TrendsRx®Drug Pipeline & News

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Pipeline Highlights: February 6, 2009 – February 27, 2009 and Recent Selected Health Care News Highlights

Selected Generic Product Approvals/Launches[1,2*]

galantamine hydrobromide (Razadyne™)	**Dosage Form; Strength**	Solution, oral; 4 mg/mL
	Approval Date†	January 30, 2009
	Anticipated Launch Date‡	TBD
	Comments	The reference brand is used for the treatment of mild to moderate dementia of the Alzheimer's type. This product is AA-rated and will be available from a single generics manufacturer.
tinidazole (Tindamax®)	**Dosage Form; Strength**	Tablet; 500 mg
	Approval Date†	February 2009
	Anticipated Launch Date‡	February 2009
	Comments	The reference brand is used for the treatment of trichomoniasis caused by *T. vaginalis* ; giardiasis caused by *G. lamblia* in both adults and pediatric patients older than three years of age; intestinal amebiasis and amebic liver abscess caused by *E. histolytica* in both adults and pediatric patients older than three years of age; bacterial vaginosis in non-pregnant women. BioComp Pharma, Inc. will launch the authorized generic version of Tindamax tablets
minocycline HCl (Solodyn™)	**Dosage Form; Strengths**	Tablet, extended-release, oral; 45 mg, 90 mg and 135 mg
	Approval Date†	February 3, 2009
	Anticipated Launch Date‡	TBD
	Comments	The reference brand is used for the treatment of only inflammatory lesions of non-nodular, moderate to severe acne vulgaris in patients 12 years of age and older. This product is AB-rated. Pursuant to a Settlement and License Agreement, the generic product will enter the market no later than November 2011.
risperidone (Risperdal®)	**Dosage Form; Strengths**	Tablet, orally disintegrating; 0.5 mg and 2 mg
	Approval Date†	February 24, 2009
	Launch Date‡	February 24, 2009
	Comments	The reference brand is used for the treatment of schizophrenia in adults and adolescents aged 13-17 years; alone, or in combination with lithium or valproate, for the short-term treatment of acute manic or mixed episodes associated with Bipolar I Disorder in adults and alone in children and adolescents aged 10-17 years; and for irritability associated with autistic disorder in children and adolescents aged 5-16 years. This product is AB-rated.

Recent Product Launches[1,2*]

Kapidex™ (dexlansoprazole) **Takeda Pharmaceuticals America Inc.**	**Dosage Form; Strengths**	Capsule, oral, delayed-release; 30 mg and 60 mg
	Indication	For the treatment of heartburn associated with non-erosive gastroesophageal reflux disease; for healing of all grades of erosive esophagitis (EE); and for maintaining healing of EE.
	Launch Date‡	February 23, 2009
Uloric® (febuxostat) **Takeda Pharmaceuticals America Inc.**	**Dosage Form; Strengths**	Tablet, oral; 40 mg and 80 mg
	Indication	For the chronic management of hyperuricemia in patients with gout.
	Launch Date	February 2009

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Recent New Drug Application (NDA) Approvals[1, 2*]

Vectical™ (calcitriol) **Galderma Laboratories LP.**	**Dosage Form; Strength**	Ointment, topical; 3 mcg/g
	Indication	For the topical treatment of mild to moderate plaque psoriasis in adults 18 years and older.
	Approval Date	January 23, 2009
	Anticipated Launch Date‡	First quarter 2009
TobraDex® ST (tobramycin/ dexamethasone) **Alcon Inc.**	**Dosage Form; Strengths**	Suspension, ophthalmic; 0.3% and 0.5%
	Indication	For the treatment of steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.
	Approval Date	February 13, 2009
	Anticipated Launch Date‡	TBD
Synvisc-One™ (hylan G-F 20) **Genzyme Corporation**	**Dosage Form; Strength**	Injection, intra-articular; 2 mL
	Indication	For the treatment of pain in osteoarthritis of the knee in patients who have failed to respond adequately to conservative non-pharmacologic therapy and simple analgesics, e.g., acetaminophen.
	Approval Date	February 26, 2009
	Anticipated Launch Date‡	TBD

Recent Supplemental New Drug Application (sNDA) Approvals[1,2*]

Apidra® SoloSTAR® (insulin glulisine [rDNA origin] injection) **Sanofi-Aventis U.S. LLC.**	**Dosage Form**	Injection, subcutaneous, pre-filled disposable pen
	Indication	For the improvement of glycemic control in adults and children with diabetes mellitus.
	Approval Date	February 24, 2009
	Comments	This is a new formulation of an already-approved product.

* Adapted from RxPipeline Services Week In Review. For more information contact: pipeline@caremark.com<mailto:pipeline@caremark.com>

† The Approval Date is established by the FDA but does not necessarily mean a generic product is available as of that date or that such product is available.

‡ A launch date/anticipated launch date may not reflect the actual availability of this medication. Due to circumstances beyond the control of CVS Caremark, information related to prospective medication launch dates is subject to change without notice. This information should not be solely relied upon for decision-making purposes.

News

Medication Safety

Information regarding selected medication safety issues can be found on the CVS Caremark Web site at www.caremark.com > Health Professional Services > Drug Safety Alerts.

