Bimatoprost Approved for Eyelash Lengthening

BY ELIZABETH MECHCATIE
Senior Writer

The Food and Drug Administration has approved bimatoprost for increasing the growth of eyelashes, a side effect of the glaucoma-treating drug that was first observed several years ago in clinical trials.

The new indication for bimatoprost 0.03% ophthalmic solution is for "the treatment of hypotrichosis of the eyelashes by increasing their growth including length, thickness and darkness." It will be marketed under the trade name Latisse by Allergan Inc., which markets the same product (Lumigan) for treating intraocular pressure in patients with open angle glaucoma or ocular hypertension. Lumigan was approved for glaucoma in 2001.

Unlike Lumigan, which is administered directly in the eye, Latisse is applied at night to the skin of the upper eyelid margin at the base of the eyelashes using a disposable applicator (one for each eye), which is to be used only once.

The new indication was approved on Dec. 26, 3 weeks after the FDA's Dermatologic and Ophthalmic Drugs Advisory Committee met to review bimatoprost for the cosmetic indication. The panel unanimously agreed that the benefit-risk profile of bimatoprost for hypotrichosis of the eyelashes was favorable.

The new indication is for 'the treatment of hypotrichosis of the eyelashes by increasing their growth.'

The panel decision was based on the efficacy data in a study comparing bimatoprost with a control vehicle in 278 people (aged 22-78 years) with hypotrichosis of the eyelashes, as well as a large bimatoprost safety database (SKIN & ALLERGY NEWS, January 2009, p. 1).

After 16 weeks, 78% of those in the bimatoprost group had at least a 1-point increase on a scale that measured eyelash prominence (the primary efficacy end point), compared with 18% of those on the vehicle, a statistically significant difference.

Exactly how bimatoprost, a prostaglandin analog, promotes eyelash growth has not been determined, but growth "is believed to occur by increasing the [percentage] of hairs in, and the duration of, the anagen or growth phase," according to the labeling. Eye pruritus, conjunctival hyperemia, and skin hyperpigmentation are listed in the label as the most common adverse events, affecting about 3%-4% of people treated. Warnings include the possibility of pigmentation of the iris (which is likely to be permanent) and the eyelids.

Allergan has agreed to conduct a 4-month, randomized, controlled study of bimatoprost solution in at least 50 black subjects, according to the FDA's approval letter. The one black patient in the hypotrichosis study was in the vehicle group. Another postmarketing requirement is that the company conduct a study of the safety and efficacy of bimatoprost in patients aged 0-17 years with hypotrichosis.

Allergan plans to launch Latisse in the first quarter of 2009, according to a written statement from the company. ■

Anti-TNF, Birth Defect Link Controversy Fueled by Study

BY DENISE NAPOLI
Associate Editor

Data from a Food and Drug Administration registry suggesting an increase in birth defects among women treated with etanercept and infliximab have rekindled controversy over the use of tumor necrosis factor blockers in pregnancy.

Authors of a new review of FDA data advise clinicians against prescribing anti-TNF agents to pregnant women based on their findings that etanercept and infliximab may be responsible for a "seemingly high number" of congenital anomalies. "Clinicians should not prescribe TNF antagonists to women during pregnancy," wrote the authors of the review.

However, conflicting preliminary data from an ongoing study by the Organization of Teratology Information Specialists (OTIS) argue that anti–tumor necrosis factor agents are safe for this population. Dr. Christina Chambers, a coinvestigator on the OTIS study, said it was alarmist to recommend avoiding anti-TNF agents in pregnancy, and said that reviews of the FDA adverse events database are "inherently biased." Based on her group's results, she said, "We're not able to draw any conclusions that suggest that we are seeing any specific pattern of defects, whether major or minor, based on the children that have been evaluated so far."

Dr. John J. Cush, who is not involved with either of these studies but who has conducted his own surveys on the issue, said in an interview that "the FDA database serves an important role in providing insight into what may be a potential hazard to those receiving these drugs."

However, he added, "There are biases regarding underreporting, sources of reports, the lack of a denominator, and a grossly underestimated numerator." Of course, all databases—including the OTIS database—have inherent biases, he cautioned.

