Hormonal Drug Approved for Prostate Cancer

BY BETSY BATES
Los Angeles Bureau

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.–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 approval of degarelix offers the medical community an effective alternative in the treatment of hormonally sensitive prostate cancer.'

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 subsequent 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. ■