Remain Alert to Black Box Warnings

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According to the Institute of Safe Medication Practices (ISMP), lamotrigine (Lamictal®), an antiepileptic drug, led all other regularly monitored drugs in reports of severe cutaneous events in 2011. The FDA has approved Lamictal for use as adjunctive therapy for partial seizures in children as young as 2 years. It is also approved as adjunctive therapy for generalized seizures in children with Lennox-Gastaut Syndrome. Lamotrigine prescribing information has a black box warning about life-threatening skin reactions, including Stevens–Johnson Syndrome (SJS), DRESS Syndrome and toxic epidermal necrolysis. Two chief concerns with lamotrigine and its use for children are lamotrigine’s interaction with Valproate (valproic acid), another anticonvulsant and mood-stabilizing drug, and the increased risk of severe rash when the two medications are used in combination.

This Claim Lesson briefly describes two pediatric cases where both children developed Stevens Johnson Syndrome pursuant to the use of lamotrigine. Our primary objective in this Claim Lesson is not to flag a “high risk” drug, but rather to encourage our policyholders to remain alert to Black Box Warnings and to develop patient tracking and monitoring systems for high risk medications.

CASE # 1

The first case involves a 14 y/o female patient with a three year history of mood swings and suicidal ideation. The patient was admitted to a behavioral health system for psychiatric care stabilization related to severe depression and acts of cutting herself. Her psychiatrist prescribed several drugs, including Lamictal®.

Two days after admission, the mother and psychiatrist discussed the addition of Lamictal® to her daily regimen of Celexa 20 mg/ day. The patient was discharged from the facility three days later.

Two weeks after discharge, the patient presented to the ED with complaints of a rash on her face, back, chest; a feeling that her throat was closing; and difficulty swallowing. The ED physician diagnosed her with SJS secondary to Lamictal®. The patient sustained sores, scarring of face, lips, mouth, esophagus, stomach, intestines and vagina.
Her parents filed a lawsuit alleging the psychiatrist improperly and wrongfully prescribed Lamictal® to stabilize the patient’s behaviors. In addition they alleged that Lamictal® was the direct and proximal cause of the patient acquiring SJS and that the patient sustained excruciating pain and disfigurement as a result.

This case was defended successfully on the basis of good expert support that the psychiatrist practiced within the standard of care in prescribing Lamictal®25 m, had used an appropriate pediatric dose, and had properly informed the patient of the risks, benefits and alternatives. His medical record was well-documented.

**CASE #2**

The second case involved a 16 y/o female whose family physician (FP) was treating her for anxiety and other problems. With a diagnosis of bipolar disorder, the FP started her on Sertraline 50 mg and Ambien 10 mg @ night; instructed her to return to the office in a month; and to schedule an appointment with a psychiatrist for further evaluation. The patient never made the appointment. Three months later, the patient developed an additional complaint of hyperactivity. The physician then prescribed Lamictal® 100 mg, ½ tab at bedtime for 7 days, then 1 tab at bedtime and discontinued the Ambien. The physician alerted the mother as to possible side effects, including a rash. This conversation, however, was not documented in the chart. A month later the patient did develop a rash and was quickly transported to the hospital with the likely diagnosis of SJS.

She suffered a tumultuous hospital course and was left with extensive discoloration and mottling of her skin and some facial disfigurement.

The case generally lacked standard of care support due to:

- An almost simultaneous administration of Lamictal®, Ambien and Sertraline (both moderately interactive with Lamictal®)
- Administration of a contraindicated dose of Lamictal® in a pediatric patient
- Questionable drug choice of Lamictal® in this case
- Failure to refer the patient to a pediatric psychiatrist for diagnosis and treatment
- An overall disregard for the Lamictal® Black Box Warning.

This case was settled for a high dollar amount.
Risk /Clinical Commentary:

With an estimated 2 to 4 million serious injuries each year, drug therapy stands as one of the most significant perils to health resulting from human activity. Major health benefits can be achieved through safer medication use, which should be a much higher priority for medicine, government, and the public. Lamotrigine accounts for a disproportionate share of severe cutaneous adverse reactions. This information raises the question of whether lamotrigine should be used only after other epilepsy drugs have failed. Also the risks of lamotrigine-associated SJS warrant additional educational efforts to patients, family, and physicians to discontinue this drug at the first sign of a rash.ii The risk of SJS can be increased in 3 waysiii:

1. co-administration of lamotrigine and Valproate or a valproate-type anticonvulsant drug. These medications interact in such a way that the clearance of both is decreased and the effective dose of lamotrigine is increased
2. exceeding the recommended dose of lamotrigine
3. exceeding the recommended escalation regimen for lamotrigine

When prescribing lamotrigine or any other drug prone to serious side effects, consider in depth patient education; use an informed consent process; document your rationale for the drug selection; and set up a patient monitoring system that engages the patient in the process.

Additional lamotrigine/ Lamictal® Resources:

http://www.rxlist.com/lamictal-drug.htm

http://professionals.epilepsy.com/medications/p_lamictal_children.html

http://www.accessdata.fda.gov/drugsatfda_docs/label/2006/020241s10s21s25s26s27,020764s3s4s18s19s20lbl.pdf


iii http://professionals.epilepsy.com/medications/p_lamictal_children.html
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MAG Mutual Risk Managers invite our policyholders’ questions. If you wish to discuss information presented in this article, or have other questions, please call us at 1-800-282-4882, and ask for Risk Management.

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