FDA to Place Limits on Opioid Drugs[4,5]

On February 6, 2009, the FDA sent letters to 16 manufacturers of extended-release opioid drug products announcing that the agency plans to establish a risk evaluation and mitigation strategy (REMS) that would help prevent misuse, abuse, and accidental or intentional overdose of these drugs. A reported rise in inappropriate prescribing of opioids and an increase in the non-medical use of these drugs prompted the FDA to develop a program to ensure that the benefits of opioids continue to outweigh the risks, while still ensuring that patients with legitimate need for these drugs will continue to have appropriate access. The REMS would consist of educating prescribers, dispensers, and patients on the safe use of opioids and

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placing restrictions on distribution of these products. The affected opioid drugs include brand and generic extended-release formulations of fentanyl, hydromorphone, methadone, morphine, oxycodone, and oxymorphone. The agency will hold a series of meetings with manufacturers, patient advocacy groups, health care professionals, consumers, and other interested parties to gain more insight on how to effectively develop a REMS for opioid drugs.

Nationwide Recall of Prescription Medications[6,7,8,9,10]

In January 2008 and February 2009, Ethex Corporation and Ther-Rx Corporation, both subsidiaries of KV Pharmaceutical Company, issued a voluntary nationwide recall of dozens of products at the wholesale and retail level. The products may have been manufactured under conditions that did not adequately comply with current Good Manufacturing Practice. Due to this recall, there is currently a shortage of the following medications:

- Metoprolol succinate extended-release (25 mg, 50 mg, 100 mg and 200 mg) tablets
- Brand-name Micro-K® (8 mEq and 10 mEq) capsules and generic potassium chloride ER (8 mEq and 10 mEq) capsules
- Brand-name Imdur® (30 mg, 60 mg and 120 mg) tablets and generic isosorbide mononitrate ER (30 mg, 60 mg and 120 mg) tablets

Some prescription prenatal vitamins and iron supplements were also recalled at the wholesale level. A list of all recalled products can be found on the FDA Web site. Patients who are using these medications and supplements should contact their physicians for follow-up care and to obtain replacement prescriptions. CVS Caremark has reviewed this medication safety issue and is prepared to answer inquiries from plan participants and physicians.

Updated Safety Information for Raptiva[11]

In the November 2008 issue of TrendsRx Drug Pipeline & News, we reported labeling changes to Raptiva (efalizumab, Genentech, Inc.), a medication used to treat adult patients with chronic moderate-to-severe plaque psoriasis. Changes included a boxed warning to highlight the risk of life-threatening infections, including progressive multifocal leukoencephalopathy (PML). PML is a rare, serious and progressive neurologic disease caused by a virus that affects the central nervous system. It usually occurs in people whose immune systems have been severely weakened or suppressed as a result of medical treatment. The FDA issued a public health advisory on February 19, 2009 based on three confirmed cases and one possible case of PML in patients who were treated with Raptiva continuously for more than three years. None of the patients had been receiving other treatments that could be linked to the development of PML.

Healthcare providers are strongly encouraged to alert patients starting Raptiva about the risk of PML and to monitor those currently being treated to enable early detection of disease development. Some of the signs and symptoms of PML include weakness, loss of coordination, changes in vision, difficulty speaking and, sometimes, personality changes. Due to this risk, sales of Raptiva are being suspended in Canada and Europe. In the United States, the FDA is currently making plans to evaluate the risks and benefits of the drug. The FDA is asking health care providers and patients to report possible cases of PML through the MedWatch program by phone, toll-free, at 1-800-FDA-1088 or via the Internet at http://www.fda.gov/medwatch/index.html.

FDA Requires Boxed Warning and Risk Mitigation Strategy for Metoclopramide-Containing Drugs[12]

On February 26, 2009, the FDA announced that manufacturers of brand and generic metoclopramide must add a boxed warning to their drug labels about the risk of developing tardive dyskinesia. Metoclopramide is a medicine used to treat gastrointestinal disorders. Long-term use or high doses can lead to tardive dyskinesia, a disorder characterized by involuntary and repetitive movements of the body. Symptoms of tardive dyskinesia may not always subside or resolve after discontinuing metoclopramide. Manufacturers will be required to implement a REMS to ensure that patients are educated about the risks inherent in long-term use of metoclopramide.

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Clinical Guidelines

New Guidelines on Chronic Opioid Therapy[13]

The American Pain Society and the American Academy of Pain Medicine have published a comprehensive clinical practice guideline on opioid pain medications for patients with chronic, non-cancer pain. The new recommendations require prescriber knowledge of the principles of opioid treatment and the management of risks associated with abuse, addiction and diversion. The following are highlights of the new recommendations:

- Clinicians must properly assess patients' propensity for substance abuse, misuse, or addiction prior to initiating chronic opioid therapy.
- Patients should be monitored regularly for compliance and possible abuse, and their dosages should be adjusted to changing therapeutic needs.
- Methadone should not be used to treat breakthrough pain or on an as-needed basis, due to its long duration of action. Dosing recommendations and conversion algorithms are presented in the guideline.
- Patients who need high doses of opioids (200 mg daily of morphine or equivalent) should be monitored regularly for adverse events and their treatment modified accordingly.
- Clinicians should routinely incorporate non-pharmacologic interventions, such as physical therapy and psychotherapy, for pain.
- Patients should be counseled regarding mental and physical impairments that may occur during opioid therapy and how they may affect driving and work safety.
- Clinicians should understand current federal and state laws, regulatory guidelines, and policy statements that govern the medical use of opioids.

Information about the new guidelines can be found in the February issue of the *Journal of Pain*.

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