

**DRUG NAME: Degarelix****SYNONYM(S):** degarelix acetate**COMMON TRADE NAME(S):** FIRMAGON®**CLASSIFICATION:** hormonal agent*Special pediatric considerations are noted when applicable, otherwise adult provisions apply.***MECHANISM OF ACTION:**

Degarelix is a selective gonadotropin-releasing hormone (GnRH) receptor antagonist (also known as luteinizing hormone-releasing hormone [LHRH] antagonist). It binds immediately, competitively, and reversibly to the pituitary GnRH receptors, and reduces the release of luteinizing hormone, follicle-stimulating hormone, and consequently testosterone by the testes. Degarelix does not induce a testosterone surge or clinical flare, therefore co-administration with an anti-androgen is not required. Medical castration levels are achieved in 96% of patients after 3 days.<sup>1,2</sup>

**PHARMACOKINETICS:**

Distribution	rapid initially, then slowly due to depot formation <sup>1,3</sup> ; higher concentration increases half-life and decreases C <sub>max</sub> <sup>4</sup> ; time to peak 37-42 h	
	cross blood brain barrier?	no information found
	volume of distribution <sup>5</sup>	>1000 L
	plasma protein binding	~90%
Metabolism	hepatobiliary, via peptide hydrolysis <sup>3</sup>	
	active metabolite(s)	no information found
	inactive metabolite(s)	no information found
Excretion	mainly excreted as peptide fragments in feces	
	urine <sup>2</sup>	20-30% (unchanged)
	feces <sup>3</sup>	70-80%
	terminal half life	starting dose: 43-53 days <sup>1,2</sup> ; maintenance dose: 28 days
	clearance <sup>4</sup>	~9 L/h

Adapted from standard reference<sup>1</sup> unless specified otherwise.**USES:****Primary uses:**

\*Prostate cancer

\*Health Canada approved indication

**Other uses:****SPECIAL PRECAUTIONS:****Contraindications:**

- history of hypersensitivity reaction to degarelix<sup>1</sup>
- women who are or may become pregnant<sup>1</sup>

**Caution:**

- Hypertension and myocardial infarction have been reported with degarelix. Screening for and treatment/prevention of **cardiovascular disease** is recommended.<sup>1</sup>
- **QT/QTc prolongation** is associated with degarelix. Use with caution in patients with congenital long QT syndrome, electrolyte abnormalities, or congestive heart failure, or taking concurrent medications which prolong the QTc interval or induce torsades de pointes.<sup>1</sup>

**Special populations:** Degarelix is not intended for use in women and children.<sup>1</sup>

**Carcinogenicity:** Malignant lymphoma and squamous cell carcinoma have been reported post-marketing.<sup>3</sup>

**Mutagenicity:** Not mutagenic in Ames test. Degarelix is not clastogenic in mammalian *in vitro* and *in vivo* chromosome tests.<sup>5</sup>

**Fertility:** Reversible infertility has been reported in both male and female rats.<sup>1</sup>

**Pregnancy:** FDA Pregnancy Category X.<sup>3</sup> Studies in animals or humans have shown fetal abnormalities, or there is evidence of fetal risk based on human experience, or both, and the risk of the use of the drug in pregnant women clearly outweighs any possible benefit.

In animal studies, increased early post-implantation loss, embryo/fetal lethality and abortion, increased minor skeletal abnormalities and variants have been reported.<sup>1</sup>

**Breastfeeding** is not recommended due to the potential secretion into breast milk.

**SIDE EFFECTS:**

The table includes adverse events that presented during drug treatment but may not necessarily have a causal relationship with the drug. Because clinical trials are conducted under very specific conditions, the adverse event rates observed may not reflect the rates observed in clinical practice. Adverse events are generally included if they were reported in more than 1% of patients in the product monograph or pivotal trials, and/or determined to be clinically important.

