Reglan and Tardive Dyskinesia - Black Box Warning May Not Be Enough to Protect Patients

The Case

Although the association between Reglan (metoclopramide) and Tardive Dyskinesia (TD) is common knowledge, in February 2009 the FDA mandated a ‘Black Box’ warning of this complication on the drug’s product information material. The “black box” clearly states that drugs containing metoclopramide can cause TD with long term use (three months or longer for people under age 65; a month for people over age 65). It is important to mention that an associated reaction is not necessarily proof of causation, but as drug manufacturers are aware, an association can adversely impact drug use/sales. Physicians should not count on patients to read nor question what is written in the drug circulars when they prescribe any drug. The patient should clearly understand the potential problems with taking a drug like Reglan, and why careful monitoring and follow-ups are essential.

Over two million people in the U.S. are taking some form of metoclopramide-containing medication which the FDA reports are now the most widely used medications known to cause Tardive Dyskinesia.

This may account for why patients are filing TD lawsuits, alleging the improper prescription of Reglan. The facts in these cases all have a common theme; frequent and long-term use of Reglan.

Case #1
This 70+ year old female patient had a history of hypertension, GERD, cholecystectomy, recurrent pancreatitis, gastroparesis, poor appetite, and multiple somatic complaints. She had been on Propulsid until it was removed from the US market. She stated, “It [Propulsid] helped all my problems”. In the following years the patient continued to suffer from pancreatitis for which her gastroenterologist (GI) prescribed Reglan prior to the evening meal. When the GI increased the Reglan dose from 5 mg to 10 mg, he received a phone message from the pharmacist: “Patients who are 65 and older are at risk using Reglan 10 mg. Is there anything else she can take or may we lower the dose to 5 mg?” The GI’s response: “Try Reglan 5 mg before meals and at bedtime #360 with 2 refills.” The GI continued to write Reglan refills, 5-10mg, four times per day, with one year follow-up office visits. Over the course of three years, the patient began experiencing tongue protrusion. The patient’s neurological symptoms slowly progressed, with involuntary mouth smacking and eye blinking, eventually progressing to whole-body abnormal movements. The patient was diagnosed with TD. Her prognosis was poor, and she now requires round the clock attendant care.

**Allegations**

The GI knew or should have known of the danger of neurological complications for prolonged Reglan use, even before the Black Box warning issued in February 2009.

The GI should have closely monitored the patient, given her age and gender, including regular in-person examinations, at frequent intervals, assessing the patient for the continued need for Reglan, and for the early development of any side effects.

Despite being warned by the pharmacist and asked to lower the dose, the GI negligently increased the patient’s dose of Reglan from 5 mg to 10 mg, as well as increased the frequency of administration.

**Disposition**

The case settled on behalf of the GI physician and his organization for a substantial sum of money.

**Case #2**

This female patient in her late 60’s presented to the GI who performed an upper GI and colonoscopy. Upper GI study results revealed grade 1 reflux esophagitis, hiatal hernia, non-bleeding erythematous gastropathy and normal duodenum. Her colonoscopy revealed a 3mm polyp in the rectum and internal hemorrhoids. She was instructed on an anti-reflux regimen and given Aciphex. On her return visit the patient was given samples of Nexium. Six months later the patient returned to the GI with complaints of a chronic cough. The GI diagnosed GERD and ordered a gastric emptying study. The gastric emptying scan revealed delayed gastric emptying half time. She prescribed Reglan 10 mg. The patient returned to the GI in three months; her cough was much improved. The GI diagnosed GERD and gastroparesis. She continued the patient on Nexium and Reglan, instructing her to return for a follow-up in six months.

In the meantime, and for the next year, the patient was being seen by her primary care physician (PCP) for treatment of anxiety and depression. The PCP noted that none of the multiple medications he had prescribed had been effective for controlling the patient’s anxiety and depression. He started the patient on Klonopin and Prozac, eventually increasing the doses of these two drugs. The PCP was aware that the patient was on Nexium and Reglan. During this time the patient was also being seen by her endocrinologist for continued difficulties controlling her diabetes and complaints of severe peripheral neuropathy. The endocrinologist had records of the patient’s recent cardiac nuclear stress test which revealed decreased exercise tolerance and baseline hypertension. She was unaware that the patient was on Reglan.

