**Drug Monograph**



## A - Drug Name

# degarelix

**COMMON TRADE NAME(S):** Firmagon®

back to top

## B - Mechanism of Action and Pharmacokinetics

Degarelix, a synthetic decapeptide is a gonadotropin-releasing hormone (GnRH) receptor antagonist and reduces the release of LH/FSH. Unlike earlier compounds, degarelix has only weak histamine releasing activity.

Marketing approval was based on testosterone suppression to castrate levels over a 1 year treatment period. Evidence of palliation of improved survival has not been demonstrated.

| | | |
|---|---|---|
| Absorption | Linear pharmacokinetics with no accumulation. Pharmacokinetics dependent upon concentration at injection site (↓ exposure with ↑ concentration). | |
| Distribution | Distributed throughout total body water | |
| | Cross blood brain barrier? | No information found. |
| | PPB | 90% (alpha-glycoprotein and albumin) |
| Metabolism | Undergoes hydrolysis by peptidases and proteases in the hepatobiliary system. Not a substrate, inducer, nor inhibitor of CYP 450 or p-glycoprotein. | |
| | Active metabolites | No |

| | | |
|---|---|---|
| | Inactive metabolites | Peptide fragments |
| Elimination | Biphasic elimination | |
| | Half-life | 43 days(starting dose); 31 days (maintenance dose) |
| | Urine | 20-30% (unchanged) |
| | Clearance | Hepatobiliary: 70-80% |
| | Clearance | 35-50 mL/h/kg |

back to top

## C - Indications and Status

**Health Canada Approvals:**

- Prostate cancer

Refer to the product monograph for a full list and details of approved indications.

back to top

## D - Adverse Effects

**Emetogenic Potential:** Not applicable

**Extravasation Potential:** None

The following table contains adverse effects reported mainly in the controlled study at the recommended dose.

| ORGAN SITE | SIDE EFFECT* (%) | ONSET** |
|---|---|---|
| Cardiovascular | Arterial thromboembolism (1%) | E |
| | Atrioventricular block (rare) | E |
| | Hypertension (6%) | E |
| | QT interval prolonged (20%) | E |
| Gastrointestinal | Constipation (5%) | E |
| | Diarrhea | I E |
| | Nausea (4%) | I |
| | Weight gain (9%) | E |
| General | Fatigue (3%) | E |
| | Flu-like symptoms (5%) | I |
| Hematological | Anemia (3%) | E |
| Hepatobiliary | ↑ LFTs (10%) ( <1% Grade 3) | E |
| Hypersensitivity | Hypersensitivity (rare) | I |
| Immune | Antibody response (46%) | D |
| Injection site | Injection site reaction (35%) (2% severe) | I |
| Metabolic / Endocrine | Abnormal electrolyte(s) | E |
| | ↑ Cholesterol (3%) | E |
| | Hyperglycemia | E |
| Musculoskeletal | Muscle weakness (less common) | E |
| | Musculoskeletal pain (6%) | E |
| | Osteoporosis (3%) | D |
| Nervous System | Dizziness (<5%) | E |
| | Headache (<5%) | E |
| | Insomnia (<5%) | E |
| Renal | Creatinine increased (2%) | E |
| Reproductive and breast disorders | Androgen deprivation symptoms (26%) (hot flashes, erectile dysfunction, gynecomastia) | E |

| | | |
|---|---|---|
| Urinary | Urinary symptoms (5%) (including infection) | E |

* "*Incidence*" may refer to an absolute value or the higher value from a reported range.
"*Rare*" may refer to events with < 1% incidence, reported in post-marketing, phase 1 studies, isolated data or anecdotal reports.

** I = *immediate* (onset in hours to days) E = *early* (days to weeks)
D = *delayed* (weeks to months) L = *late* (months to years)

The most common side effects for degarelix include injection site reaction, androgen deprivation symptoms, QT interval prolonged, ↑ LFTs, weight gain, hypertension, musculoskeletal pain, constipation and flu-like symptoms.

Pain, erythema, swelling, nodule and induration were the most common **injection site reactions** and primarily occurred with the first dose. These reactions were mostly transient and usually resolved after a few days. Reported serious injection site reactions include injection site infection, abscess and necrosis that could require surgical treatment/drainage.

Mild, transient increases in **LFTs** have been observed, and were not accompanied by a rise in bilirubin or clinical symptoms.

Men treated with **androgen deprivation** (including orchiectomy, GnRH agonists and antiandrogens) are at increased risk of developing heart disease, QTc prolongation, poor glucose tolerance and osteoporosis. However, degarelix has no intrinsic effect on the QTc.

**Anti-degarelix antibodies** are commonly reported but do not seem to have any clinical sequelae on safety or efficacy.

back to top

## E - Dosing

Refer to protocol by which patient is being treated.

***Adults:***

**Starting dose:** 240 mg subcut once (given as 2 x 120 mg injections at 40 mg/mL)

**One month later, start:**

**Maintenance**: 80 mg subcut (1 injection at 20 mg/mL) monthly

***Dosage with Hepatic Impairment:***

Although drug exposure is 10-18% lower in mild to moderate hepatic impairment, no dosage adjustment is required in these patients. Exercise caution in patients with severe hepatic impairment as no studies have been conducted in this population.

***Dosage with Renal Impairment:***

Drug clearance decreases by 23% in patients with moderate renal impairment (< 50 mL/min); however, no dosage adjustment is required in mild to moderate renal impairment. Exercise caution in patients with severe renal impairment as there is insufficient data available in this population.

