteria back to secondary care:

1. Deterioration in lower urinary tract symptoms
2. Bone pain
3. Lower limb neurology (refer to A&E for same day review)
4. Suspicion of spinal cord compression (refer to A&E for same day review)
5. Development of adverse effects as listed above and documented within the SPC linked above
6. If patient refuses degarelix injections
7. If patient fails to attend appointments for degarelix

Barts Health NHS Trust urology team contact details are documented in the table in section 10.

9. Monitoring and Responsibilities

- **Hospital specialist:**

1. Ensure that the patient/carer is an informed recipient in therapy.
2. Ensure that patients understand their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate). Issue any local patient information leaflets where appropriate.

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3. Ensure baseline investigations are appropriate before commencing treatment. Give the patient a patient held booklet for result monitoring if appropriate.
4. Degarelix is initiated in secondary care. Where initiated in secondary care prescribe for one month (initiation dose only). Send a letter to the GP requesting shared care for this patient and the date for the first maintenance dose. The letter must state that the first maintenance dose is to be given via the GP one month after the day that the initiation dose was administered and must be continued monthly thereafter in primary care.
5. Clinical and laboratory supervision of the patient by blood monitoring and routine clinic follow-up on a regular 3-4 monthly basis.
6. Send a letter/results notification to the GP after each clinic attendance ensuring current dose, most recent blood results and frequency of monitoring are stated.
7. Evaluation of any reported adverse effects by GP or patient.
8. Advise GP on review, duration or discontinuation of treatment where necessary.
9. Inform GP of patients who do not attend clinic appointments.
10. Ensure that backup advice is available at all times

- **General Practitioner:**

1. Degarelix can be initiated in secondary care by urology or oncology specialists. Ensure patient is an informed recipient of therapy and baseline investigations are appropriate before commencing treatment.
2. Ensure that patients understand their treatment regimen and any monitoring or follow up that is required (using advocacy if appropriate).
3. Check and reinforce patient understanding of the nature, effect and potential side effects of the drug before prescribing it and contact the specialist for clarification where appropriate.
4. Monitor patient's overall health and well-being.
5. Report any adverse events to the consultant, where appropriate.
6. Report any adverse events to the CHM, where appropriate.
7. Help in monitoring the progression of disease and side effects of treatment
8. Report to urology consultant if degarelix is withheld or not administered for any reason.

- **Patient or parent/carer:**

1. Report any adverse effects to their GP and/or specialist.
2. Ensure they have a clear understanding of their treatment.
3. Report any changes in disease symptoms to GP and/or specialist. Alert GP and/or specialist of any changes of circumstance which could affect management of disease e.g. plans for pregnancy.
4. Take/ administer the medication as prescribed.
5. Undertake any monitoring as requested by the GP and/or specialist

10. Contact Information

Royal London Hospital switchboard	02073777000
Whipps Cross University Hospital switchboard	02085395522
Newham University Hospital switchboard	02074767000
St Barts Hospital switchboard	02073777000
Urology Consultant on-call	via switchboard
Whipps Cross Urology Registrar on-call working hours (9am-5pm Monday to Friday)	Bleep via switchboard 2500
Whipps Cross Urology SHO working hours (9am-5pm Monday to Friday)	Bleep via switchboard 2621 or 2622
Urology Registrar on-call out of hours	via switchboard
Urology Specialist Nurse	via switchboard
Urology Specialist Pharmacist	02032460134

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11. References

British Medical Association., Royal Pharmaceutical Society. 2019. British National Formulary: Degarelix monograph (online application). Version 2.1.28.

Ferring Pharmaceuticals Ltd. 2017. Firmagon 120mg injection: Summary of product characterisitics (online). Available at: https://www.medicines.org.uk/emc/product/6537/smpc (accessed 05 January 2020)

NICE. 2008. Clinical Guideline 75: Metastatic spinal cord compression: Diagnosis and management of adults at risk of and with metastatic spinal cord compression (online). Available at: https://www.nice.org.uk/guidance/cg75 (accessed 05 January 2020)

NICE. 2016. Technology Appraisal 404: Degarelix for treating advanced hormone-dependent prostate cancer (online). Available at: https://www.nice.org.uk/guidance/ta404 (accessed 05 January 2020)

12. Document Management

Document ratification and history	
Produced by:	Rakhee Mistry (Highly Specialist Pharmacist Renal and Urology)
Approved by:	Barts Health Drugs and Therapeutics Committee (DTC) Waltham Forest and East London Medicines Optimisation and Commissioning Committee (WELMOCC)
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Appendix 1.

Shared Care Guideline: Prescribing Agreement

Section A: To be completed by the hospital consultant initiating the treatment

GP Practice Details:	**Patient Details:**
Name:	Name:
Tel No:	DOB:
Email (nhs.net):	NHS Number (10 digits):

Consultant Details:
Consultant Name:
Secretary Contact Details:
Tel No:
Email (nhs.net):

Diagnosis:	**Drug Name (to be prescribed by GP):** **Dose:** **Frequency:**

I will review the patient in clinic in weeks / months (*Delete as appropriate)*.

Dear

Your patient started treatment with the above drug for the above diagnosis on (insert date) and in my view; his/her condition is now stable.

The patient has given consent to treatment under a shared care prescribing agreement and has agreed to comply with instructions and follow up requirements.

I am requesting your agreement to sharing the care of this patient from (insert date) in accordance with the attached Shared Care Prescribing Guideline.

This patient was reviewed on (insert date). These are the results relevant for the drug and/or condition, as outlined in the shared care document:

Test	Baseline	Date

Please continue to monitor the patient as outlined in the shared care guidelines. Refer to the attached guidelines for monitoring criteria.

Other relevant information:

Consultant Signature:	Date:

Section B: To be completed by the GP and returned to the hospital consultant as detailed in Section A above [If returned via e-mail, use NHS.net email account ONLY]

Please sign and return your agreement to shared care within 14 days of receiving this request.

☐ Yes, I accept sharing care as per shared care prescribing guideline.

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☐ No, I am not willing to undertake shared care for this patient for the following reason: (Please give reason)		
GP Name:	GP Signature:	Date:

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