

Hormonal Drug Approved for Prostate Cancer

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The Food and Drug Administration has approved an injectable gonadotrophin-releasing hormone (GnRH) antagonist for the treatment of advanced prostate cancer. It is the first new agent cleared to treat the disease since 2004.

Degarelix, which will launch in Europe in early 2009 under the name Firmagon, was shown in phase III trials to outpace leuprolide (Lupron) in rapidly suppressing testosterone, without the androgen flare associated with Lupron and other luteinizing hormone-releasing hormone (LHRH) agonists.

Potential trade names for the new drug in the United States are still being reviewed with the FDA, according to a statement issued by Parsippany, N.J.–

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based Ferring Pharmaceuticals USA following the approval late last year. After those discussions are complete, an immediate commercial release of the drug is planned.

The drug offers a new spin on hormone treatment for advanced prostate cancer, directly binding to GnRH receptors on pituitary cells, rather than working more circuitously, through hypothalamic downregulation of LH secretion, like LHRH agonists.

The more direct route achieves very rapid and sustained testosterone suppression, clinical trial data confirmed.

In a 12-month, randomized, open-label phase III study of 610 patients, testosterone was suppressed to 0.5 ng/mL or less within 3 days in 96.1% and 95.5% of patients receiving either of two dosing regimens of degarelix and no patients in the comparative leuprolide group (BJU Int. 2008;102:1531-8).

By day 14 of the study, castrate levels of testosterone were demonstrated in 99% of degarelix patients compared with 18% receiving leuprolide.

"Use of a GnRH receptor antagonist is a highly efficient way to stop the production of testosterone," Dr. Neal Shore, medical director of the Carolina Urologic Research Center, Myrtle Beach, S.C., said in the statement.

"The approval of degarelix offers the medical community an effective alternative in the treatment of hormonally sensitive prostate cancer," said Dr. Shore, a clinical trial investigator and advisor to Ferring.

One potential advantage of degarelix over LHRH agonists is the avoidance of early stimulation of hormone receptors during LH downregulation. Antiandrogen therapy is required to prevent this brief testosterone "surge," and subse-

quent tumor growth, the FDA said.

The most frequent adverse events seen in clinical trials of degarelix were injection site reactions, including pain, redness, and swelling; hot flashes; increased weight; fatigue; and increases in serum levels of transaminases and gamma-glutamyltransferase (GGT).

Reactions were rated as grade 1 or 2 (mild to moderate) in 99% of patients.

The approved dosage for degarelix is

initially 240 mg given in equal, divided injections, followed by monthly single injections of 80 mg.

Degarelix had a much less tumultuous journey through the FDA approval process than did Provenge, an experimental immunotherapeutic agent that received a recommendation from an FDA panel in March. The agency withheld approval in May, requesting more efficacy data. Supplemental trial data

should be complete in 2009, with approval possible in the second half of the year. The panel and the agency agreed on approval of degarelix based on phase III trial data.

"There is an ongoing need for additional treatment options for these patients," Dr. Richard Pazdur, director of the FDA's Office of Oncology Drug Products, Center for Drug Evaluation and Research, said in a statement. ■

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Indications and usage

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Important safety information

Levemir® is contraindicated in patients hypersensitive to insulin detemir or one of its excipients.

Hypoglycemia is the most common adverse effect of all insulin therapies, including Levemir®. As with other insulins, the timing of hypoglycemic events may differ among various insulin preparations. Glucose monitoring is recommended for all patients with diabetes. Levemir® is not to be used in insulin infusion pumps. Any change of insulin dose should be made cautiously and only under medical supervision. Concomitant oral antidiabetes treatment may require adjustment.

Inadequate dosing or discontinuation of treatment may lead to hyperglycemia and, in patients with type 1 diabetes, diabetic ketoacidosis. Levemir® should not be diluted or mixed with any

other insulin preparations. Insulin may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy. Dose and timing of administration may need to be adjusted to reduce the risk of hypoglycemia in patients being switched to Levemir® from other intermediate or long-acting insulin preparations. The dose of Levemir® may need to be adjusted in patients with renal or hepatic impairment.

Other adverse events commonly associated with insulin therapy may include injection site reactions (on average, 3% to 4% of patients in clinical trials) such as lipodystrophy, redness, pain, itching, hives, swelling, and inflammation.

*Whether these observed differences represent true differences in the effects of Levemir®, NPH insulin, and insulin glargine is not known, since these trials were not blinded and the protocols (eg, diet and exercise instructions and monitoring) were not specifically directed at exploring hypotheses related to weight effects of the treatments compared. The clinical significance of the observed differences in weight has not been established.

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Please see brief summary of Prescribing Information on adjacent page.

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