

## HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use **TRADENAME** safely and effectively. See full prescribing information for **TRADENAME**.

**TRADENAME**<sup>®</sup> (degarelix for injection) for subcutaneous administration

Initial U.S. Approval: 2008

### -----INDICATIONS AND USAGE-----

**TRADENAME** is a GnRH receptor antagonist indicated for treatment of patients with advanced prostate cancer. (1)

### -----DOSAGE AND ADMINISTRATION-----

- **TRADENAME** is for subcutaneous administration only and is not to be administered intravenously.
- Treatment is started with a dose of 240 mg given as two injections of 120 mg each.
- The starting dose is followed by maintenance doses of 80 mg administered as a single injection every 28 days. (2)

### -----DOSAGE FORMS AND STRENGTHS-----

- **TRADENAME** (degarelix for injection) 120 mg per vial
- **TRADENAME** (degarelix for injection) 80 mg per vial

### -----CONTRAINDICATIONS-----

Degarelix is contraindicated in:

- Patients with previous hypersensitivity reactions to **TRADENAME**. (4)

- Pregnancy Category X. Fetal harm can occur when administered to pregnant women. (4)

### -----WARNINGS AND PRECAUTIONS-----

- Long-term androgen deprivation therapy prolongs the QT interval. Consider risks and benefits. (5.2)

### -----ADVERSE REACTIONS-----

The most commonly observed adverse reactions (≥10%) during **TRADENAME** therapy included injection site reactions (e.g., pain, erythema, swelling or induration), hot flashes, increased weight, and increases in serum levels of transaminases and gamma-glutamyltransferase (GGT). (6)

**To report SUSPECTED ADVERSE REACTIONS, contact Ferring at 1-888-FERRING (1-888-337-7464) or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

### -----DRUG INTERACTIONS-----

Clinically significant CYP450 pharmacokinetic drug-drug interactions are unlikely. (7)

### -----USE IN SPECIFIC POPULATIONS-----

There is no need to adjust the dose for the elderly or in patients with mild or moderate liver or kidney function impairment. Patients with severe liver or kidney dysfunction have not been studied and caution is therefore warranted. (8)

**See 17 for PATIENT COUNSELING INFORMATION (and FDA approved patient labeling)**

Revised:12/2008

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## FULL PRESCRIBING INFORMATION

### 1 INDICATIONS AND USAGE

TRADENAME is a GnRH receptor antagonist indicated for treatment of patients with advanced prostate cancer.

### 2 DOSAGE AND ADMINISTRATION

TRADENAME is for subcutaneous administration only and is not to be administered intravenously.

Dosing information:

Starting dose	Maintenance dose – Administration every 28 days
240 mg given as two subcutaneous injections of 120 mg at a concentration of 40 mg/mL	80 mg given as one subcutaneous injection at a concentration of 20 mg/mL

The first maintenance dose should be given 28 days after the starting dose.

TRADENAME is administered as a subcutaneous injection in the abdominal region. As with other drugs administered by subcutaneous injection, the injection site should vary periodically. Injections should be given in areas of the abdomen that will not be exposed to pressure, e.g. not close to waistband or belt nor close to the ribs.

TRADENAME is supplied as a powder to be reconstituted with Sterile Water for Injection, USP.

The reconstitution procedure needs to be carefully followed. Administration of other concentrations is not recommended. See Instructions for Proper Use below.

#### Instructions for Proper Use

##### NOTE:

- Gloves should be worn during preparation and administration.
- Reconstituted drug must be administered within one hour after addition of Sterile Water for Injection, USP (WFI).
- Keep the vial vertical at all times
- Do not shake the vials
- Follow aseptic technique

#### TRADENAME 120 mg

The Treatment Initiation pack contains 2 vials of TRADENAME 120 mg that must be prepared for 2 subcutaneous injections. Hence, the instructions here below need to be repeated a second time.

Prepare TRADENAME 120 mg for reconstitution by gathering the following:

- 6 mL of Sterile Water for Injection, USP (WFI); Do not use Bacteriostatic Water for Injection.
- 2 reconstitution needles – 21G / 2 inch
- 2 administration needles for subcutaneous injection – 27 G / 1-1/4 inch
- 2 injection syringes (5 mL)

