HAUTE AUTORITÉ DE SANTÉ

TRANSPARENCY COMMITTEE
SUMMARY
20 APRIL 2022

The legally binding text is the original French opinion version

degarelix
FIRMAGON 80 mg and 120 mg powder and solvent for solution for injection

New indications

Key points

Favourable opinion for reimbursement in:

- Treatment of high-risk localised or locally advanced hormone dependent prostate cancer in combination with radiotherapy.
- Neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced hormone dependent prostate cancer.

What therapeutic improvement?

No clinical added value in the therapeutic strategy.

Role in the care pathway?

The current guidelines for the treatment of advanced hormone-dependent (locally advanced or metastatic) or high-risk localised prostate cancer recommend:

- at the high-risk localised or locally advanced stage: androgen deprivation hormone therapy using a GnRH agonist or antagonist combined with adjuvant external radiotherapy for 2 to 3 years (neo-adjuvant use may also be considered for 4 to 6 months).

It should be noted that the care pathway has recently evolved, with, in particular, the integration of second-generation androgen receptor antagonists since 2019, in combination with androgen deprivation therapy (ADT) in patients with non-metastatic castration-resistant prostate cancer (nmCRPC): apalutamide (ERLEADA), enzalutamide (XTANDI) or darolutamide (NUBEQA), in high-risk patients (PSA doubling time ≤ 10 months).

- at the metastatic stage:

o In hormone-sensitive patients (mHSPC), ADT should be used in combination with second-generation androgen receptor antagonists [apalutamide (ERLEADA)] or enzalutamide (XTANDI) or abiraterone acetate (ZYTIGA) in combination with prednisone or prednisolone in newly diagnosed high-risk patients, or with docetaxel in patients eligible for chemotherapy and who cannot receive the previously mentioned treatments. External radiotherapy may potentially be used for low-volume tumours.

o In castration-resistant patients (mCRPC), castration should be maintained and chemotherapy (docetaxel, cabazitaxel in patients previously treated with docetaxel) or second-generation hormone therapy [abiraterone acetate (ZYTIGA), enzalutamide (XTANDI)] may be proposed. It should be noted that radium 223 (XOFIGO) only has an MA in the event of bone metastases after two prior treatment lines.

Androgen deprivation therapy as neo-adjuvant or adjuvant treatment along with external radiotherapy in locally advanced or high-risk localised tumours, and at metastatic stages, includes two treatment classes, a GnRH antagonist, FIRMAGON (degarelix), and GnRH agonists (groserelin, triptorelin, leuprorelin). In the event of treatment with a GnRH agonist alone, temporary hypertestosteronaemia (flare up effect) may be observed. This effect is not observed with degarelix. A first-generation antiandrogen (bicalutamide, nilutamide, flutamide) generally used to be combined with the GnRH agonist for a short period of time in order to prevent the clinical consequences of serum testosterone peaks. Since the arrival of second-generation androgen receptor antagonists in combination with androgen deprivation therapy and the evolution of the care pathway, the use of first-generation antiandrogens has been limited (only in the context of complete androgen blockade).

Role of FIRMAGON (degarelix) in the care pathway

FIRMAGON (degarelix) is an alternative to GnRH agonists as a first-line treatment in the care pathway for hormone-dependent prostate cancer at high-risk localised and locally advanced stages as neo-adjuvant treatment prior to radiotherapy or in combination with radiotherapy. At present, the recommended duration of androgen deprivation hormone therapy using a GnRH agonist or antagonist combined with adjuvant external radiotherapy is 2 to 3 years (neoadjuvant use may also be considered for 4 to 6 months).

COMMITTEE'S CONCLUSIONS

Considering all of this information and further to debate and voting, the Committee considers:

Clinical benefit

Treatment of high-risk localised or locally advanced hormone dependent prostate cancer in combination with radiotherapy

◗ Prostate cancer is a serious, life-threatening disease.

◗ FIRMAGON (degarelix) is a curative medicinal product.

◗ The efficacy/adverse effects ratio of FIRMAGON (degarelix) proprietary medicinal products is high.

◗ There are medicinal alternatives (GnRH analogues).

◗ These proprietary medicinal products, in combination with radiotherapy, are a first-line treatment in the care pathway for high-risk localised or locally advanced hormone dependent prostate cancer.

Public health benefit
Considering:

- the seriousness of the disease and its incidence,
- the medical need partially met by GnRH analogues,
- the lack of additional response to the identified need, given the absence of any demonstrated additional impact on morbidity and mortality compared to GnRH analogues, and on quality of life,
- the lack of data on a potential impact on the organisation of care,

FIRMAGON (degarelix) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of FIRMAGON (degarelix) is substantial in the treatment of high-risk localised or locally advanced hormone dependent prostate cancer in combination with radiotherapy.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use in the treatment of high-risk localised or locally advanced hormone dependent prostate cancer in combination with radiotherapy and at the MA dosages.

Neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced hormone dependent prostate cancer

◗ Prostate cancer is a serious, life-threatening disease.

◗ FIRMAGON (degarelix) is a curative medicinal product.

◗ The efficacy/adverse effects ratio of FIRMAGON (degarelix) proprietary medicinal products is high.

◗ There are medicinal alternatives.

◗ These proprietary medicinal products are first-line treatments.

Public health benefit
Considering:

- the seriousness of the disease and its incidence,
- the medical need partially met by GnRH analogues,
- the lack of additional response to the identified need, given the absence of any demonstrated additional impact on morbidity and mortality compared to GnRH analogues, and on quality of life,
- the lack of data on a potential impact on the organisation of care,

FIRMAGON (degarelix) is unlikely to have an additional impact on public health.

Considering all these elements, the Committee deems that the clinical benefit of FIRMAGON (degarelix) is substantial as neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced hormone dependent prostate cancer.

The Committee issues a favourable opinion for inclusion in both the hospital formulary list and the retail formulary list of reimbursed proprietary medicinal products approved for use as neo-adjuvant treatment prior to radiotherapy in patients with high-risk localised or locally advanced hormone dependent prostate cancer and at the MA dosages.

- **Recommended reimbursement rate: 65%**

Clinical Added Value

Considering:
- demonstration of the non-inferiority of degarelix as neo-adjuvant treatment compared to the goserelin + bicalutamide combination in terms of mean variation in total prostate volume between inclusion and week 12 in a randomised, open-label study,
- the absence of any clinical study having specifically evaluated the efficacy and safety of FIRMAGON (degarelix) in combination with radiotherapy in the treatment of high-risk localised or locally advanced hormone dependent prostate cancer,
- the safety profile, which is deemed to be acceptable,

the Committee considers that FIRMAGON (degarelix) provides no clinical added value (CAV V) in the treatment of high-risk localised or locally advanced hormone dependent prostate cancer, as neo-adjuvant treatment prior to radiotherapy or in combination with radiotherapy.