FIRMAGON® (degarelix)

A practitioner's guide to managing CV risk in patients with advanced hormone-dependent prostate cancer

Why is it important to consider ADT modality for patients with pre-existing CVD?

- Men with PCa are at an increased risk of CVD.[1] Men with PCa and pre-existing CVD treated with ADT are at an even greater risk.[1] ADT modality should be considered in order to reduce the risk of further CV events in patients[1]

Consider the right ADT modality for patients with pre-existing CVD to help minimise additional CV risk[1]

How to identify patients with pre-existing CVD using the STAMP tool[2]

STAMP – Identification of patients with CVD	
S	Stroke
T	Transient ischaemic attack
A	Abdominal aortic aneurysm or other aortic disease
M	Myocardial infarction, angina, or previous coronary revascularisation
P	Peripheral arterial disease

Adapted from Kenk M, et al. 2020[2]

If your advanced hormone-dependent PCa patient has any of the listed conditions, consider the use of Firmagon®, which has been associated with reduced CV events vs LHRH agonists in patients with these pre-existing conditions[3–8]

What is Firmagon®?

- Firmagon® is currently the only GnRH antagonist that is commercially available in the UK to treat adult male patients with advanced hormone-dependent PCa[9,10]
- Firmagon® is proposed as the GnRH antagonist treatment option of choice for men in this clinical setting

What is the evidence?

In a **retrospective pooled analysis** (N=2,328) of PCa patients with pre-existing CVD, initiating Firmagon® compared with LHRH agonist therapy, **the absolute risk reduction during the first year was 8.2%** and the NNT to avoid one CV event or death was 12[3]

In a **prospective randomised trial** of 80 patients with pre-existing CVD,* nine patients developed a MACCE. **Eight (20.5%) of these patients randomised to an LHRH agonist had a MACCE compared with one (2.4%) treated with the antagonist** (p=0.013; NNT=6)[4]

**Study did not meet its primary endpoint of endothelial dysfunction, but did meet the predefined secondary endpoint of developing a new CV event. MACCEs were defined as death, myocardial infarction, cerebrovascular event and heart catheterisation with stent insertion.*

ADT, androgen deprivation therapy; CV, cardiovascular; CVD, cardiovascular disease; GnRH, gonadotrophin-releasing hormone; LHRH, luteinising hormone-releasing hormone; MACCE, major adverse cardiac and cerebral event; NNT, number needed to treat; PCa, prostate cancer.

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What is the evidence? (continued)

Real-world data from a UK primary care database of patients treated with LHRH agonists or Firmagon® (N=9,081) showed that **significantly more patients treated with an agonist had a CV event after initiation of therapy compared with Firmagon®** (6.9% vs 17.7%; 0.39 [0.191, 0.799]; p=0.01; NNT=9)[5]

An **Italian observational study** carried out to evaluate incidence of CV events in a large cohort (N=9,785) concluded that the **incidence rate of CV events was significantly higher in patients treated with LHRH agonists rather than Firmagon®** (8.80 vs 6.24 per 100 person-year, p=0.002)[6]

Results from a **pharmacovigilance study** reported **higher increased odds of cardiac events in patients treated with LHRH agonists** (805 [7.7%]) vs in patients treated with a GnRH antagonist (102 [6.4%])[7]

In a **Phase III HERO trial**,† 622 patients received an oral GnRH antagonist and 308 received an LHRH agonist over 48 weeks. **Incidence of MACE was 2.9% in the GnRH antagonist group and 6.2% in the LHRH agonist group** (HR: 0.46; 95% CI: 0.24–0.88)[8]

†The oral GnRH antagonist is not available in the UK. In the study design, MACE were not a primary or secondary endpoint but reported as a prespecified safety analysis. MACE were defined as nonfatal myocardial infarction, nonfatal stroke, and death from any cause.