1. Draw up 3 mL WFI with a reconstitution needle (21G / 2 in).

2. Inject the WFI slowly into the TRADENAME 120 mg vial. To keep the product and syringe sterile, do not remove the syringe and the needle.
3. Keeping the vial in an upright position, swirl it very gently until the liquid looks clear and without undissolved powder or particles. If the powder adheres to the vial over the liquid surface, the vial can be tilted slightly to dissolve powder. Avoid shaking to prevent foam formation. A ring of small air bubbles on the surface of the liquid is acceptable. The reconstitution procedure may take up to 15 minutes.
4. Tilt the vial slightly and keep the needle in the lowest part of the vial. Withdraw 3 mL of TRADENAME 120 mg without turning the vial upside down.
5. Exchange the reconstitution needle with the administration needle for deep subcutaneous injection (27G / 1-1/4 in). Remove any air bubbles.
6. Inject 3 mL of TRADENAME 120 mg subcutaneously immediately after reconstitution.
  - Grasp the skin of the abdomen, elevate the subcutaneous tissue. Insert the needle deeply at an angle of not less than 45 degrees.
  - Gently pull back the plunger to check if blood is aspirated. If blood appears in the syringe, the reconstituted product can no longer be used. Discontinue the procedure and discard the syringe and the needle (reconstitute a new dose for the patient).
7. Repeat reconstitution procedure for the second dose. Choose a different injection site and inject 3 mL.

#### TRADENAME 80 mg

The Treatment Maintenance pack contains 1 vial of TRADENAME 80 mg that must be prepared for subcutaneous injection.

Prepare TRADENAME 80 mg for reconstitution by gathering the following:

- 4.2 mL of Sterile Water for Injection, USP (WFI); Do not use Bacteriostatic Water for Injection
  - 1 reconstitution needle – 21G / 2 inch
  - 1 administration needle for sc injection – 27 G / 1-1/4 inch
  - 1 injection syringe (5 mL)
1. Draw up 4.2 mL WFI with the reconstitution needle (21G / 2 in).
  2. Inject the WFI slowly into the TRADENAME 80 mg vial. To keep the product and syringe sterile, do not remove the syringe and the needle.
  3. Keeping the vial in an upright position, swirl it very gently until the liquid looks clear and without undissolved powder or particles. If the powder adheres to the vial over the liquid surface, the vial can be tilted slightly to dissolve powder. Avoid shaking to prevent foam formation. A ring of small air bubbles on the surface of the liquid is acceptable. The reconstitution procedure may take up to 15 minutes.
  4. Tilt the vial slightly and keep the needle in the lowest part of the vial. Withdraw 4 mL of TRADENAME 80 mg without turning the vial upside down.
  5. Exchange the reconstitution needle with the administration needle for deep subcutaneous injection (27G / 1-1/4 in). Remove any air bubbles.
  6. Inject 4 mL of TRADENAME 80 mg subcutaneously immediately after reconstitution.

- Grasp the skin of the abdomen, elevate the subcutaneous tissue. Insert the needle deeply at an angle of not less than 45 degrees.
- Gently pull back the plunger to check if blood is aspirated. If blood appears in the syringe, the reconstituted product can no longer be used. Discontinue the procedure and discard the syringe and the needle (reconstitute a new dose for the patient).

### 3 DOSAGE FORMS AND STRENGTHS

#### Starting dose

Powder for injection 120 mg:

One vial of TRADENAME 120 mg contains 120 mg degarelix. Each vial is to be reconstituted with 3 mL of Sterile Water for Injection. 3 mL is withdrawn to deliver 120 mg degarelix at a concentration of 40 mg/mL.

One starting dose comprises 240 mg given as two 3 mL injections of 120 mg each.

#### Maintenance dose

Powder for injection 80 mg:

One vial of TRADENAME 80 mg contains to 80 mg degarelix. Each vial is to be reconstituted with 4.2 mL of Sterile Water for Injection. 4 mL is withdrawn to deliver 80 mg degarelix at a concentration of 20 mg/mL.

One maintenance dose comprises 80 mg given as one 4 mL injection.

### 4 CONTRAINDICATIONS

TRADENAME is contraindicated in patients with known hypersensitivity to degarelix or to any of the product components.

Degarelix is contraindicated in women who are or may become pregnant. Degarelix can cause fetal harm when administered to a pregnant woman. Degarelix given to rabbits during organogenesis at doses that were 0.02% of the clinical loading dose (240 mg) on a mg/m<sup>2</sup> basis caused embryo/fetal lethality and abortion. When degarelix was given to female rats during organogenesis, at doses that were just 0.036% of the clinical loading dose on a mg/m<sup>2</sup> basis, there was an increase post implantation loss and a decrease in the number of live fetuses. If this drug is used during pregnancy, or if the patient becomes pregnant while taking this drug, the patient should be apprised of the potential hazard to the fetus.

