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## FDA NEWS

### FDA Warns of Confusion Between Risperidone and Ropinirole

The FDA has issued a Drug Safety Communication regarding medication errors involving **Risperdal** (risperidone) and **Requip** (ropinirole). The agency has evaluated 226 wrong drug medication errors involving these two orthographically similar drugs. In addition to both brand and generic names being similar, the two drugs share the same dosage form, frequency of dosing, and strengths. The FDA has requested that the manufacturers adopt tall man lettering (risperiDONE and rOPINIRole), and the agency also suggests the following:

- **Patients should check the name and appearance of the tablets in their prescription bottle. If something looks different, talk to your pharmacist**
- **Prescribers should clearly print the drug name on written prescriptions**
- **Pharmacists are advised to physically separate the stocks of these two drugs wherever they are stored**

## .....NEW DRUGS.....NEW DRUGS.....NEW DRUGS.....

**EDARBI** (Azilsartan medoxomil).
**Category:** Antihypertensive (ARB).
**Initial dose:** 80 mg once daily, taken with or without food.
**MDD:** 80 mg.

The FDA has approved Takeda Pharmaceutical's Edarbi, which brings to eight the number of angiotensin receptor blockers (ARBs) available in the U.S. Edarbi is indicated for the treatment of hypertension. While the recommended dose is 80 mg daily, a starting dose of 40 mg daily should be considered for patients who are treated with high doses of diuretics. As is the case with all ARBs, use in pregnancy should be avoided. Edarbi is among a growing number of products which, according to their manufacturers, must be dispensed and stored in their original containers and can not be repackaged due to stability concerns.

**OXECTA** (Oxycodone HCl).
**Category:** Analgesic (Opioid Agonist).
**Initial dose:** 5 to 15 mg every 4 to 6 hours as needed for pain.
**MDD:** Not applicable.

Pfizer, Inc., and Acura Pharmaceuticals will market Oxecta, a new, immediate-release form of Oxycodone HCl which incorporates Acura's AVERSION technology, which is designed to deter common forms of prescription drug abuse. For example, the active ingredient will form a gel to prevent injection, and is formulated to irritate nasal passages to discourage inhalation. Originally, the tablet was to have also contained niacin to deter intentional overdose, but it was removed after the FDA objected. Oxecta will be available in 5 mg and 7.5 mg tablets.

**DIFICID** (Fidaxomicin).
**Category:** Antibiotic (Macrolide).
**Initial dose:** 200 mg twice daily with or without food for *C. difficile*-associated diarrhea.
**MDD:** 400 mg.

Optimer Pharmaceuticals has been granted FDA approval to market Dificid, a new Macrolide antibiotic indicated for the treatment of *Clostridium difficile*-associated diarrhea. Symptomatic *C. difficile* infection, once limited to hospitalized patients taking antibiotics, is now being seen more often among healthier patients in the community setting. In addition to watery diarrhea, the toxin produced by the infection can also cause pseudomembranous colitis. In clinical trials, Dificid was shown to be equally as effective as Vancomycin in treating the infection, but superior in preventing relapses. In order to prevent the development of drug resistant bacteria, Dificid should only be used for infections proven or strongly suspected to be caused by *C. difficile*. The most common adverse effects are nausea, vomiting, and abdominal pain.

**TRADJENTA** (Linagliptin).
**Category:** Antidiabetic (DPP-IV Inhibitor).
**Initial dose:** 5 mg once daily with or without food.
**MDD:** 5 mg.

The FDA has approved the third dipeptidyl peptidase-4 (DPP-IV) inhibitor for the treatment of type 2 diabetes mellitus. Tradjenta, co-marketed by Boehringer Ingelheim and Eli Lilly, can be used as monotherapy, or in combination with other oral antidiabetic agents. Unlike its competitors, **Januvia** and **Onglyza**, Tradjenta does not require dosage adjustment when used in patients with renal or hepatic impairment.

