U.S. Food and Drug Administration
Protecting and Promoting *Your* Health

Drug Safety Communications

FDA Drug Safety Communication: Anti-seizure drug Potiga (ezogabine) linked to retinal abnormalities and blue skin discoloration

Safety Announcement

[04-26-2013] The U.S. Food and Drug Administration (FDA) is warning the public that the anti-seizure medication Potiga (ezogabine) can cause blue skin discoloration (See photos in Appendix 1) and eye abnormalities characterized by pigment changes in the retina. FDA does not currently know if these changes are reversible. All patients taking Potiga should have a baseline eye exam, followed by periodic eye exams. FDA is working with the manufacturer to gather and evaluate all available information to better understand these events. FDA will update the public when more information is available.

Pigment changes in the retina have the potential to cause serious eye disease with loss of vision. It is not yet known whether the retinal pigment changes caused by Potiga lead to visual impairment, although several patients have been reported to have impaired visual acuity.

The skin discoloration in the reported cases appeared as blue pigmentation, predominantly on or around the lips or in the nail beds of the fingers or toes, but more widespread involvement of the face and legs has also been reported. Scleral and conjunctival discoloration, on the white of the eye and inside eyelids, has been observed as well. The skin discoloration generally occurred after four years of treatment with Potiga, but has appeared sooner in some patients (See Data Summary). In some cases, retinal abnormalities have been observed in the absence of skin discoloration.

In light of this new safety information, all patients taking Potiga or about to start Potiga should have an eye exam, followed by periodic eye exams thereafter (See Information for Health Care Professionals). Potiga should be discontinued if ophthalmic changes are observed unless no other treatment options are available. If a patient develops skin discoloration, serious consideration should be given to changing to an alternate medication.

Patients should not stop taking Potiga or any anti-seizure medication without talking to their health care professional, as stopping anti-seizure treatment suddenly can precipitate withdrawal seizures, a serious and life-threatening medical problem.

FACTS about Potiga

- Approved as adjunctive (added on to other anti-seizure medications) treatment of partial-onset seizures in adult patients 18 years and older.
- From marketing in April 2012 through February 2013, approximately 10,900 prescriptions were dispensed[1] and approximately 2,900 patients received a dispensed prescription for ezogabine

from outpatient retail pharmacies.[2] Based on sales distribution data, the majority of all ezogabine bottles (78% of ezogabine sales) were distributed to outpatient retail pharmacies.[3]

Footnotes

1 IMS Vector One®: National (VONA). April 2012-February 2013. Extracted March 2013.

2 IMS Vector One®: Total Patient Tracker (TPT). April 2012-February 2013. Extracted March 2013.

3 IMS Health National Sales Perspectives™. Year 2012. Extracted March 2013.

Additional Information for Patients

- If you are taking Potiga and develop any changes in your vision or any discoloration of your skin, including of your lips and nail beds, contact your health care professional right away.
- Do not stop taking Potiga without talking to your health care professional. Stopping such treatment suddenly can cause serious and life-threatening medical problems such as recurrence of seizures.
- Discuss any questions or concerns about Potiga with your health care professional.
- Report any side effects you experience to your health care professional and the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

Additional Information for Health Care Professionals

- All patients taking Potiga should have a baseline eye exam and periodic eye exams that should include visual acuity testing and dilated fundus photography, and may include fluorescein angiograms (FA), ocular coherence tomography (OCT), perimetry, and electroretinograms (ERG).
- The latency of retinal abnormalities after treatment initiation is unknown, although all known cases of retinal abnormalities were reported after an exposure to Potiga of at least three years. It is not known if retinal abnormalities can begin earlier in treatment. The rate of progression of retinal abnormalities, the best method of detection of these abnormalities, and the optimal frequency of periodic ophthalmologic monitoring are also unknown.
- Approximately one-third of patients who had eye examinations have been found to have retinal pigment changes and approximately one-third of these patients had no skin discoloration.
- Report adverse events involving Potiga to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

Data Summary

To date, the retinal abnormalities and skin discoloration observed with Potiga have been reported only in patients who were originally enrolled in Potiga clinical trials, and who have generally taken the drug for a long period of time in two ongoing extension studies (extensions of the clinical trials; 555 patients) and an ongoing compassionate use study (50 patients). Of the patients in the extension studies, 272 have received treatment for at least two years, and 212 patients have received treatment for at least three years.