### 5 WARNINGS AND PRECAUTIONS

#### 5.1 Use in Pregnancy

##### **Pregnancy Category X**

Women who are or may become pregnant should not take TRADENAME. [*see Contraindications (4) and Use in Specific Populations (8.1)*]

#### 5.2 Effect on QT/QTc Interval

Long-term androgen deprivation therapy prolongs the QT interval. Physicians should consider whether the benefits of androgen deprivation therapy outweigh the potential risks in patients with congenital long QT syndrome, electrolyte abnormalities, or congestive heart failure and in patients taking Class IA (e.g. quinidine, procainamide) or Class III (e.g. amiodarone, sotalol) antiarrhythmic medications.

In the randomized, active-controlled trial comparing TRADENAME to leuprolide, periodic electrocardiograms were performed. Seven patients, three (<1%) in the pooled degarelix group and four (2%) patients in the leuprolide 7.5 mg group, had a QTcF  $\geq$  500 ms. From baseline to end of study the median change for TRADENAME was 12.3 msec and for leuprolide was 16.7 msec.

### **5.3 Laboratory Testing**

Therapy with TRADENAME results in suppression of the pituitary gonadal system. Results of diagnostic tests of the pituitary gonadotropic and gonadal functions conducted during and after TRADENAME may be affected.

The therapeutic effect of TRADENAME should be monitored by measuring serum concentrations of prostate-specific antigen (PSA) periodically. If PSA increases, serum concentrations of testosterone should be measured.

## **6 ADVERSE REACTIONS**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

A total of 1325 patients with prostate cancer received TRADENAME either as a monthly treatment (60-160 mg) or as a single dose (up to 320 mg). A total of 1032 patients (78%) were treated for at least 6 months and 853 patients (64%) were treated for one year or more. The most commonly observed adverse reactions during TRADENAME therapy included injection site reactions (e.g. pain, erythema, swelling or induration), hot flashes, increased weight, fatigue, and increases in serum levels of transaminases and gamma-glutamyltransferase (GGT). The majority of the adverse reactions were Grade 1 or 2, with Grade 3/4 adverse reaction incidences of 1% or less.

TRADENAME was studied in an active-controlled trial (N = 610) in which patients with prostate cancer were randomized to receive TRADENAME (subcutaneous) or leuprolide (intramuscular) monthly for 12 months. Adverse reactions reported in 5% of patients or more are shown in Table 1.

**Table 1. Adverse Reactions Reported in  $\geq 5\%$  of Patients in an Active Controlled Study**

	TRADENAME 240/160 mg (subcutaneous) N = 202	TRADENAME 240/80 mg (subcutaneous) N = 207	leuprolide 7.5 mg (intramuscular) N = 201
	%	%	%
Percentage of subjects with adverse events	83	79	78
<i>Body as a whole</i>			
Injection site adverse events	44	35	<1
Weight increase	11	9	12
Fatigue	6	3	6
Chills	4	5	0
<i>Cardiovascular system</i>			
Hot flash	26	26	21
Hypertension	7	6	4
<i>Musculoskeletal system</i>			
Back pain	6	6	8
Arthralgia	4	5	9
<i>Urogenital system</i>			
Urinary tract infection	2	5	9
<i>Digestive system</i>			
Increases in Transaminases and GGT	10	10	5
Constipation	3	5	5

The most frequently reported adverse reactions at the injection sites were pain (28%), erythema (17%), swelling (6%), induration (4%) and nodule (3%). These adverse reactions were mostly transient, of mild to moderate intensity, occurred primarily with the starting dose and led to few discontinuations (<1%). Grade 3 injection site reactions occurred in 2% or less of patients receiving degarelix.

Hepatic laboratory abnormalities were primarily Grade 1 or 2 and were generally reversible. Grade 3 hepatic laboratory abnormalities occurred in less than 1% of patients.

In 1-5% of patients the following adverse reactions, not already listed, were considered related to TRADENAME by the investigator:

*Body as a whole:* Asthenia, fever, night sweats; *Digestive system:* Nausea; *Nervous system:* Dizziness, headache, insomnia.

The following adverse reactions, not already listed, were reported to be drug-related by the investigator in  $\geq 1\%$  of patients: erectile dysfunction, gynecomastia, hyperhidrosis, testicular atrophy, and diarrhea.

Changes in bone density:

Decreased bone density has been reported in the medical literature in men who have had orchiectomy or who have been treated with a GnRH agonist. It can be anticipated that long periods of medical castration in men will result in decreased bone density.