## FDA Sets New Requirements for Sunscreen Products

The U.S. Food and Drug administration (FDA) has announced new rules for sunscreen products, part of an ongoing effort by the agency to ensure that these products meet modern-day standards for safety and effectiveness. The new regulations, which are to take effect by the summer of 2012, include:

- **Sunscreens must pass FDA's broad spectrum test procedure, which measures a product's UVA protection relative to its UVB protection, in order to be labeled "Broad Spectrum."**
- **Only broad spectrum sunscreens with an SPF value of 15 or higher can claim to reduce the risk of skin cancer and early skin aging.**
- **Sunscreens may not be labeled "waterproof," "sweatproof," or "sunblock," as these claims overstate effectiveness. "Water resistant" claims must state whether the sunscreen remains effective for 40 minutes or 80 minutes while swimming or sweating, based on standard testing.**

# MEDICAID UPDATE

*Information Regarding the New York State Medicaid Program*

### Preferred Drug Program Update

Effective May 4, 2011, **Pantoprazole** was added to the list of preferred Proton Pump Inhibitors (PPIs), joining **Nexium**, **Omeprazole**, and **Prilosec OTC** as the only PPIs covered without prior authorization.

As of June 1, 2011, **Claritin-D**, **Zyrtec-D**, and generics will not be covered without prior authorization.

### Lost/Stolen Override No Longer Acceptable

Effective June 1, 2011, the New York State Medicaid program discontinued the **"04"** override for early fill rejections. This override was designated for lost or stolen medication. Beneficiaries claiming lost or stolen medication must now contact their prescriber, who may initiate a prior authorization request by contacting the Bureau of Pharmacy Policy and Operations at (**518) 486-3209**. Approval will *not* be granted for lost or stolen controlled substances. Medicaid discontinued the other early fill override, **"03"** for vacation supply, in July of 2010.

### DUR Recommendations Now Available on Website

The Department of Health has published a list of frequency, quantity, and duration limits for specific drugs identified by the Drug Utilization Review Board. The list is available at ***https://newyork.fhsc.com***. Some examples of the limitations recommended by the board include:

**Maxalt:** 24 tablets every 30 days

**Sumatriptan:** 18 tablets every 30 days

**Regranex:** Two 15-gram tubes in a lifetime (now requires prior authorization before dispensing)

**Solaraze:** 100 grams dispensed as a 90-day supply once per year

**Vusion:** 100 grams dispensed as a 90-day supply

# LAW REVIEW

*Regulatory Issues Affecting Pharmacy in New York State*

## U.S. Supreme Court Rules on Two Pharmacy-Related Cases

On June 24, 2011, the U.S. Supreme court ruled on two cases involving pharmacy: one pertaining to the liability of generic drug manufacturers who fail to warn patients about risks associated with their products, the other questioning the legality of a Vermont law banning "data mining" of prescription information from pharmacies.

### Pliva vs. Mensing: A Claim of Metoclopramide-induced Tardive Dyskinesia

In March of 2001, Gladys Mensing, a 76-year old Minnesota resident, was prescribed Reglan for diabetic gastroparesis, and her prescription was filled generically with metoclopramide. Ms. Mensing continued to take metoclopramide for the next four years and eventually developed symptoms of tardive dyskinesia, an often irreversible movement disorder known to be associated with long term use of metoclopramide, especially in the elderly, women, and diabetics. The FDA added a black box warning about this risk to the metoclopramide label, but not until 2009. The patient sued the drug's manufacturers, including Wyeth, maker of the brand name, for failure to warn doctors and patients of a known hazard of their product. The case against Wyeth was dismissed because, according to state law, a company owes no duty to persons who do not use their product specifically. The case against the generic companies, Pliva and Actavis, was originally denied but was upheld on appeal, which led to the manufacturers petitioning the Supreme Court to hear the case. The Court, by a vote of 5 to 4, ruled in favor of the drug companies, stating that the federal law prohibiting generic manufacturers from unilaterally changing their drug labels pre-empts state laws on failure to warn. Justice Clarence Thomas, writing for the majority, found that it would be impossible for the company to comply with both the state law requiring a label change to warn consumers of risks, and the federal law prohibiting such a change by a generic manufacturer, whose label must always be identical to the brand name label. Justice Sonia Sotomayor, speaking for the minority, pointed out that "a drug consumer's right to compensation for inadequate warnings now turns on the happenstance of whether the pharmacist filled her prescription with a brand-name drug or a generic."