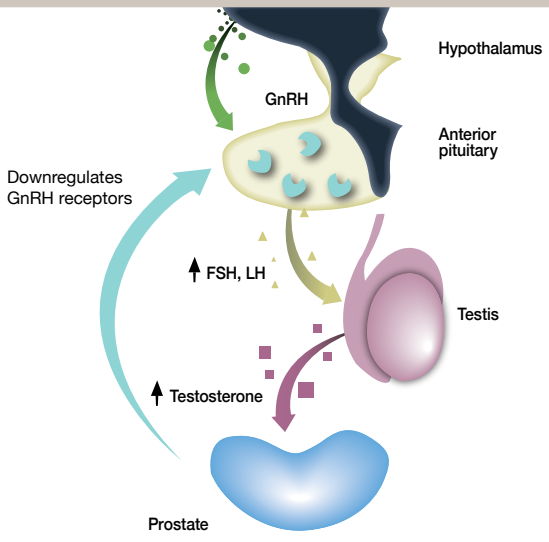
New guidelines refer to studies indicating lower CV morbidity associated with GnRH antagonists compared with LHRH agonists, and recommend considering their use in PCa patients with CV comorbidities[11,12]

Firmagon®: A different class of ADT

- Firmagon® is a different class of ADT providing better overall disease control and improved outcomes with regards to controlling symptoms,[13] preventing CV events,[13] and delaying disease progression[14,15] vs LHRH agonists[13]
- Firmagon® blocks GnRH receptors leading to immediate and profound suppression of LH, FSH and testosterone[16]

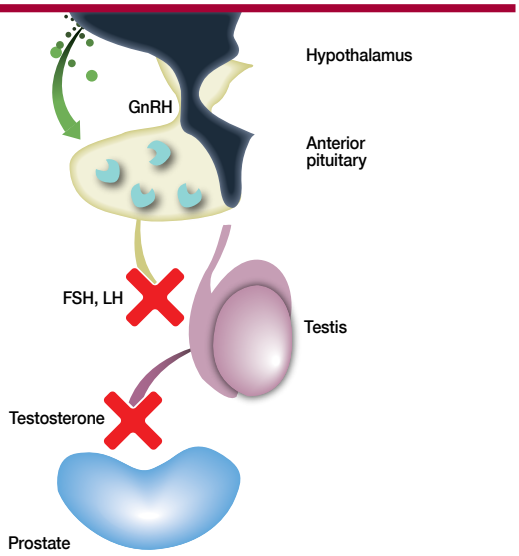
LHRH agonists

LHRH agonists initially overstimulate GnRH receptors leading to an increase of LH and testosterone before causing suppression



GnRH antagonists

GnRH antagonists block GnRH receptors leading to immediate and profound suppression of LH, FSH and testosterone



Adapted from Drudge-Coates L. 2009[16]

ADT, androgen deprivation therapy; CI, confidence interval; CV, cardiovascular; FSH, follicle-stimulating hormone; GnRH, gonadotrophin-releasing hormone; HR, hazard ratio; LH, luteinising hormone; LHRH, luteinising hormone-releasing hormone; MACE, major adverse cardiac event; NNT, number needed to treat; PCa, prostate cancer.

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Firmagon® dosing and administration: Start and stay

- Firmagon® is administered via monthly injection, starting with an initial 240 mg dose, and continued with 80 mg maintenance doses[9,10]

Watch how to reconstitute and administer Firmagon®
www.ferringukhub.co.uk/urology/firmagon/
Follow the link and scroll down to the bottom of the page to watch the reconstitution and administration video.

First month of treatment
240 mg administered as TWO deep subcutaneous injections of 120 mg each (NB. 3 x 80 mg injections are not equivalent)[9]

INITIATION DOSE

Monthly administration from Month 2 onwards
80 mg administered as ONE deep subcutaneous injection[10]

MAINTENANCE DOSE

A careful CV risk assessment should be considered in all PCa patients receiving ADT.[17] Firmagon® is currently the only GnRH antagonist that is commercially available in the UK to treat adult male patients with advanced hormone-dependent PCa[9,10]

For additional information, please contact medical.uk@ferring.com

ADT, androgen deprivation therapy; CV, cardiovascular; GnRH, gonadotrophin-releasing hormone; PCa, prostate cancer.