Anti-degarelix antibody development has been observed in 10% of patients after treatment with TRADENAME

for 1 year. There is no indication that the efficacy or safety of TRADENAME treatment is affected by antibody formation.

## **7 DRUG INTERACTIONS**

No drug-drug interaction studies were conducted.

Degarelix is not a substrate for the human CYP450 system. Degarelix is not an inducer or inhibitor of the CYP450 system *in vitro*. Therefore, clinically significant CYP450 pharmacokinetic drug-drug interactions are unlikely.

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

Category X [see *Contraindications (4) and Warnings and Precautions (5.1)*]

Women who are or may become pregnant should not take TRADENAME.

When degarelix was given to rabbits during early organogenesis at doses of 0.002 mg/kg/day (about 0.02% of the clinical loading dose on a mg/m<sup>2</sup> basis), there was an increase in early post-implantation loss. Degarelix given to rabbits during mid and late organogenesis at doses of 0.006 mg/kg/day (about 0.05% of the clinical loading dose on a mg/m<sup>2</sup> basis) caused embryo/fetal lethality and abortion. When degarelix was given to female rats during early organogenesis, at doses of 0.0045 mg/kg/day (about 0.036% of the clinical loading dose on a mg/m<sup>2</sup> basis), there was an increase in early post-implantation loss. When degarelix was given to female rats during mid and late organogenesis, at doses of 0.045 mg/kg/day (about 0.36% of the clinical loading dose on a mg/m<sup>2</sup> basis), there was an increase in the number of minor skeletal abnormalities and variants.

### **8.3 Nursing Mothers**

TRADENAME is not indicated for use in women and is contraindicated in women who are or who may become pregnant. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from degarelix, a decision should be made whether to discontinue nursing or discontinue the drug taking into account the importance of the drug to the mother.

### **8.4 Pediatric Use**

Safety and effectiveness in pediatric patients have not been established.

### **8.5 Geriatric Use**

Of the total number of subjects in clinical studies of TRADENAME, 82% were age 65 and over, while 42% were age 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, but greater sensitivity of some older individuals cannot be ruled out.

### **8.6 Renal Impairment**

No pharmacokinetic studies in renally impaired patients have been conducted. At least 20-30% of a given dose of degarelix is excreted unchanged in the urine.

A population pharmacokinetic analysis of data from the randomized study demonstrated that there is no significant effect of mild renal impairment [creatinine clearance (CrCL) 50-80 mL/min] on either the degarelix concentration or testosterone concentration. Data on patients with moderate or severe renal impairment is limited and therefore degarelix should be used with caution in patients with CrCL < 50 mL/min.

## 8.7 Hepatic Impairment

Patients with hepatic impairment were excluded from the randomized trial.

A single dose of 1 mg degarelix administered as an intravenous infusion over 1 hour was studied in 16 non-prostate cancer patients with either mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment. Compared to non-prostate cancer patients with normal liver function, the exposure of degarelix decreased by 10% and 18% in patients with mild and moderate hepatic impairment, respectively. Therefore, dose adjustment is not necessary in patients with mild or moderate hepatic impairment. However, since hepatic impairment can lower degarelix exposure, it is recommended that in patients with hepatic impairment testosterone concentrations should be monitored on a monthly basis until medical castration is achieved. Once medical castration is achieved, an every-other-month testosterone monitoring approach could be considered.

Patients with severe hepatic dysfunction have not been studied and caution is therefore warranted in this group.

## 10 OVERDOSAGE

There have been no reports of overdose with TRADENAME. In the case of overdose, however, discontinue TRADENAME, treat the patient symptomatically, and institute supportive measures.

As with all prescription drugs, this medicine should be kept out of the reach of children.

SEE TRADENAME PATIENT COUNSELING INFORMATION

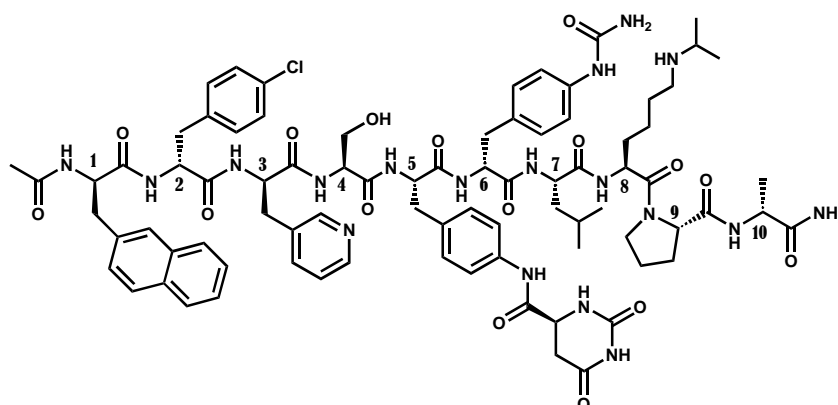
## 11 DESCRIPTION

TRADENAME is a sterile lyophilized powder for injection containing degarelix (as the acetate) and mannitol. Degarelix is a synthetic linear decapeptide amide containing seven unnatural amino acids, five of which are D-amino acids. The acetate salt of degarelix is a white to off-white amorphous powder of low density as obtained after lyophilization.

