June 6, 2013

IMPORTANT DRUG WARNING

Subject: Pregnancy Category D: Fetal skeletal abnormalities reported with continuous administration beyond 5-7 days of MAGNESIUM SULFATE INJECTION, USP during pregnancy.

Dear Health Care Professional,

Fresenius Kabi USA, LLC (Fresenius Kabi) would like to inform you of important new safety information for Magnesium Sulfate Injection, USP 50%, marketed by Fresenius Kabi. The new information concerns continuous maternal administration of magnesium sulfate. Magnesium sulfate can lead to fetal abnormalities when administered beyond 5-7 days to pregnant women. There are retrospective epidemiological studies and case reports documenting fetal abnormalities such as hypocalcemia, skeletal demineralization, osteopenia and other skeletal abnormalities with continuous maternal administration of magnesium sulfate for more than 5-7 days. In addition, case reports of neonatal fracture have been submitted to the FDA Adverse Event Reporting System. Health care professionals are advised against using magnesium sulfate injection for more than 5-7 days to stop pre-term labor in pregnant women. This use of the drug is off-label, which means that the efficacy and safety of such use have not been established**.**

Health Care Professionals are advised that the pregnancy category has changed for magnesium sulfate injection from category A to D. Magnesium sulfate injection should be used during pregnancy only if clearly needed. If this drug is used during pregnancy, the woman should be apprised of the potential harm to the fetus.

In collaboration with the Food and Drug Administration (FDA), Fresenius Kabi has updated its prescribing information for magnesium sulfate injection to include the following updated warnings and new safety information in the **WARNINGS, PREGNANCY CATEGORY,** and **DOSAGE AND ADMINISTRATION** sections.

WARNINGS:

FETAL HARM: Continuous administration of magnesium sulfate beyond 5-7 days to pregnant women can lead to hypocalcemia and bone abnormalities in the developing fetus. These bone abnormalities include skeletal demineralization and osteopenia. In addition, cases of neonatal fracture have been reported. The shortest duration of treatment that can lead to fetal harm is not known. Magnesium sulfate should be used during pregnancy only if clearly needed. If magnesium sulfate is given for treatment of preterm labor, the woman should be informed that the efficacy and safety of such use have not been established and that use of magnesium sulfate beyond 5-7 days may cause fetal abnormalities.

PREGNANCY CATEGORY D

Teratogenic effects

Magnesium sulfate can cause fetal abnormalities when administered beyond 5-7 days to pregnant women. There are retrospective epidemiological studies and case reports documenting fetal abnormalities such as hypocalcemia, skeletal demineralization, osteopenia and other skeletal abnormalities with continuous maternal administration of magnesium sulfate for more than 5-7 days. Magnesium sulfate injection should be used during pregnancy only if clearly needed. If this drug is used during pregnancy, the woman should be apprised of the potential harm to the fetus.

Labor and delivery

Continuous administration of magnesium sulfate is an unapproved treatment for preterm labor. The safety and efficacy of such use have not been established. The administration of magnesium sulfate outside of its approved indication in pregnant women should be by trained obstetrical personnel in a hospital setting with appropriate obstetrical care facilities.

DOSAGE AND ADMINISTRATION:

Dosage of magnesium sulfate must be carefully adjusted according to individual requirements and response, and administration of the drug should be discontinued as soon as the desired effect is obtained.

Both IV and IM administration are appropriate. IM administration of the undiluted 50% solution results in therapeutic plasma levels in 60 minutes, whereas IV doses will provide a therapeutic level almost immediately. The rate of IV injection should generally not exceed 150 mg/minute (1.5 mL of a 10% concentration or its equivalent), except in severe eclampsia with seizures. Continuous maternal administration of magnesium sulfate in pregnancy beyond 5-7 days can cause fetal abnormalities.

Prescribing Information:

This letter is not intended to provide a complete description of the indications, dosage and administration, risks and benefits associated with the use of Magnesium Sulfate Injection, USP.

Please find attached a copy of Magnesium Sulfate Injection, USP 50% prescribing information.

This communication and product information is available on the Fresenius Kabi, USA web site at www.APPpharma.com.

For additional information on this subject, please review the FDA Drug Safety Communication posted at http://www.fda.gov/Drugs/DrugSafety/ucm353333.htm.

Reporting Adverse Events:

To report adverse events experienced with the use of this product, call Fresenius-Kabi USA Vigilance and Medical Affairs at 1-800-551-7176, Monday – Friday, between the hours of 8 a.m. and 5 p.m. (CST), or e-mail apppatientsafety@APPpharma.com.

Adverse events may also be reported to the FDA's MedWatch Adverse Event Reporting program either online, by regular mail or by fax.

- **Online**: www.fda.gov/medwatch/report.htm
- **Regular Mail**: use postage-paid FDA form 3500 available at: www.fda.gov/MedWatch/getforms.htm. Mail to MedWatch 5600 Fishers Lane, Rockville, MD 20852-9787
- **Fax**: 1-800-FDA-0178

Sincerely,

Elizabeth M. Hartnett
Senior Director, Vigilance and Medical Affairs