### Sorrell vs. IMS: Is the Use of Data Mining Information Free Speech?

In 2007, the state of Vermont enacted The Prescription Confidentiality Law, which prohibits pharmacies from selling prescriber-identifiable information to data mining companies. Data mining companies, such as IMS Health, Inc, a respondent in this case, buy information from pharmacies which discloses the prescribing practices of individual practitioners. The data miners analyze this information and produce reports which are then sold to pharmaceutical manufacturers, who use the information to target specific prescribers to "detail." "Detailing" is the process by which pharmaceutical company representatives ("drug reps") visit physicians offices to persuade them to prescribe a particular product sold by their company. The stated purpose of the law was to protect doctors from "intrusive marketing," which could lead them to make medical decisions based on "incomplete and biased information." The law was challenged by data miners and an association of brand-name drug manufacturers. In a 6 to 3 vote, the Court struck down the Vermont law, labeling it a violation of free speech. Delivering the majority opinion, Justice Anthony M. Kennedy found that the law violated the First Amendment by restricting speech based on the content of the speech and based on the identity of the speaker. "That the State finds expression too persuasive," he wrote, "does not permit it to quiet the speech or burden its messenger." Justice Stephen G. Breyer dissented, arguing that is incorrect to "apply a strict First Amendment standard virtually as a matter of course when a court reviews ordinary economic regulatory programs….At best, the court opens a Pandora's box of First Amendment challenges to ordinary regulatory practices that may only incidentally affect a commercial message."

*Feature Article..*

# NEW FDA RESTRICTIONS ON SIMVASTATIN THERAPY

**The U.S. Food and Drug Administration (FDA)** has announced new restrictions, contraindications, and dose limitations for the use of the cholesterol-lowering agent simvastatin (Zocor®). The agency's decision was based upon a review of data suggesting an increased risk of serious adverse reactions when the drug was prescribed at its highest approved dose or given concomitantly with certain medications that interact with simvastatin.

## FDA Safety Communication on Zocor

On June 8, 2011, the FDA issued a drug safety communication regarding the use of Zocor (simvastatin). Their recommendations (see right and below) were based on a review of data from the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) trial. SEARCH was a 7-year, randomized, double-blind clinical trial comparing the safety and effectiveness of simvastatin 80 mg to simvastatin 20 mg. In the trial, 52 patients in the 80 mg group versus only 1 patient in the 20 mg group developed myopathy (defined as unexplained muscle weakness or pain with a serum creatine kinase [CK] greater than 10 times the upper limit of normal). In addition, 22 patients in the higher-dose group developed rhabdomyolysis (CK >40 times normal). No patients in the lower-dose group experienced rhabdomyolysis. The risks for myopathy and rhabdomyolysis were highest in the first 12 months of treatment and were increased in both elderly and female patient populations.

## FDA Recommendations Regarding Simvastatin 80 mg

The FDA has published the following guidelines pertaining to the use of the highest approved dose of simvastatin (80 mg):

- **Maintain patients on simvastatin 80 mg *only* if they have been taking this dose for 12 months or more without evidence of toxicity**
- **Do not start new patients on simvastatin 80 mg**
- **Patients who do not reach their LDL-C goal on simvastatin 40 mg should be switched to an alternative agent that provides greater LDL-C lowering**

## Updated FDA Contraindications and Dose Limitations of Zocor Therapy

| Contraindicated with Simvastatin | Do not exceed 10 mg of Simvastatin daily with: | Do not exceed 20 mg of Simvastatin daily with: |
|---|---|---|
| • Clarithromycin<br>• Cyclosporine<br>• Danazol<br>• Erythromycin<br>• Gemfibrozil<br>• HIV Protease Inhibitors<br>• Itraconazole<br>• Ketoconazole<br>• Nefazodone<br>• Posaconazole<br>• Telithromycin | • Amiodarone<br>• Diltiazem<br>• Verapamil | • Amlodipine<br>• Ranolazine |