At her six-month follow-up with the GI, the GI noted the patient was doing well with no cough or new GI symptoms. She continued the patient’s Nexium and advised her to return to the office as needed. Less than a month later the patient returned to the GI complaining of regurgitation and cough when she lay down. She stated she was unable to sleep. The GI continued her Nexium and prescribed Reglan 10 mg (120# with 11 refills). Three days later an upper GI study revealed hiatal hernia and gastric mucosal abnormality characterized by erythema. The GI’s impression included gastroparesis secondary to Type 1 Diabetes. She advised the patient to continue Reglan and Nexium. A month later the GI increased the patient’s Reglan dose to 15 mg. The patient continued to see her PCP and endocrinologist for...
her other problems. Twelve months later the endocrinologist saw symptoms of TD, noting the patient was on Reglan. The patient called the GI who advised her to stop the Reglan. The patient had developed facial twitching, tremors, fatigue and slurred speech. The PCP ordered a neurology consult. The neurologist’s impression was Tardive Dyskinesia secondary to Reglan.

Disposition

The case settled for a very large amount on behalf of the GI physician and his organization. Experts were supportive of the PCP and her case was successfully defended.

Allegations against the GI

Failed to safely prescribe Reglan; failed to properly assess the patient during her Reglan use; failed to properly and timely monitor the patient for side effects and symptoms related to the administration and use of Reglan; improperly prescribed Reglan to the patient who was known to be taking anti-anxiety and anti depression medications; failed to provide follow-up care after prescribing high dose of Reglan with multiple refills; failed to discontinue/withdraw the patient’s prescription when the FDA black box warning was issued in 2/09; and failed to inform her of the contraindication for the long term use of the drug Reglan including signs and symptoms of Tardive Dyskinesia.

Allegations against the PCP

The PCP failed to diagnose TD; failed to properly assess the patient during the duration of her Reglan use; failed to discontinue the use of Reglan despite knowing the patient was taking high dose Reglan for an extended period of time for over a year; failed to provide and perform neurologic examinations during the pertinent time period with regard to Reglan use; failed to diagnose symptoms of TD in a timely manner, including but not limited to tremors and other neurologic symptoms.

Risk Management Commentary

These two recent lawsuits serve to remind individual physicians of the liability they share with the drug manufacturer for Tardive Dyskinesia associated with the long-term use of Reglan. The FDA states that metoclopramide is “approved for the short-term (no longer than 3 months) treatment of gastrointestinal disorders,” but warns that “frequent and long-term use of metoclopramide has been linked to Tardive Dyskinesia,” stating that older women are at the greatest risk for developing symptoms. It is recommended that patients discuss the medication with their physicians and it should not be used for more than 90 days unless the doctor’s assessment determines that “the benefits outweigh the risks.”

Tardive Dyskinesia is a miserable, disabling and irreversible condition. While it is recognized that sometimes Reglan is the only drug that helps control the symptoms of certain conditions like gastroparesis, it becomes incumbent upon physicians prescribing Reglan or other drugs containing metoclopramide to ensure and document that:

- Reglan is the best option for the patient’s clinical circumstance
- There are no existing therapeutic alternatives
- Standard dosing is being utilized
- The patient is taking the drug as prescribed, and complying with regular follow-up visits. In some cases, it’s better to insist the patient return for multiple office visits, rather than providing a prescription with multiple refills.
- You have warned the patient via informed consent of the risks and benefits of the drug, alternative treatments, if any, the symptoms of Tardive Dyskinesia, and that these symptoms may be permanent. Consider the increased risk of diabetics developing TD while taking Reglan for gastroparesis.
The information provided in this resource does not constitute legal, medical or any other professional advice, nor does it establish a standard of care. This resource has been created as an aid to you in your practice. The ultimate decision on how to use the information provided rests solely with you, the PolicyOwner.

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