The skin discoloration has generally occurred after long treatment intervals (mean: 4.04 years; median: 4.1 years; range: 0.8 to 7 years). All but two patients were exposed for a period of two years or longer. As of April 23, 2013, 38 patients had developed skin discoloration out of the estimated 605 patients (6.3%). All patients, however, have not yet been examined. Of the 38 patients reported to have skin discoloration, 36 were treated with the drug for at least two years.

Of 89 patients still remaining in the ongoing studies, 36 had eye examinations that included a funduscopic and corrected visual acuity examination. It is not yet known how many of these 36 patients also had skin discoloration. Eleven of the 36 patients have been found to have retinal pigmentary abnormalities. Four of the 11 patients did not have skin discoloration at the time of exam. Five patients had worse than 20/20 visual acuity. One of these patients had visual acuity of 20/160 in one eye, while the remaining four had visual acuity of 20/25 to 20/40 in one or both eyes. No baseline visual acuity assessment is available for these patients.

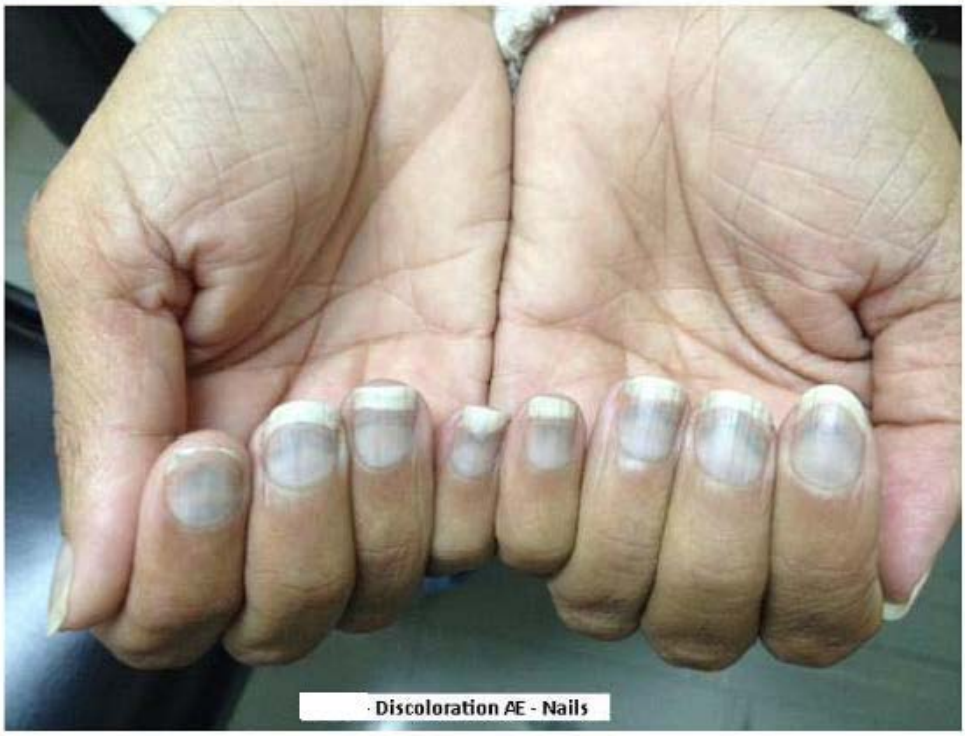
One of the 11 patients with retinal pigmentary abnormalities had a full panel of diagnostic retinal studies, which revealed findings consistent with a retinal dystrophy. In this patient, mild reduction of visual acuity was noted (20/25), and additional visual testing indicated abnormal electroretinography (ERG), bone spicule pattern on funduscopic exam, perivascular hyperfluorescence on fluorescein angiography, and decreased sensitivity on visual field testing. In the other ten patients, complete data on retinal function have not yet been reported.

Information on the consequences, reversibility, time to onset, and pathophysiology of the retinal and skin abnormalities remains incomplete. Ophthalmologic and skin examinations on other patients exposed to Potiga in the studies previously discussed have been requested and will be reviewed.

The possibility of more extensive systemic involvement has not been excluded.

Photos

Discoloration AE - Lips



Discoloration AE - Nails