The chemical name of degarelix is D-Alaninamide, N-acetyl-3-(2-naphthalenyl)-D-alanyl-4-chloro-D-phenylalanyl-3-(3-pyridinyl)-D-alanyl-L-seryl-4-[[[(4S)-hexahydro-2,6-dioxo-4-pyrimidinyl]carbonyl]amino]-L-phenylalanyl-4-[(aminocarbonyl)amino]-D-phenylalanyl-L-leucyl-N6-(1-methylethyl)-L-lysyl-L-prolyl. It has an empirical formula of  $C_{82}H_{103}N_{18}O_{16}Cl$  and a molecular weight of 1632.3 Da.



Degarelix has the following structural formula:



TRADENAME delivers degarelix acetate, equivalent to 120 mg of degarelix for the starting dose, and 80 mg of degarelix for the maintenance dose. The 80 mg vial contains 200 mg mannitol and the 120 mg vial contains 150 mg mannitol.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

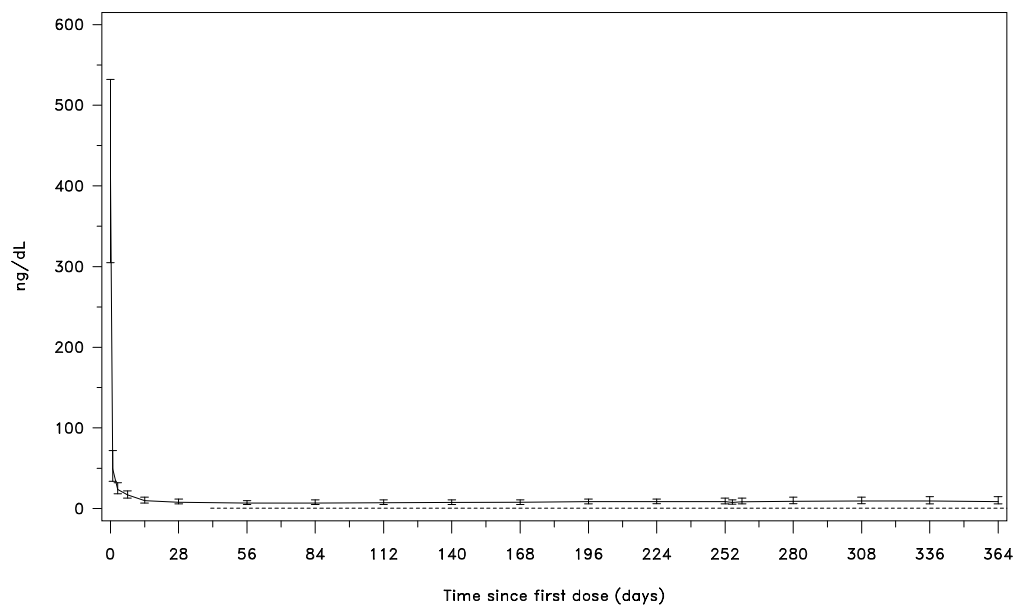
Degarelix is a GnRH receptor antagonist. It binds reversibly to the pituitary GnRH receptors, thereby reducing the release of gonadotropins and consequently testosterone.

### 12.2 Pharmacodynamics

A single dose of 240 mg TRADENAME causes a decrease in the plasma concentrations of luteinizing hormone (LH) and follicle stimulating hormone (FSH), and subsequently testosterone.

TRADENAME is effective in achieving and maintaining testosterone suppression below the castration level of 50 ng/dL.

**Figure 1: Plasma Testosterone Levels from Day 0 to 364 for Degarelix 240 mg/80 mg (Median with Interquartile Ranges)**



### 12.3 Pharmacokinetics

#### *Absorption*

TRADENAME forms a depot upon subcutaneous administration, from which degarelix is released to the circulation. Following administration of TRADENAME 240 mg at a product concentration of 40 mg/mL, the mean C<sub>max</sub> was 26.2 ng/mL (coefficient of variation, CV 83%) and the mean AUC was 1054 ng-day/mL (CV 35%). Typically C<sub>max</sub> occurred within 2 days after subcutaneous administration. In prostate cancer patients at a product concentration of 40 mg/mL, the pharmacokinetics of degarelix were linear over a dose range of 120 to 240 mg. The pharmacokinetic behavior of the drug is strongly influenced by its concentration in the injection solution.