"Nonetheless, there is no reason or convincing data to emphatically deny effective anti-TNF therapy to patients who need it to control their disease, either before or during pregnancy," said Dr. Cush, director of the clinical rheumatology program at Baylor Research Institute in Dallas.

The review of the FDA adverse events database, led by Dr. John D. Carter, involved more than 120,000 adverse events for all entries between 1999 and 2005 found with the keywords "congenital anomaly," "congenital anomalies," "birth defect," and "birth defects." A total of 41 children with 61 congenital anomalies born to 40 different mothers who were taking a TNF antagonist during pregnancy were recorded (J. Rheumatol. 2008 Dec. 15 [doi:10.3899/jrheum. 080545]).

Overall, 22 of these mothers had been taking etanercept at some point during their pregnancy; 19 had been taking infliximab. "In all 41 cases, the TNF-α antagonist was considered the 'primary suspect' as the cause of the birth defect," wrote Dr. Carter of the division of rheumatology at the University of South Florida, Tampa.

A total of 34 different types of birth defects were seen, 19 of which were part of the VACTERL spectrum.

In an interview, Dr. Chambers took issue with the VACTERL findings, noting that to include children's defects as part of the VACTERL spectrum means that they must exhibit at least three of the seven defects in the spectrum—not just one. And though the authors emphasize that 24 of 41 children (59%) "had one or more congenital anomalies that are part of VACTERL," only one was diagnosed with the pattern of associated birth defects within the original study period, according to Dr. Chambers.

Dr. Carter said that he thinks women of childbearing age taking anti-TNFs should be strongly encouraged to use contraception, as they are with known teratogenic drugs such as Accutane.

Dr. Carter did not declare any conflicts of interest with regard to his study. Dr. Chambers said she did not have any personal conflicts, but that OTIS receives grant funding from nine different pharmaceutical companies, two of which are manufacturers of anti-TNFs. Dr. Cush has served as a consultant or advisor to, or received grant money from, multiple pharmaceutical companies, including the makers of the three anti-TNFs looked at in these studies. ■

Topical Lidocaine Comes With Risks, Warns FDA

BY ELIZABETH MECHCATIE
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The use of topical lidocaine products to mitigate pain has the potential to cause life-threatening events, according to a public health advisory issued by the Food and Drug Administration Jan. 16.

"Before recommending a topical anesthetic for any purpose, doctors should determine if the desired amount of pain relief can be achieved safely with a topical anesthetic or if a different treatment would be more appropriate," the FDA alert says. If a topical anesthetic is considered the best choice, the lowest amount necessary to adequately relieve pain should be used, the agency recommends.

The advisory does not mention any reports of adverse events associated with the use of topical anesthetics in this context, but refers to a February 2007 FDA advisory that described two young women who died after applying a topical anesthetic to their legs after laser hair removal—and to a recently published study that evaluated the effect of lidocaine in relieving discomfort during mammograms (Radiology 2008;248:765-72).

In the study of 418 women aged 32-89 undergoing a screening mammogram, who expected to experience discomfort during the test, discomfort was significantly lower among those who were premedicated with 4% lidocaine gel, than among those premedicated with acetaminophen or ibuprofen.

In the study, topical lidocaine was spread over a wide area and covered with plastic, and no serious adverse effects were reported. But the FDA statement points out that the study was not large enough to determine whether this use could be associated with uncommon, serious reactions, and adds that the agency "remains concerned about the potential for topical anesthetics to cause serious and life-threatening adverse effects when applied to a large area of skin or when the area of application is covered."

When a topical anesthetic is recommended, patients need to apply the product sparingly, should avoid broken or irritated skin; and should be counseled that the risk of adverse effects is increased when a wrapping or dressing is used to cover the skin, the advisory recommends.

In the 2007 alert, the FDA said that in two separate incidents, women in their 20s had seizures and went into comas after applying topical products that contained a high concentration of lidocaine and tetracaine to their legs, and wrapped their legs in plastic wrap to increase the anesthetic effects. ■

The advisory is available at: www.fda.gov/cder/drug/advisory/topical_anesthetics 2009.htm.