

Drug Monograph

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A - Drug Name

degarelix

SYNONYM(S): FE200486**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).
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Distribution

Distributed throughout total body water

Cross blood brain barrier?	No information found.
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PPB	90% (alpha-glycoprotein and albumin)
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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

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C - Indications and Status

Health Canada Approvals:

Testosterone suppression in patients with advanced prostate cancer in whom androgen deprivation is warranted.

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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.
Dose-limiting side effects are underlined.

** 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.

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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.

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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.

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- For further details regarding proper reconstitution of degarelix, refer to the most updated Product Monograph.

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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:

- Embryotoxicity: Yes
- Fertility effects: Documented in animals
Reversible infertility has been observed in animal studies.
- Fetotoxicity: Yes
Degarelix is **contraindicated** in pregnancy and in women of child-bearing potential.
Adequate contraception should be used during treatment, and for at least **6 months** after the last dose.
- Genotoxicity: No information available
- Mutagenicity: No
- Excretion into breast milk: Unknown
Breastfeeding is not recommended.

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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****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](#)

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J - Supplementary Public Funding

ODB - General Benefit (
[ODB Formulary](#)
)

- degarelix ()

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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.

August 2018 Updated adverse effects (severe injection site reactions, hypersensitivity, antibody formation), and warnings.

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L - Disclaimer

Refer to the [New Drug Funding Program](#) or [Ontario Public Drug Programs](#) websites for the most up-to-date public funding information.

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