***Dosage in the elderly:***

No dose adjustment required.

***Children:***

Not indicated for use in patients < 18 years of age.

back to top

## F - Administration Guidelines

- Outpatient prescription for administration at Cancer Centre or at physician's office.
- For **subcutaneous** injection in the abdomen.
- Dosage strength and concentration of injection differ between starting and maintenance doses. The concentrations recommended in the dosing section should be used, since the pharmacokinetics of degarelix are strongly concentration-dependent.
- Gloves should be worn during preparation and administration.
- Reconstitute using sterile water for injection (SWI) as directed in the product monograph. Reconstitution procedure may take up to 15 minutes.
- Do not shake the vial(s). Swirl gently during reconstitution.
- Resulting solution should be clear and free of undissolved powder or particles.
- Reconstituted product must be administered within 2 hours after addition of SWI.
- Ensure injection site is free of pressure from belts, waistbands, other clothing, or ribs. Rotate injection sites.
- For further details regarding proper reconstitution of degarelix, refer to the most updated Product Monograph.

back to top

## G - Special Precautions

### Contraindications:

- Patients who have hypersensitivity to degarelix or to any of its excipients.

### Other Warnings/Precautions:

- Fatigue and dizziness are common adverse reactions with degarelix and caution must be exercised with driving and operating machines.
- Long-term androgen deprivation prolongs the QT interval. Although a thorough QT study showed that there was no intrinsic effect of degarelix on heart rate, QT/QTc, PR intervals, QRS duration, or T or U wave morphology in healthy men, caution should be exercised in patients with congenital long QT syndrome, electrolyte abnormalities, congestive heart failure, and in patients taking antiarrhythmic medications.

### Other Drug Properties:

- Carcinogenicity: Yes

### Pregnancy and Lactation:

- Mutagenicity: No
- Genotoxicity: No information available
- Embryotoxicity: Yes
- Fetotoxicity: Yes
- Pregnancy:
  Degarelix is **contraindicated** in patients who are or may become pregnant. Adequate contraception should be used during treatment, and for at least 6 months after the last dose. (general recommendation)
- Breastfeeding:
  Degarelix is **only indicated in patients with prostate cancer**. There are no data on the presence of degarelix in human milk.
- Fertility effects: Probable
  Documented in animal studies

back to top

## H - Interactions

Clinically significant drug-drug interactions are unlikely other than those listed below.

Degarelix suppresses the pituitary-gonadal axis. Results of diagnostic tests for pituitary or gonadal functions may be affected.

| AGENT | EFFECT | MECHANISM | MANAGEMENT |
|---|---|---|---|
| Drugs that may prolong QT (i.e. Amiodarone, procainamide, sotalol, venlafaxine, amitriptyline, sunitinib, methadone, chloroquine, clarithromycin, haloperidol, fluconazole, moxifloxacin, domperidone, ondansetron, etc) | ↑ risk of QT interval prolongation | Additive | Caution; monitor closely. |

back to top

## I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

### Recommended Clinical Monitoring

| Monitor Type | Monitor Frequency |
|---|---|
| Creatinine | Baseline and as clinically indicated. |
| Electrolytes, including calcium, magnesium, potassium, sodium | Baseline and as clinically indicated. |
| Liver function tests | Baseline and as clinically indicated. |
| Blood glucose | Baseline and as clinically indicated. |
| ECG | Baseline and as clinically indicated. |
| Testosterone concentrations | In patients with hepatic impairment: monthly until medical castration is achieved then every 2 months. |
| Clinical assessment for local reactions, diabetes, osteoporosis, cardiovascular changes, hot flashes | Baseline and as clinically indicated. |

Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

back to top

## J - Supplementary Public Funding

**ODB - General Benefit (ODB Formulary )**

- degarelix ()

back to top

## K - References

Degarelix acetate: e-AHFS. Accessed December 30, 2009.

Frampton JE and Lyseng-Williamson KA. Degarelix. Drugs 2009; 69(14): 1967-76.

Prescribing Information: Firmagon® (degarelix acetate). Ferring Pharmaceuticals Inc. (US), Feb 2009.

Product Monograph: Firmagon® (degarelix acetate). Ferring Pharmaceuticals, March 18, 2016.

**February 2025** Updated Pregnancy and Lactation section

back to top

## L - Disclaimer

*Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.*

*The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.*

*The format and content of the drug monographs, regimen monographs, appendices and symptom management information contained in the Formulary will change as they are reviewed and revised on a periodic basis. The date of last revision will be visible on each page of the monograph and regimen. Since standards of usage are constantly evolving, it is advised that the Formulary not be used as the sole source of information. It is strongly recommended that original references or product monograph be consulted prior to using a chemotherapy regimen for the first time.*

*Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.*

*While care has been taken in the preparation of the information contained in the Formulary, such information is provided on an “as-is” basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information’s quality, accuracy, currency, completeness, or reliability.*

*CCO and the Formulary’s content providers shall have no liability, whether direct, indirect, consequential, contingent, special, or incidental, related to or arising from the information in the Formulary or its use thereof, whether based on breach of contract or tort (including negligence), and even if advised of the possibility thereof. Anyone using the information in the Formulary does so at his or her own risk, and by using such information, agrees to indemnify CCO*

*and its content providers from any and all liability, loss, damages, costs and expenses (including legal fees and expenses) arising from such person's use of the information in the Formulary.*

back to top