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

Drug Safety Communications

FDA warns about a serious lung condition in infants and newborns treated with Proglycem (diazoxide)

Safety Announcement

[7-16-2015] The U.S. Food and Drug Administration (FDA) is warning that a serious lung condition called pulmonary hypertension, which is high pressure in the blood vessels leading to the lungs, has been reported in infants and newborns treated with Proglycem (diazoxide) for low blood sugar. In all cases, the pulmonary hypertension resolved or improved after Proglycem was stopped. We are continuing to investigate this safety issue and will determine whether changes are needed in the Proglycem prescribing information.

Proglycem is usually given in the hospital, and health care professionals should closely monitor babies receiving it, especially those with risk factors for pulmonary hypertension such as meconium aspiration syndrome, respiratory distress syndrome, transient tachypnea of the newborn, pneumonia, sepsis, congenital diaphragmatic hernia, and congenital heart disease. Stop Proglycem treatment if pulmonary hypertension is identified.

Parents and caregivers of any child receiving Proglycem should watch for signs of difficulty breathing such as flaring nostrils, grunting, unusual movement of their child's chest, rapid breathing, difficulty feeding, or a bluish color of the lips or skin. Immediately alert your child's health care professionals if you see any of these signs, and talk to them if you have any questions or concerns about Proglycem.

Proglycem is used to treat low blood sugar levels due to certain medical conditions that cause the release of too much insulin from the pancreas. Proglycem works mainly by blocking the pancreas from releasing insulin; this action helps to increase blood sugar.

We searched the FDA Adverse Event Reporting System (FAERS) database[1] and the medical literature[2-4] and identified 11 cases of pulmonary hypertension in infants and newborns treated with diazoxide, the active ingredient in Proglycem, since the drug was approved in 1973. FAERS includes only reports submitted to FDA, so there are likely additional cases about which we are unaware. In addition to having other serious medical conditions, most of these babies also were at high risk for developing pulmonary hypertension, a condition in which the pressure in the blood vessels leading to the lungs is too high. This makes it harder for the heart to pump blood to the lungs, and it can cause heart failure and lower oxygen in the blood. The babies affected developed

pulmonary hypertension within a day to a few months after starting Proglycem, and they were hospitalized or had their neonatal intensive care unit (NICU) hospitalization extended because of the condition. All of them either recovered or improved after Proglycem was discontinued.

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

Facts about Proglycem (diazoxide)

- Proglycem is used to treat low blood sugar levels due to certain conditions that can cause the release of too much insulin in the blood.
- The medicine works mainly by blocking insulin release from the pancreas; this action helps to increase blood sugar.
- Proglycem is available as a liquid that is taken by mouth.
- Infants and newborns treated with Proglycem generally receive it while they are hospitalized.

Additional Information for Parents and Caregivers

- There have been reports of a rare but serious condition of high pressure in the blood vessels leading to the lungs, called pulmonary hypertension, in infants and newborns treated with Proglycem (diazoxide) for low blood sugar. In these cases, the condition resolved or improved once Proglycem treatment was stopped.
- If your child is receiving Proglycem, watch for signs of difficulty breathing such as flaring nostrils, grunting, unusual movement of your child's chest, rapid breathing, difficulty feeding, or a bluish color of the lips or skin.
- Talk to your child's health care professional if you have any questions or concerns about Proglycem.
- Report side effects from Proglycem to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Additional Information for Health Care Professionals

- There have been reports of pulmonary hypertension occurring in infants and neonates treated with Proglycem (diazoxide). The pulmonary hypertension either resolved or improved when Proglycem was discontinued.
- Monitor patients, especially those with risk factors for pulmonary hypertension, for signs of respiratory distress, including tachypnea, flaring nostrils, grunting, and chest wall retractions. Other signs can include feeding intolerance and cyanosis.
- Common risk factors for pulmonary hypertension include meconium aspiration syndrome, respiratory distress syndrome, transient tachypnea of the newborn, pneumonia, sepsis, congenital diaphgragmatic hernia, and congenital heart disease.
- Discontinue Proglycem if pulmonary hypertension is identified.

- Report adverse events involving Proglycem to the FDA MedWatch program, using the information in the "Contact FDA" box at the bottom of this page.

Data Summary

FDA searched the FDA Adverse Event Reporting System (FAERS) database[1] for reports dating from May 28, 1973 (the date of approval), through March 11, 2015, and the medical literature[2-4] and identified a total of 11 cases of pulmonary hypertension associated with diazoxide. Seven cases were identified in FAERS, and four cases were identified in the medical literature.

Patients in the seven FAERS cases were infants or neonates born at gestational ages of 34 to 41 weeks. All of the patients received diazoxide for hypoglycemia caused by inappropriate endogenous insulin secretion. Diazoxide was started within the first 30 days of life in five of the seven cases. Most of the cases reported at least one risk factor for developing pulmonary hypertension, including congenital heart disease, meconium aspiration, and streptococcal infection. All seven patients were hospitalized or had their neonatal intensive care unit (NICU) hospitalization extended because of pulmonary hypertension. Extensive medical interventions were required to treat the severity of the pulmonary hypertension or manage the clinical condition of the patient. Interventions included initiation of oxygen supplementation, mechanical ventilation, and the use of vasodilator medications such as sildenafil and nitric oxide. There were no fatalities. All seven patients improved after diazoxide was discontinued (i.e., positive dechallenge). Five of the seven cases reported resolution of the pulmonary hypertension, while the remaining two cases reported an improvement. Of the five cases with resolution of the pulmonary hypertension, two cases documented a normal echocardiogram after discontinuing diazoxide.

In addition to the FAERS data, four cases of diazoxide-associated pulmonary hypertension occurring in infants or neonates were identified in three published reports.[1-3] In all four cases, the pulmonary hypertension was reported to have resolved after diazoxide was discontinued.

References

1. Food and Drug Administration. FDA Adverse Event Reporting System (FAERS). http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm. Last updated September 8, 2014. Accessed June 30, 2015.

2. Yildizdas D, Erdem S, Küçükosmanoglu O, Yilmaz M, Yüksel B. Pulmonary hypertension, heart failure and neutropenia due to diazoxide therapy. Adv Ther 2008;25:515-9.

3. Demirel F, Unal S, Çetin II, Esen I, Arasli A. Pulmonary hypertension and reopening of the ductus arteriosus in an infant treated with diazoxide. J Pediatr Endocrinol Metab 2011;24:603-5.

4. Gerardin M, Denizot S, Texier R, et al. Pulmonary hypertension in newborns treated with diazoxide: about two cases. Fundam Clin Pharm 2010;24(s1):81.