

The FDA's MedWatch program safety labeling changes for boxed warnings are compiled quarterly for drugs and therapeutic biologics where important changes have been made to the safety information. These and other label changes are searchable in the Drug Safety Labeling Changes (SLC) database, where data are available to the public in downloadable and searchable formats. Boxed warnings are ordinarily used to highlight either adverse reactions so serious in proportion to the potential benefit from the drug that it is essential that it be considered in assessing the risks and benefits of using the drug; or serious adverse reactions that can be prevented/reduced in frequency or severity by appropriate use of the drug; or FDA approved the drug with restrictions to ensure safe use because FDA concluded that the drug can be safely used only if distribution or use is restricted.

PRANDIMET (METFORMIN HYDROCHLORIDE; REPAGLINIDE):

Edited boxed warning April 7, 2017

Post-marketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension, and resistant bradyarrhythmias. The onset of metformin-associated lactic acidosis is often subtle, accompanied only by non-specific symptoms such as malaise, myalgias, respiratory distress, somnolence, and abdominal pain. Metformin-associated lactic acidosis was characterized by elevated blood lactate levels (> 5 mmol/Liter), anion gap acidosis (without evidence of ketonuria or ketonemia), an increased lactate/pyruvate ratio; and metformin plasma levels generally > 5 mcg/mL.

Risk factors for metformin-associated lactic acidosis include renal impairment, concomitant use of certain drugs (eg, carbonic anhydrase inhibitors such as topiramate), age 65 years old or greater, having a radiological study with contrast, surgery and other procedures, hypoxic states (eg, acute congestive heart failure), excessive alcohol intake, and hepatic impairment.

Steps to reduce the risk of and manage metformin-associated lactic acidosis in these high risk groups are provided in the full prescribing information.

If metformin-associated lactic acidosis is suspected, immediately discontinue PrandiMet and institute general supportive measures in a hospital setting. Prompt hemodialysis is recommended.

AVANDAMET (METFORMIN HYDROCHLORIDE; ROSIGLITAZONE MALEATE):

Edited and updated boxed warning April 7, 2017

WARNING: CONGESTIVE HEART FAILURE and LACTIC ACIDOSIS

Rosiglitazone maleate: CONGESTIVE HEART FAILURE

- Thiazolidinediones, including rosiglitazone, cause or exacerbate congestive heart failure in some patients. After initiation of Avandamet, and after dose increases, observe patients carefully for signs and symptoms of heart failure (including excessive, rapid weight gain, dyspnea, and/or edema). If these signs and symptoms develop, the heart failure should be managed according to current standards of care. Furthermore, discontinuation or dose reduction of Avandamet must be considered.
- Avandamet is not recommended in patients with symptomatic heart failure. Initiation of Avandamet in patients with established NYHA Class III or IV heart failure is contraindicated.

Metformin hydrochloride: LACTIC ACIDOSIS

- Postmarketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension, and resistant bradyarrhythmias. The onset of metformin-associated lactic acidosis is often subtle, accompanied only by nonspecific symptoms such as malaise, myalgias, respiratory distress, somnolence, and abdominal pain. Metformin-associated lactic acidosis was characterized by elevated blood lactate levels (> 5 mmol/L), anion gap acidosis (without evidence of ketonuria or ketonemia), and increased lactate/pyruvate ratio; and metformin plasma levels generally > 5 mcg/mL.
- Risk factors for metformin-associated lactic acidosis include renal impairment, concomitant use of certain drugs (eg, carbonic anhydrase inhibitors such as topiramate), age 65 years old or greater, having a radiological study with contrast, surgery and other procedures, hypoxic states (eg, acute congestive heart failure), excessive alcohol intake, and hepatic impairment. Steps to reduce the risk of and manage metformin-associated lactic acidosis in these high-risk groups are provided in the Full Prescribing Information.
- If metformin-associated lactic acidosis is suspected, immediately discontinue Avandamet and institute general supportive measures in a hospital setting. Prompt hemodialysis is recommended.

OPTIRAY (160, 240, 300, 320, AND 350):

Edited boxed warning April 7, 2017

PLR conversion, addition of the following:

WARNING: NOT FOR INTRATHECAL USE

Inadvertent intrathecal administration may cause death, convulsions, cerebral hemorrhage, coma, paralysis, arachnoiditis, acute renal failure, cardiac arrest, seizures, rhabdomyolysis, hyperthermia, and brain edema.

SABRIL (VIGABATRIN):

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WARNING: PERMANENT VISION LOSS

Because of the risk of permanent vision loss, Sabril is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the Vigabatrin REMS Program. Further information is available at www.vigabatrinREMS.com or 1-866-244-8175.

GLUMETZA (METFORMIN HYDROCHLORIDE):

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LACTIC ACIDOSIS

Postmarketing cases of metformin-associated lactic acidosis have resulted in death, hypothermia, hypotension, and resistant bradyarrhythmias. The onset of metformin-associated lactic acidosis is often subtle, accompanied only by nonspecific symptoms such as malaise, myalgias, respiratory distress, somnolence, and abdominal pain. Metformin-associated lactic acidosis was characterized by elevated blood lactate levels (> 5 mmol/Liter), anion gap acidosis (without evidence of ketonuria or ketonemia), an increased lactate/pyruvate ratio, and metformin plasma levels generally > 5 mcg/mL.

Risk factors for metformin-associated lactic acidosis include renal impairment, concomitant use of certain drugs (eg, carbonic anhydrase inhibitors such as topiramate), age 65 years old or greater, having a radiological study with contrast, surgery and other procedures, hypoxic states (eg, acute congestive heart failure), excessive alcohol intake, and hepatic impairment.

Steps to reduce the risk of and manage metformin-associated lactic acidosis in these high risk groups are provided in the full prescribing information.

If metformin-associated lactic acidosis is suspected, immediately discontinue Glumetza and institute general supportive measures in a hospital setting. Prompt hemodialysis is recommended.

VALCYTE (VALGANCICLOVIR HYDROCHLORIDE):

Edited boxed warning April 7, 2017

WARNING: HEMATOLOGIC TOXICITY, IMPAIRMENT OF FERTILITY, FETAL TOXICITY, MUTAGENESIS AND CARCINOGENESIS

- Hematologic Toxicity: Severe leukopenia, neutropenia, anemia, thrombocytopenia, pancytopenia, and bone marrow failure including aplastic anemia have been reported in patients treated with Valcyte.
- Impairment of Fertility: Based on animal data, Valcyte may cause temporary or permanent inhibition of spermatogenesis in males and suppression of fertility in females.

