Degarelix *(Firmagon®)* AMBER 0

Advanced hormone-dependent prostate cancer with spinal metastases - to be read in conjunction with the SPC

Background

Degarelix is a GnRH antagonist indicated for the treatment of adult male patients with advanced hormone-dependent prostate cancer. Degarelix must be prescribed in accordance with NICE TA 404 (Degarelix for treating advanced hormone dependent prostate cancer) for those patients with:

- Advanced hormone dependent prostate cancer with spinal metastases

Degarelix competitively and reversibly binds to the pituitary GnRH receptors, thereby reducing the release of the gonadotrophins, luteinizing hormone (LH) and follicle stimulating hormone (FSH), which in turn reduces the secretion of testosterone by the testes. GnRH is also known as LHRH. Unlike LHRH agonists, GnRH antagonists do not induce a LH surge with subsequent testosterone surge / tumour stimulation and therefore no potential for symptomatic flares after the initiation of treatment.

Dosage and Administration

For instructions on reconstitution and administration of degarelix, please consult the latest version of the Summary of Product Characteristics (SPC) at www.medicines.org.uk/emc/ for full details.

Degarelix is for subcutaneous use ONLY and should not be administered intravenously. Intramuscular administration is not recommended as it has not been studied.

Degarelix is administered as a subcutaneous injection in the abdominal region. The injection site should vary periodically. Injections should be given in areas where the patient will not be exposed to pressure, e.g. not close to waistband or belt and not close to the ribs.

Starting Dose (to be prescribed and administered by secondary care):

- 240mg administered as 2 subcutaneous injections of 120mg each

Maintenance Dose (to be prescribed and administered in primary care):

- **80mg** administered monthly as 1 subcutaneous injection, starting one month after the starting dose and continued monthly, indefinitely

There is no need to adjust the dose for the elderly or in patients with mild or moderate impairment of liver or kidney function. Patients with severe liver or kidney impairment have not been studied and caution is therefore warranted.

Monitoring

Baseline – Specialist

- Serum PSA
- FBC
- U&E
- LFT
- Bone Profile

Every 6-months – GP

- Serum PSA

Missed Dose – by more than 2-weeks

- Serum PSA

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Patients should be referred back to secondary care if they have any one of the following symptoms:

- PSA above threshold (PSA rise of ≥50% from baseline in six months **OR** two consecutive PSA measurements of >20ng/ml)
- Deterioration in lower urinary tract symptoms
- Bone pain

Patients who have the following symptoms should be urgently re-referred on the same day (**if metastatic spinal cord compression is suspected the patient should be urgently referred direct to accident and emergency**):

- Lower limb neuropathy
- Suspicion of spinal cord compression

Contraindications and Cautions for Use

Contraindications: Hypersensitivity to the active substance or to any of the excipients (mannitol E421).

Special Warnings and Precautions: Long-term androgen deprivation therapy may prolong the QT interval. The benefit/risk ratio must be thoroughly appraised in patients with a history of a corrected QT interval over 450ms, in patients with a history of or risk factors for torsades de pointes and in patients receiving concomitant medicinal products that might prolong the QT interval as degarelix has not been studied in these patients.

Monitoring of liver function in patients with known or suspected hepatic disorder is advised during treatment.

Degarelix has not been studied in patients with severe renal impairment, patients with a history of severe untreated asthma, anaphylactic reactions or severe urticaria, or angioedema.

Bone density changes have not been studied during treatment with degarelix. However, it can be anticipated that long periods of testosterone suppression in men will have effects on bone density.

A reduction in glucose tolerance has been observed in men who have had orchiectomy or who have been treated with a GnRH agonist. Development or aggravation of diabetes may occur. Diabetic patients may require more frequent monitoring of blood glucose when receiving androgen deprivation therapy. The effect of degarelix on insulin and glucose levels has not been studied.

Cardiovascular disease such as stroke and myocardial infarction has been reported in the medical literature in patients with androgen deprivation therapy. Therefore, all cardiovascular risk factors should be taken into account when prescribing degarelix.

Side Effects

Very common (≥ 1/10): hot flush, injection site adverse reactions.

Common (≥ 1/100 to < 1/10): anaemia, weight increase, insomnia, dizziness, headache, diarrhoea, nausea, liver transaminases increased, hyperhidrosis (incl. night sweats), rash, musculoskeletal pain and discomfort, gynaecomastia, testicular atrophy, erectile dysfunction, chills, pyrexia, fatigue, Influenza-like illness.

Uncommon (≥ 1/1000 to < 1/100): hypersensitivity, hyperglycemia / diabetes mellitus, cholesterol increased, weight decreased, appetite decreased, changes in blood calcium, depression, libido decreased, mental impairment, hypoaesthesia, vision blurred, cardiac arrhythmia (incl. atrial fibrillation), palpitations, QT prolongation, hypertension, vasovagal reaction (incl. hypotension), dyspnoea, constipation, vomiting, abdominal pain, abdominal discomfort, dry mouth, bilirubin increased, alkaline

phosphatase increased, urticaria, skin nodule, alopecia, pruritus, erythema, osteoporosis / osteopenia, arthralgia, muscular weakness, muscle spasms, joint swelling / stiffness, pollakiuria, micturition urgency, dysuria, nocturia, renal impairment, incontinence, testicular pain, breast pain, pelvic pain, genital irritation, ejaculation failure, malaise, peripheral oedema.

Rare (≥ 1/10,000 to < 1/1,000): neutropenic fever, anaphylactic reactions, myocardial infarction, cardiac failure.

Always consult the latest version of the SPC at www.medicines.org.uk/emc/ for full details.

Drug Interactions

No formal drug-drug interaction studies have been performed.

Since androgen deprivation treatment may prolong the QT interval, the concomitant use of degarelix with medicinal products known to prolong the QT interval or medicinal products able to induce torsades 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.

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.

This is not an exhaustive list of side effects, cautions, contra-indications or interactions please refer to the BNF or Summary of Product Characteristics for more information.