## FDA Comparison of LDL-lowering Efficacy of Statins and Statin-based Therapies

| Zocor (simvastatin) | Crestor (rosuvastatin) | Lescol (fluvastatin) | Lipitor (atorvastatin) | Livalo (pitavastatin) | Mevacor (lovastatin) | Pravachol (pravastatin) | Vytorin (ezetimibe/ simvastatin) |
|---|---|---|---|---|---|---|---|
| 10 mg | ----- | 40 mg | ----- | 1 mg | 20 mg | 20 mg | ----- |
| 20 mg | ----- | 80 mg | 10 mg | 2 mg | 40 or 80 mg | 40 mg | ----- |
| 40 mg | 5 mg | ---- | 20 mg | 4 mg | 80 mg | 80 mg | 10/10 mg |
| 80 mg | 10 mg | ----- | 40 mg | ----- | ----- | ----- | 10/20 mg |
| ----- | 20 mg | ----- | 80 mg | ----- | ----- | ----- | 10/40 mg |
| ----- | 40 mg | ----- | ----- | ----- | ----- | ----- | 10/80 mg |

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# ASK PRN...

**Considering the fact that Nucynta (tapentadol) is a Schedule II narcotic, why isn't the chemically similar drug Ultram (tramadol) a controlled substance?**

When tramadol was approved by the FDA in 1995, the manufacturer claimed that the drug possessed only very weak narcotic effects, and it was not scheduled as a controlled substance. More recent data has demonstrated that opioid activity is the primary mechanism of the drug's pharmacological effect. According to the DEA, numerous reports of abuse and dependence have been received, and the drug is most commonly abused by narcotic addicts, chronic pain patients, and heath care professionals. Abrupt cessation of tramadol can produce a withdrawal syndrome typical of opioid drugs, which is marked by flu-like symptoms, restlessness, and drug craving. While tramadol is currently not a federal controlled substance under the Controlled Substance Act (CSA), a number of states have taken independent action to curb abuse and diversion of the drug. As of July 1, 2011, tramadol will be listed as a Schedule IV controlled substance in the state of Wyoming. It is already designated as a C-IV in the states of Arkansas, Kentucky, and Tennessee. A number of other agents which are non-controlled federally have been scheduled as controlled substances by individual states seeking to restrict their distribution. **Soma** (carisoprodol) is a scheduled drug in 17 states, and, in New York, **chorionic gonadotropin** is listed in Schedule III, although it is not controlled under the CSA. In some cases, states list drugs in a higher schedule than the federal government does; anabolic steroids are listed in Schedule III federally, but are Schedule II in New York State. **Pseudoephedrine**, a restricted OTC nationally, is a controlled substance in 11 states.

**GOT QUESTIONS? WE HAVE ANSWERS!**
**Send your questions to us at:**
***askprn@prnnewsletter.com***

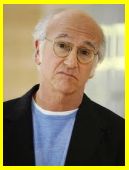
*PRN welcomes your questions on any topics relating to the practice of pharmacy. All answers are researched by our staff and, when necessary, discussed with the appropriate regulatory agencies. The information provided is not intended as legal advice, nor is it a substitute for professional judgment in clinical practice.*

## DID YOU KNOW?

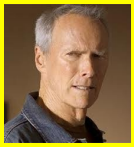
DID YOU KNOW that Metformin was *not* the first biguanide antidiabetic drug marketed in the United States? Introduced by Ciba-Geigy in 1959 and sold under the trade name **DBI**, Phenformin was the first biguanide used to treat diabetes. Reports of lactic acidosis started appearing shortly after Phenformin was approved, but it wasn't until 1977 that Secretary of Health, Education, and Welfare Joseph A. Califano, Jr., citing "imminent hazard." ordered the drug removed from the market.[1] Nearly 20 years would pass before another biguanide was approved for use in the United States. Metformin first reached pharmacy shelves in 1995, and remains a mainstay of diabetic pharmacotherapy to this day.

## PHARMACY FUN

**It's rebus time again - celebrity edition! The first reader to submit the correct answers to *puzzle@prnnewsletter.com* will receive a custom-printed *PRN* binder. (Hint: all three drugs are in the same general pharmacological category)**

1.  + "M"

2.  + A + 

3.  + A +  + "N"

Answers to last month's ***PHARMACY FUN***:
1. Mentax 2. Betaxolol 3. Cefotaxime 4. Taxol 5. Metaxalone 6. Staxyn

**References:**
1. Robert Reinhold, "Califano, Citing 'Imminent Hazard,' Orders Drug for Diabetes Taken Off the Market," *New York Times*, July 26, 1977.