References

1. Higano CS, et al. *N Engl J Med.* 2020;382:2257–2259; **2.** Kenk M, et al. *Can Urol Assoc J.* 2020;14:E458–464; **3.** Albertsen PC, et al. *Eur Urol.* 2014;65:565–573; **4.** Margel D, et al. *J Urol.* 2019;202:1199–1208; **5.** Davey P and Kirby M, *J Urol.* 2020;203(45):e250–251; **6.** Perrone V, et al. *Ther Clin Risk Manag.* 2020;16:393–401; **7.** Cone EB, et al. *BJU Int.* 2020;126:9–10; **8.** Shore ND, et al. *N Engl J Med.* 2020;382:2187–2196; **9.** Firmagon® (degarelix) 120mg injection Summary of Product Characteristics. August 2020; **10.** Firmagon® (degarelix). 80mg injection Summary of Product Characteristics. August 2020; **11.** Mottet N, et al. EAU Guidelines. 2021; 67–68; **12.** Kokorovic A, et al. CUA Guideline. 2021; 3–12; **13.** Klotz L, et al. *Eur Urol.* 2014;66:1101–1108; **14.** Crawford ED, et al. *Urology.* 2014;83:1122–1128; **15.** Boccon-Gibod L, et al. *Ther Adv Urol.* 2011;3:127–140; **16.** Drudge-Coates L, *Int J Urol Nurs.* 2009;3:85–92; **17.** Cereda V, et al. *Heart Fail Rev.* 2020 June 4. doi: 10.1007/s10741-020-09984-2. [Epub ahead of print].

Prescribing information (PI)

Prescribing Information: Firmagon® (degarelix) 120mg and 80mg powder and solvent for solution for injection. **Please consult the full Summary of Product Characteristics before prescribing. Name of Product:** Firmagon 120mg and 80mg powder and solvent for solution for injection. **Composition:** Each vial contains 120mg or 80mg degarelix (as acetate). **Indication:** Firmagon is a gonadotrophin releasing hormone (GnRH) antagonist indicated for treatment of adult male patients with advanced hormone-dependent prostate cancer. **Dosage and administration**: For subcutaneous use only. Starting dose – 240mg administered as two subcutaneous injections of 120mg each. Maintenance dose – 80mg administered monthly as one subcutaneous injection. **Contraindications:** Hypersensitivity to the active substance or to any of the excipients. **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 450 msec, 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 Firmagon has not been studied in these patients. A thorough QT study showed that there was no intrinsic effect of Firmagon on QT/QTc interval. Monitoring of liver function in patients with known or suspected hepatic disorder is advised during treatment. Firmagon 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. It can be anticipated that long periods of testosterone suppression in men will have effects on bone density. Diabetic patients may require more frequent monitoring of blood glucose when receiving androgen deprivation therapy. 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. **Side Effects**: Very Common: hot flush, injection site adverse reactions. Common: 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: 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: neutropenic fever, anaphylactic reactions, myocardial infarction, cardiac failure. Please consult the full Summary of Product Characteristics for further information about side effects. **Presentation:** Firmagon 120mg contains 2 vials of 120mg powder for solution for injection and 2 solvent prefilled syringes, 2 vial adaptors and 2 administration needles. Firmagon 80mg contains 1 vial of 80mg powder for solution for injection and 1 solvent pre-filled syringe, 1 vial adaptor and administration needle. Solvent for both 120mg and 80mg: Water for injection. **Marketing Authorisation Number:** 80mg: EU/1/08/504/001, 120mg: EU/1/08/504/002. **Marketing Authorisation Holder:** Ferring Pharmaceuticals A/S, Kay Fiskers Plads 11, DK-2300 Copenhagen S, Denmark. **Legal category:** POM. **Basic NHS price:** Firmagon 120mg - £260.00; Firmagon 80mg - £129.37 **Date of preparation:** July 2018. Firmagon® is a registered trademark. **PI Job Code:** FN/1250/2018/UK(1).

Adverse events should be reported.
Reporting forms and information can be found at www.mhra.gov.uk/yellowcard.
Adverse events should also be reported to Ferring Pharmaceuticals Ltd.
Tel: 0800 111 4126. Email: medical.uk@ferring.com

Ferring Pharmaceuticals Ltd., Drayton Hall, Church Road, West Drayton, UB7 7PS. Telephone: 0844 931 0050, Fax: 0844 931 0057, www.ferring.co.uk

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