#### *Distribution*

The distribution volume of degarelix after intravenous (> 1 L/kg) or subcutaneous administration (> 1000L) indicates that degarelix is distributed throughout total body water. *In vitro* plasma protein binding of degarelix is estimated to be approximately 90%.

#### *Metabolism*

Degarelix is subject to peptide hydrolysis during the passage of the hepato-biliary system and is mainly excreted as peptide fragments in the feces. No quantitatively significant metabolites were detected in plasma samples after subcutaneous administration. *In vitro* studies have shown that degarelix is not a substrate, inducer or inhibitor of the CYP450 or p-glycoprotein transporter systems.

### *Excretion*

Following subcutaneous administration of 240 mg TRADENAME at a concentration of 40 mg/mL to prostate cancer patients, degarelix is eliminated in a biphasic fashion, with a median terminal half-life of approximately 53 days. The long half-life after subcutaneous administration is a consequence of a very slow release of degarelix from the TRADENAME depot formed at the injection site(s). Approximately 20-30% of a given dose of degarelix was renally excreted, suggesting that approximately 70-80% is excreted via the hepato-biliary system in humans. Following subcutaneous administration of degarelix to prostate cancer patients the clearance is approximately 9 L/hr.

### *Effect of Age, Weight and Race*

There was no effect of age, weight or race on the degarelix pharmacokinetic parameters or testosterone concentration.

## **13 NONCLINICAL TOXICOLOGY**

### **13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility**

Degarelix was administered subcutaneously to rats every 2 weeks for 2 years at doses of 2, 10 and 25 mg/kg (about 9, 45 and 120% of the recommended human loading dose on a mg/m<sup>2</sup> basis). Long term treatment with degarelix at 25 mg/kg caused an increase in the combined incidence of benign hemangiomas plus malignant hemangiosarcomas in females.

Degarelix was administered subcutaneously to mice every 2 weeks for 2 years at doses of 2, 10 and 50 mg/kg (about 5, 22 and 120% of the recommended human loading dose (240 mg) on a mg/m<sup>2</sup> basis). There was no statistically significant increase in tumor incidence associated with this treatment.

Degarelix did not cause genetic damage in standard *in vitro* assays (bacterial mutation, human lymphocyte chromosome aberration) nor in *in vivo* rodent bone marrow micronucleus tests.

Single degarelix doses of  $\geq 1$  mg/kg (about 5% of the clinical loading dose on a mg/m<sup>2</sup> basis) caused reversible infertility in male rats. Single doses of  $\geq 0.1$  mg/kg (about 0.5% of the clinical loading dose on a mg/m<sup>2</sup> basis) caused a decrease in fertility in female rats.

## **14 CLINICAL STUDIES**

The safety and efficacy of TRADENAME were evaluated in an open-label, multi-center, randomized, parallel-group study in patients with prostate cancer. A total of 620 patients were randomized to receive one of two TRADENAME dosing regimens or leuprolide for one year:

- a. TRADENAME at a starting dose of 240 mg (40 mg/mL) followed by monthly doses of 160 mg (40 mg/mL) subcutaneously,
- b. TRADENAME at a starting dose of 240 mg (40 mg/mL) followed by monthly doses of 80 mg (20 mg/mL) subcutaneously,
- c. leuprolide 7.5 mg intramuscularly monthly.

Serum levels of testosterone were measured at screening, on days 0, 1, 3, 7, 14, and 28 in the first month, and then monthly until the end of the study.

The clinical trial population (n=610) across all treatment arms had an overall median age of approximately 73 (range 50 to 98). The ethnic/racial distribution was 84% white, 6% black and 10% others. Disease stage was distributed approximately as follows: 20% metastatic, 29% locally advanced (T3/T4 Nx M0 or N1 M0), 31% localized (T1 or T2 N0 M0) and 20% classified as other (including patients whose disease metastatic status could not be determined definitively - or patients with PSA relapse after primary curative therapy). In addition, the median testosterone baseline value across treatment arms was approximately 400 ng/dL.

The primary objective was to demonstrate that TRADENAME is effective with respect to achieving and maintaining testosterone suppression to castration levels ( $T \leq 50$  ng/dL), during 12 months treatment. The results are shown in Table 2.

