About FDA

Drug Safety Oversight Board Meeting, June 18, 2009

Public Summary

The Executive Director updated the Board on risk communications [Public Health Advisories (PHAs), Early Communications about Ongoing Safety Reviews (ECs), and Information for Healthcare Professionals (HCP)] posted and in development since the May 21, 2009 meeting.

The following is a list of the posted risk communications:

- June 4, 2009 - Propylthiouracil and hepatic failure[1]
- June 11, 2009 - Increased mortality associated with CNI conversion to sirolimus in transplant patients[2]
- June 12, 2009 - Singulair and neuropsychiatric events[3]
- June 15, 2009 - Cardiovascular risk and Stimulant Medications in Children with ADHD[4]
- June 16, 2009 - Zicam Cold Remedy Intranasal Products[5]
- June 17, 2009 - Cefepime and increased mortality[6]

The Drug Safety Oversight Board discussed reports of metabolic acidosis, metabolic acidosis with increased anion gap, and neuropsychiatric adverse events in children using polyethylene glycol (PEG) products. Metabolic acidosis is a disturbance in the body's acid-base balance and causes too much acid in the blood. In some situations, metabolic acidosis can be a mild, chronic condition; however, it may lead to shock or death in severe cases. Neuropsychiatric adverse events may include seizures, tremors, tics, headache, anxiety, lethargy, sedation, aggression, rages, obsessive-compulsive behaviors including repetitive chewing and sucking, paranoia and mood swings.

PEG is a laxative that increases the amount of water in the intestinal tract to stimulate bowel movements. There are currently 19 PEG products, prescription and over-the-counter (OTC), in the US approved for use as either as a bowel preparation prior to colonoscopy or for the treatment of constipation. All products approved for use prior to colonoscopy are prescription products with one product approved for use in children 6 months and older. There is only one PEG product available over-the-counter and it is indicated for short term use (up to 7 days) in adults and children 17 years of age or older with occasional constipation. The Constipation Guideline Committee of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition has formulated PEG product guidelines for long-term use in the management of pediatric constipation; however, this indication is not FDA approved.

The Board discussed whether the adverse event reports constituted a safety signal and what if any action should be taken for the prescription and over-the-counter preparations used. The Board was assisted by Andrea Gropman, MD who served as the Board's guest expert in pediatric neurology.

Dr. Andrea Gropman is a child neurologist and clinical geneticist at the National Institutes of Neurological Disorders and Stroke at the National Institutes of Health and the Children's National Medical Center in Washington, DC.

Some of the issues highlighted by the Board are:

1. PEG is a long-chain polymer of ethylene oxide commercially available in molecular weights of 300 g/mol to 10,000,000 g/mole. Many products contain an average molecular weight of 3350 g/mole and thus are given the name PEG-3350. PEG-3350 products exist in a stable powder form. Approved products instruct patients to dissolve the PEG-3350 powder in a liquid and use immediately. The approved products have been tested under these conditions and are stable. It is unknown if prolonged duration in solution would change the chemical properties of PEG-3350, and what the actual content of ethylene glycol or diethylene glycol or other low molecular weight PEG would be under such conditions.
2. PEG products that are available over-the-counter can be used without medical oversight.

3. There is a perception that PEG is safe because it is minimally absorbed from the stomach and intestines. However, little is known about whether absorption in children differs from adults, especially in children who are constipated, have underlying intestinal disease, or are very young.
4. Children are receiving adult doses of PEG in some cases.
5. Children may be more susceptible to variations in PEG product quality.
6. Effects of large doses of PEG given over a long duration (e.g weeks or longer) is not known.

Links on this page:

1. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm162701.htm
2. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm165015.htm
3. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm165489.htm
4. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm165858.htm
5. http://www.fda.gov/Drugs/DrugSafety/PublicHealthAdvisories/ucm166059.htm
6. http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm167254.htm