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <b>bold, italics</b>	
blood and lymphatic system/ febrile neutropenia	anemia (3%)
cardiac, see paragraph following <b>Side Effects</b> table	<b>atrio-ventricular first degree block</b> (<1%)
	<b>cardiac arrhythmia</b> (<1%)
	<b>myocardial infarction</b> (1%)
gastrointestinal	<i>emetogenic potential: rare</i> <sup>6</sup>
	constipation (3-5%)
	diarrhea (≥1%)
	nausea (1-5%)
general disorders and administration site conditions	<i>extravasation hazard: none</i> <sup>7</sup>
	asthenia (1-5%)
	chills (3-5%); transient, occurs within hours of dosing
	fatigue (≥3%) <sup>1,3</sup>
	fever (≥1%); transient, occurs within hours of dosing <sup>1,3</sup>
	influenza-like illness (1%); transient, occurs within hours of dosing

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <b>bold, italics</b>	
	<b>injection site reactions</b> (35-44%, severe ≤2%), including pain (28%), erythema (17%), swelling (6%), indurations (4%), nodule (3-4%), infection (1%), itching and soreness; primarily with starting dose, transient <sup>1,3</sup>
immune system	hypersensitivity (including anaphylaxis, urticaria, rash, pruritus, and angioedema) (<1%) <sup>1,3</sup>
infections and infestations	urinary tract infection (1-5%)
injury, poisoning, and procedural complications	fracture (<1%)
investigations	blood urea nitrogen increase (15%)
	creatinine increase (2%)
	gamma-glutamyltransferase increase (2-10%, severe <1%); reversible
	hypercholesterolemia (3-6%)
	<b>QT/QTc interval prolongation</b> (20%)
	transaminases increase (2-47%, severe <1%); reversible <sup>1,3</sup>
	weight decrease (≥10%) <sup>3</sup>
	weight increase (7-11%)
metabolism and nutrition	hyperglycemia/diabetes mellitus (<1%)
	hyperkalemia (6%)
musculoskeletal and connective tissue	arthralgia (3-5%)
	back pain (6%)
	musculoskeletal/connective tissue events (17%) <sup>4</sup>
	osteoarthritis (<1%) <sup>3</sup>
	<b>osteoporosis</b> or <b>osteopenia</b> (<1%); see paragraph following <b>Side Effects</b> table
neoplasms	malignant lymphoma, squamous cell carcinoma (<1%) <sup>3</sup>
nervous system	cerebrovascular accident (<1%) <sup>3</sup>
	dizziness (1-5%)
	headache (1-5%)
	vaso-vagal reaction (<1%)
psychiatric	depression, mental status changes (<1%) <sup>3</sup>
	insomnia (1-5%)
renal and urinary	pollakiuria, micturition urgency (<1%)
	renal impairment (<1%)
reproductive system and breast disorders	<b>erectile dysfunction, impotence</b> (≥1%) <sup>1-3</sup> ; see paragraph following <b>Side Effects</b> table
	gynecomastia (≥1%)
	<b>libido, decreased</b> <sup>2,3</sup> ; see paragraph following <b>Side Effects</b> table
	testicular atrophy (≥1%)
skin and subcutaneous	hyperhidrosis (≥1%)

ORGAN SITE	SIDE EFFECT
Clinically important side effects are in <b><i>bold, italics</i></b>	
tissue	night sweats (1-5%)
vascular	<b><i>hot flashes</i></b> (25-26%)
	hypertension (6-7%)

Adapted from standard reference<sup>1</sup> unless specified otherwise.

Orchiectomy and/or ***long-term androgen deprivation therapy*** has been associated with an increased risk of heart disease and QT prolongation and decreased glucose tolerance and bone density. The expected physiological effects of testosterone suppression (i.e., hot flashes, decreased libido, and erectile dysfunction) have been reported with GnRH agonist and are anticipated with GnRH antagonists with a comparable incidence.<sup>1,8</sup>

### INTERACTIONS:

Degarelix is associated with QT/QTc interval prolongation. Concurrent therapy with drugs associated with QTc prolongation and/or torsades de pointes should be used with caution<sup>1</sup>; consider monitoring for QT prolongation or cardiac arrhythmias.<sup>3</sup>

