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

Drug Safety Communications

FDA Drug Safety Communication: FDA reporting mental health drug ziprasidone (Geodon) associated with rare but potentially fatal skin reactions

Safety Announcement

[12-11-2014] The U.S. Food and Drug Administration (FDA) is warning that the antipsychotic drug ziprasidone (marketed under the brand name, Geodon, and its generics) is associated with a rare but serious skin reaction that can progress to affect other parts of the body. A new warning has been added to the Geodon drug label to describe the serious condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS). Patients who have a fever with a rash and/or swollen lymph glands should seek urgent medical care. Health care professionals should immediately stop treatment with ziprasidone if DRESS is suspected.

Ziprasidone is an antipsychotic drug used to treat the serious mental health disorders schizophrenia and bipolar I disorder. Ziprasidone helps restore certain natural substances in the brain and can decrease hallucinations, delusions, other psychotic symptoms, and mania. To work properly, ziprasidone should be taken every day as prescribed. Patients should not stop taking their medicine or change their dose without first talking to their health care professional.

DRESS may start as a rash that can spread to all parts of the body. It can include fever, swollen lymph nodes, and inflammation of organs such as the liver, kidney, lungs, heart, or pancreas. DRESS also causes a higher-than-normal number of a particular type of white blood cell called eosinophils in the blood. DRESS can lead to death.

FDA reviewed information from six patients in whom the signs and symptoms of DRESS appeared between 11 and 30 days after ziprasidone treatment was started. None of these patients died (see Data Summary). Based on this information, FDA required the manufacturer of Geodon to add a new warning for DRESS to the *Warnings and Precautions* section of the drug labels for the capsule, oral suspension, and injection formulations.

We urge health care professionals and patients to report side effects involving ziprasidone to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

Facts about ziprasidone (Geodon)

- Ziprasidone is an atypical antipsychotic drug used to treat schizophrenia and bipolar I disorder.
- Ziprasidone is marketed under the brand name Geodon, and as generics.

- During 2013, approximately 2.5 million prescriptions for oral formulations of ziprasidone were dispensed, and approximately 353,000 patients received a prescription for an oral formulation of ziprasidone through U.S. outpatient retail pharmacies.[1]

Additional Information for Patients

- Treatment with ziprasidone may cause you to have a rash. The rash can be severe, covering much of the body. You may also have a fever and other symptoms associated with a serious condition known as Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
- Call your health care professional(s) and seek immediate care if you develop any of the following signs or symptoms:
    - Skin rash
    - Fever
    - Swollen face
    - Swollen lymph glands
- For ziprasidone to work properly, it should be taken every day as prescribed.
- Do not stop taking ziprasidone or change your dose without first talking to your health care professional.
- Discuss any questions or concerns about ziprasidone 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

- Make sure your patients know that rash may occur with ziprasidone treatment and may progress to Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS).
- Explain the signs and symptoms of severe skin reactions to your patients and tell them when to seek immediate care.
- DRESS consists of three or more of the following:
    - cutaneous reaction (such as rash or exfoliative dermatitis)
    - eosinophilia
    - fever
    - lymphadenopathy, and
    - one or more systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, pericarditis, and pancreatitis.
- If DRESS is suspected, ziprasidone treatment should be stopped immediately.
- Report adverse reactions involving ziprasidone to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of the page.

[1] Source: IMS Health, National Prescription Audit (NPA™) and Total Patient Tracker (TPT). Year 2013, data extracted October 2014

Data Summary

FDA reviewed six worldwide cases of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) associated with ziprasidone use and reported to the FDA Adverse Event Reporting System (FAERS).

The six cases were temporally associated with ziprasidone, with a time to onset of symptoms from 11 days to one month after ziprasidone initiation. In three cases, a recurrence of symptoms was reported following the discontinuation and re-initiation of ziprasidone, with a faster time to onset following the re-initiation. Three of the cases reported concomitant use of drugs associated with DRESS. The cases reported serious outcomes, including hospitalization. There were no cases reporting death. The FAERS cases support an association between ziprasidone and the development of DRESS because of the consistency of the case characteristics to the signs and symptoms of DRESS, the temporal relationship between ziprasidone initiation and the onset of symptoms, and reportedcases of positive re-challenge.

Although there were no fatalities among the reported cases, DRESS is a potentially fatal drug reaction with a mortality rate of up to 10%.[2] The pathogenesis of DRESS is unclear; however, it is thought to be the result of a combination of genetic and immunologic factors, such as detoxification defects in the drug metabolism pathway, resulting in toxic metabolite formation and an immune response. Reactivation of viral infections (herpes virus [HHV-6, HHV-7] or Epstein-Barr Virus [EBV]) may also play a role by inducing or amplifying the immune reaction. There is currently no specific treatment for DRESS. The keys to managing DRESS are early recognition of the syndrome, discontinuation of the offending agent as soon as possible, and supportive care. Treatment with systemic corticosteroids should be considered in cases with extensive organ involvement.[2]

References

1. Source: IMS Health, National Prescription Audit (NPA™) and Total Patient Tracker (TPT). Year 2013, data extracted October 2014.
2. Husain Z, Reddy BY, Schwartz RA. DRESS syndrome: Part II. Management and therapeutics. J Am Acad Dermatol. 2013 May;68(5):709.e1-9