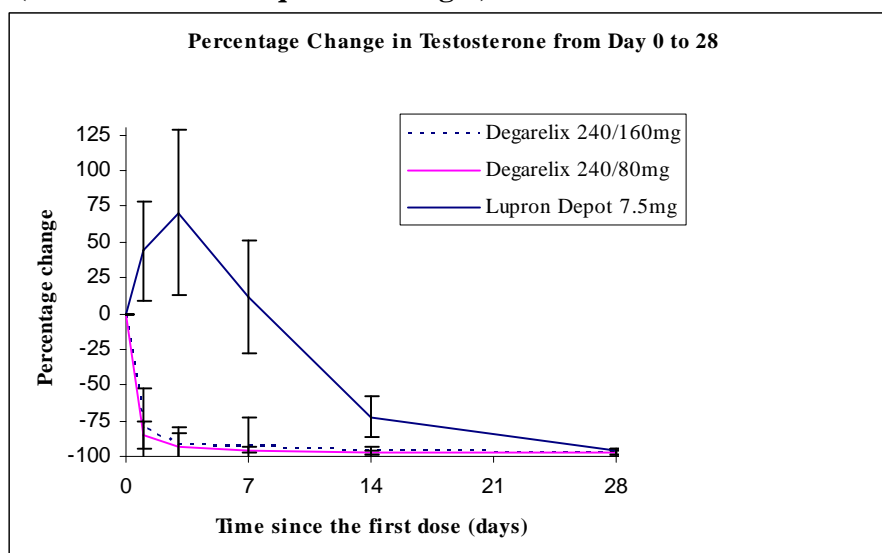
**Table 2: Medical Castration Rates (Testosterone  $\leq 50$  ng/dL) from Day 28 to Day 364**

	TRADENAME 240/160 mg N=202	TRADENAME 240/80 mg N=207	leuprolide 7.5 mg N=201
No. of Responders	199	202	194
Castration Rate (95% CIs)*	98.3% (94.8; 99.4)	97.2% (93.5; 98.8%)	96.4% (92.5; 98.2%)

\* Kaplan Meier estimates within group

Percentage changes in testosterone from baseline to day 28 (median with interquartile ranges) are shown in Figure 2 and the percentages of patients who attained the medical castration of testosterone  $\leq 50$  ng/dL are summarized in Table 3.

**Figure 2: Percentage Change in Testosterone from Baseline by Treatment Group until Day 28 (Median with Interquartile Ranges)**



**Table 3: Percentage of Patients Attaining Testosterone  $\leq$  50 ng/dL within the First 28 Days**

	Degarelix (240/160 mg) N=202	Degarelix (240/80 mg) N=207	Leuprolide (7.5 mg) N=201
Day 1	44%	52%	0%
Day 3	96%	96%	0%
Day 7	99%	99%	1%
Day 14	99%	99%	18%
Day 28	99%	100%	100%

In the clinical trial, PSA levels were monitored as a secondary endpoint. PSA levels were lowered by 64% two weeks after administration of TRADENAME, 85% after one month, 95% after three months, and remained suppressed throughout the one year of treatment. These PSA results should be interpreted with caution because of the heterogeneity of the patient population studied. No evidence has shown that the rapidity of PSA decline is related to a clinical benefit.

## 15 REFERENCES

1. NIOSH Alert: Preventing occupational exposures to antineoplastic and other hazardous drugs in healthcare settings. 2004. U.S. Department of Health and Human Services, Public Health Service, Centers for Disease Control and Prevention, National Institute for Occupational Safety and Health, DHHS (NIOSH) Publication No. 2004-165.
2. OSHA Technical Manual, TED 1-0.15A, Section VI: Chapter 2. Controlling Occupational Exposure to Hazardous Drugs. OSHA, 1999. [http://www.osha.gov/dts/osta/otm/otm\\_vi/otm\\_vi\\_2.html](http://www.osha.gov/dts/osta/otm/otm_vi/otm_vi_2.html)
3. American Society of Health-System Pharmacists. ASHP guidelines on handling hazardous drugs. *Am J Health-Syst Pharm.* 2006; 63:1172-1193.
4. Polovich, M., White, J. M., & Kelleher, L.O. (eds.) 2005. *Chemotherapy and biotherapy guidelines and recommendations for practice* (2nd. ed.) Pittsburgh, PA: Oncology Nursing Society.