### SUPPLY AND STORAGE:

***Injection:*** Ferring Pharmaceuticals supplies degarelix for injection as 80 mg and 120 mg vials of lyophilized powder for reconstitution in self-contained treatment packs: a Treatment Starter pack, a Treatment Maintenance pack and a 3-pack Treatment Maintenance pack. Each self-contained treatment pack contains pre-filled syringe(s) with solvent (sterile water for injection), vial adapter(s), plunger rod(s), and injection needle(s). The Treatment Starter pack contains 2 single-use vials of degarelix 120 mg powder. The Treatment Maintenance pack contains 1 single-use vial of degarelix 80 mg powder. The 3-pack Treatment Maintenance pack contains 3 single-use vials of degarelix 80 mg powder. Store at room temperature. Do not shake.<sup>1</sup>

***For basic information on the current brand used at the BC Cancer Agency, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.***

### SOLUTION PREPARATION AND COMPATIBILITY:

***For basic information on the current brand used at the BC Cancer Agency, see [Chemotherapy Preparation and Stability Chart](#) in Appendix.***

***Additional information:*** Reconstitution directions should be carefully followed for each kit to ensure correct final concentrations.<sup>1</sup> Administration of other concentrations is not recommended.<sup>2</sup>

***Compatibility:*** consult detailed reference

**PARENTERAL ADMINISTRATION:**

BCCA administration guideline noted in ***bold, italics***

<b><i>Subcutaneous</i></b> <sup>9</sup>	<ul style="list-style-type: none"> <li>• forms a depot after deep subcutaneous injection<sup>1</sup></li> <li>• administer in the abdominal region, in areas that will not be exposed to pressure; rotate injection sites<sup>1</sup></li> <li>• insert needle deeply at an angle of not less than 45 degrees<sup>1</sup></li> <li>• to reduce incidence of injection site reactions: inject slowly, leave needle in place for 30 seconds after injection, and then withdraw needle slowly<sup>10</sup></li> </ul>
Intramuscular	not recommended <sup>3</sup>
Direct intravenous	not recommended <sup>1</sup>
Intermittent infusion	not recommended <sup>1</sup>
Continuous infusion	not recommended <sup>1</sup>
Intraperitoneal	no information found
Intrapleural	no information found
Intrathecal	no information found
Intra-arterial	no information found
Intravesical	no information found

**DOSAGE GUIDELINES:**

Refer to protocol by which patient is being treated. Numerous dosing schedules exist and depend on disease, response, and concomitant therapy. Guidelines for dosing also include consideration of absolute neutrophil count (ANC). Dosage may be reduced, delayed or discontinued in patients with bone marrow depression due to cytotoxic/radiation therapy or with other toxicities.

**Adults:**

BCCA usual dose noted in ***bold, italics***

Cycle Length:

***Subcutaneous***<sup>1,9</sup>:

***1 month:***

***starting dose: 240 mg SC (as two injections of 120 mg) on day 1***

***maintenance dose: 80 mg SC (as a single injection) monthly, beginning one month after starting dose***

*Concurrent radiation:*

no information found

*Dosage in myelosuppression:*

modify according to protocol by which patient is being treated; if no guidelines available, refer to Appendix 6 "Dosage Modification for Myelosuppression"

*Dosage in renal failure:*

no adjustment recommended with mild or moderate impairment; no information found for severe impairment<sup>1</sup>

*Dosage in hepatic failure:*

no adjustment recommended with mild or moderate impairment; no information found for severe impairment<sup>1</sup>

*Dosage in dialysis:*

no information found

**Children:**

not intended for use in children<sup>1</sup>

**REFERENCES:**

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9. BC Cancer Agency Genitourinary Tumour Group. (GUPLHRHA) BCCA Protocol Summary for Therapy for Advanced Prostate Cancer Using LHRH Antagonist Degarelix. Vancouver, British Columbia: BC Cancer Agency; 1 Jun 2014.
10. Anne Brusby MD. Personal communication. Medical Director, Ferring Pharmaceuticals Inc.; June 2013.