

FIRMAGON[®] (degarelix) – The Facts

What is FIRMAGON[®]?

- FIRMAGON[®] is indicated for the treatment of advanced hormone-dependent prostate cancer.
- FIRMAGON[®] is a synthetic peptide gonadotropin-releasing hormone (GnRH) blocker.¹
- FIRMAGON[®] effectively blocks the GnRH receptors in the pituitary gland and stops luteinizing hormone (LH) and follicle-stimulating hormone (FSH) production, which in turn leads to a rapid, profound, and sustained suppression of testosterone.²
- FIRMAGON[®] reduces levels of prostate specific antigen (PSA) to very low levels.
- FIRMAGON[®], a GnRH blocker, offers advantages over traditional luteinizing-hormone-releasing hormone (LHRH) agonist therapy by avoiding the risk of a testosterone surge at the initiation of treatment.
- FIRMAGON[®] is administered as a subcutaneous injection.
- FIRMAGON[®] was approved in both the EU and US in 2009. Commercialisation in other key global markets started in 2009.

FIRMAGON[®] clinical studies

- The long-term suppression of testosterone and PSA and the safety of FIRMAGON[®] have been extensively studied in men with prostate cancer for whom hormone therapy was indicated. There have been more than 20 studies involving more than 2000 patients.
- Studies from Phase I through to Phase III of FIRMAGON[®] have shown a fast, profound and sustained suppression of testosterone and an enduring reduction in PSA in men with prostate cancer.^{1,2,3,4,5,6}
- The pivotal Phase III study showed that FIRMAGON[®] was non inferior to leuprolide in the percentage of patients with testosterone ≤ 0.5 ng/ml from 28 to day 364 (primary endpoint): 97.2 % (IC 95% 93.5 -98.8) of patients maintained castration levels in a 1-year study with FIRMAGON arm versus 96.4 % (IC 95% 92.5 -98.2) with leuprolide.
 - In this study, monthly administration of FIRMAGON[®] was compared with the monthly LHRH agonist leuprolide over 12 months.
 - 96.1% of study patients on FIRMAGON[®] arm achieved suppression of testosterone levels to ≤ 0.5 ng/mL (castration levels) by day 3 compared to none (0%) of the men in the leuprolide arm.
 - This median low level of testosterone suppression in the FIRMAGON[®] arm was maintained from 28 to 364 days.
 - PSA reduction was faster in men treated with FIRMAGON[®] by day 14 compared to men treated with leuprolide (64% vs. 18%), demonstrating a more rapid response to treatment.

- FIRMAGON[®] and leuprolide's different mechanisms of action explained these results. The immediate onset of action of FIRMAGON[®] achieves a suppression of testosterone and PSA reduction more rapidly than leuprolide, and the reduced levels of testosterone and PSA were sustained throughout the treatment period.
- In addition, FIRMAGON[®] as a monotherapy achieved faster testosterone suppression and PSA reduction vs. leuprolide with no need for antiandrogen supplements at the initiation of treatment to prevent the possibility of clinical 'flare'.
- Results from a pre-defined secondary endpoint showed that compared to leuprolide, FIRMAGON[®] reduced the risk of PSA progression or death by 34% (HR =0.664 – 95%CI, 0.385-1.146)⁷ Further studies are needed to confirm these findings. In a subset of patients with more advanced disease (PSA>20 ng/ml at diagnosis), analysis of the time taken for the first 25% to experience PSA progression showed that FIRMAGON can delay PSA progression by 7 months compared to leuprolide.⁸
- A further analysis of secondary endpoints suggests that FIRMAGON[®] offers a greater reduction of serum alkaline phosphatase (S-ALP) than leuprolide, in patients with metastatic disease. In prostate cancer, elevated S-ALP levels are associated with progression of skeletal metastases as well as being significant predictors of early death.⁹
- Data from the ongoing FIRMAGON[®] extension study (CS21a) demonstrated the long-term efficacy and tolerability of FIRMAGON[®] and support its use as first-line androgen deprivation therapy.
 - After the one year phase III study, all patients were offered the option to receive FIRMAGON on a voluntary basis as part of the open-label extension study; this included patients who continued to receive FIRMAGON[®] and those who crossed over from leuprolide to FIRMAGON[®].
 - Beyond 1 year, the rate of PSA failure or death decreased in patients switched from leuprolide to FIRMAGON[®].⁸
 - Data from the extension trial suggest that patients starting on leuprolide experienced improved PSA control after switching to FIRMAGON[®].⁸
- Recent data from two Phase III trials comparing FIRMAGON[®] with a combination of LHRH agonist goserelin plus bicalutamide in men with advanced hormone-dependent prostate cancer, showed that FIRMAGON[®] was non inferior to the LHRH agonist at reducing total prostate volume and offered better relief from lower urinary tract symptoms (LUTS).^{10,11} LUTS can have a major negative impact on quality of life for men with prostate cancer.^{12,13}
 - The Phase IIIb CS30 trial assessed FIRMAGON[®] as a neoadjuvant hormone therapy in men with intermediate to high-risk prostate cancer. Week 12 results showed FIRMAGON[®] was non-inferior to goserelin plus bicalutamide

at prostate shrinking (mean percent change in prostate volume: -36.0% for FIRMAGON[®] vs. -35.3% for goserelin plus bicalutamide). In addition, FIRMAGON[®] demonstrated more pronounced LUTS relief compared to goserelin plus bicalutamide.

- The Phase IIIb CS31 trial assessed the ability of FIRMAGON[®] to decrease prostate cancer volume in a range of prostate cancer patients. Week 12 results showed prostate volume reduction achieved by FIRMAGON[®] was similar to the combination therapy of goserelin plus bicalutamide and that FIRMAGON[®] had a significantly more pronounced positive effect on LUTS.

FIRMAGON[®] side effect profile¹⁴

- In general, FIRMAGON[®] has been well tolerated in clinical studies. Most of the treatment related side effects associated with FIRMAGON[®] are related to androgen deprivation.
- The most frequently reported adverse events (>10 percent) during treatment with FIRMAGON[®] were hot flushes, injection site reaction and redness, which was usually associated with the first dose. Other common adverse events include injection site swelling, node and hardness, chills, fever or influenza-like illness after the injection, trouble sleeping, tiredness, weakness, dizziness, headache, increased weight, nausea, elevated levels of some liver enzymes and excessive sweating (including night sweats).

References

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- ¹⁴ FIRMAGON[®] Summary of Product Characteristics (European Union countries), July 2009.