## 16 HOW SUPPLIED/STORAGE AND HANDLING

TRADENAME is available as:

- NDC 55566-8401-1, Starting dose – One carton contains:  
Two vials each with 120 mg powder for injection
- NDC 55566-8301-1, Maintenance dose – One carton contains:  
One vial with 80 mg powder for injection

Store at 25°C (77°F); excursions permitted to 15-30°C (59-86°F).

Caution should be exercised in handling and preparing the solution of TRADENAME. Several guidelines on proper handling and disposal of anticancer drugs have been published.<sup>1-4</sup> To minimize the risk of dermal exposure, always wear impervious gloves when handling TRADENAME. If TRADENAME solution contacts the skin, immediately wash the skin thoroughly with soap and water. If TRADENAME contacts mucous membranes, the membranes should be flushed immediately and thoroughly with water [see *Contraindications (4) and Nonclinical Toxicology (13.1)*].

## 17 PATIENT COUNSELING INFORMATION

(See FDA-approved Patient Labeling 17.2)

### 17.1 Information

- Patients should be instructed to read the Patient Labeling carefully.
- Patients should be informed of the possible side effects of androgen deprivation therapy, including hot flashes, flushing of the skin, increased weight, decreased sex drive, and difficulties with erectile function. Possible side effects related to therapy with TRADENAME include redness, swelling, and itching at the injection site; these are usually mild, self limiting, and decrease within three days.

### 17.2 FDA-approved Patient Labeling

TRADENAME (phonetic spelling of TRADENAME)  
(degarelix for injection)

Read this patient information leaflet before you start taking TRADENAME and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or your treatment.

#### What is TRADENAME?

TRADENAME is a prescription medicine used in the treatment of advanced prostate cancer.

It is not known if TRADENAME is safe or effective in children.

#### Who should not use TRADENAME?

TRADENAME should not be given to:

- people who are allergic to any of the other ingredients in TRADENAME. See the end of this leaflet for a complete list of ingredients in TRADENAME
- women who are pregnant or may become pregnant

Talk to your healthcare provider before getting TRADENAME if you have any of these conditions.

#### What should I tell my healthcare provider before receiving TRADENAME?

**Before receiving TRADENAME, tell your healthcare provider about all your medical conditions, including if you:**

- have any heart problems
- have problems with balance of your body salts or electrolytes, such as sodium, potassium, calcium, and magnesium
- have kidney or liver problems
- are breast-feeding or plan to breast-feed. It is not known if TRADENAME passes into your breast milk. You and your healthcare provider should decide if you will take TRADENAME or breast feed. You should not do both without talking with your healthcare provider.

**Tell your healthcare provider about all the medicines you take**, including prescription and nonprescription medicines, vitamins, and herbal supplements. Especially tell your healthcare provider if you are taking or have taken any medicines for your heart.

Know the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist when you get a new medicine.

### **How should I receive TRADENAME?**

You will receive an injection of TRADENAME from your healthcare provider.

- The injection site will always be in the abdominal area but will change within that area with the next doses of TRADENAME.
- The injected medicine gives you a continuous release of TRADENAME over one month.
- Two injections are given as a first dose and the following monthly doses are one injection.
- Make sure your injection site is free of any pressure from belts, waistbands or other types of clothing.
- Always set up an appointment for your next injection.
- If you miss a dose of TRADENAME, or if you think you forgot to get your monthly dose of TRADENAME, talk to your healthcare provider about how to get your next dose.

### **What are the possible side effects of TRADENAME?**

The common side effects include:

- hot flashes
- injection site pain, redness, and swelling, especially with the first dose
- weight gain
- increase in some liver enzymes
- tiredness
- hypertension
- back and joint pain
- chills
- urinary tract infection
- decreased sex drive and trouble with erectile function (impotence)

These are not all the possible side effects. For more information, ask your healthcare provider or pharmacist.

Tell your healthcare provider if you have any side effect that bothers you or that does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

### **General information about the safe and effective use of TRADENAME.**

Medicines are sometimes prescribed for conditions that are not mentioned in the patient leaflet. Do not use TRADENAME for a condition for which it was not prescribed. Do not give TRADENAME to other people, even if they have the same symptoms that you have. It may harm them.

This patient information leaflet summarizes the most important information about TRADENAME. If you would like more information, talk with your healthcare provider. You can ask your pharmacist or healthcare provider for information about TRADENAME that is written for health professionals.

For more information, go to [www.TRADENAME.com](http://www.TRADENAME.com) or call 1-888-FERRING (1-888-337-7464)

**What are the ingredients in TRADENAME?**

Active ingredient: degarelix (as acetate)

Inactive ingredient: mannitol

Manufactured for: Ferring Pharmaceuticals Inc.