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TrendsRx® Drug Pipeline & News
A bi-weekly publication highlighting recent events in the pharmaceutical industry

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News Highlights from January 31 – February 11, 2005

EXECUTIVE SUMMARY

This issue of TrendsRx® Drug Pipeline and News contains information regarding recent NDA approvals, product launches, and recent drug safety information. Each issue will contain up-to-date pipeline information, as well as select information regarding drug safety, updated national clinical guidelines, and clinical studies of interest. Contact your Caremark Account Representative for additional information regarding any of the pipeline or other information contained in this product.

PIPELINE

Yentreve® (duloxetine) Withdraws NDA for the Treatment of Stress Urinary Incontinence[1] On January 28, 2005, Lilly and Boehringer Ingelheim Pharmaceuticals Inc. withdrew their New Drug Application (NDA) for Yentreve for the treatment of stress and urinary incontinence. The application was withdrawn because the U.S. Food and Drug Administration (FDA) indicated that there was not sufficient data to support approval. Lilly and Boehringer Ingelheim stated that they plan to evaluate all options to decide what steps to take next regarding duloxetine and this indication.

FDA Clears the Way for Generic Versions of Transdermal Patches to Treat Chronic Pain[1,2] On January 28, 2005, the FDA granted approval to Mylan Technologies, Inc., for the first generic version of Duragesic® Patch (fentanyl transdermal system)[1], which is used to treat patients suffering from severe chronic pain that cannot be managed with alternative analgesics.[2] The original Duragesic Transdermal System was approved in August 1990.[2] Fentanyl is a Schedule II controlled substance.[2]

Recent NDA Approvals[1]

Drug Name	Indication(s)	Drug Class	Approval Date	Route of Administration	Comments
Nascobal® (cyanocobalamin, USP) Nasal Spray; manufactured by Nastech Pharmaceutical/Questcor Pharmaceuticals	The treatment of vitamin B_{12} deficiency in patients with pernicious anemia and other malabsorptive conditions that can result in vitamin B_{12} deficiency such as gastric bypass surgery, Crohn's Disease, HIV/AIDS, and Multiple Sclerosis	Vitamin	02/01/2005	Intranasal	Nascobal Nasal Spray is intended to provide a treatment alternative to the already approved Nascobal Nasal Gel.

Recent Product Launches[1]

Drug Name	Indication(s)	Drug Class	Launch Date	Route of Administration	Comments
Abraxane™ for Injectable Suspension (paclitaxel protein-bound particles for injectable suspension) (albumin-bound); manufactured by American Pharmaceutical Partners, Inc.	The treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy	Protein-bound taxane	02/08/2005	Injection-infusion	

First Generic Approvals/Launches[1]

Generic Drug Name	Reference Brand	Dosage Form/Strength(s)	Approval Date	Launch Date	Comments
terconazole	Terazol 7®	Vaginal Cream, 0.4%	Jan 20	Jan 28	
levofloxacin	Levaquin®	Tablets, 750 mg	Jan 26	pending	Teva has been awarded 180 days of market exclusivity. Shipment will not commence at least until a decision is made on the pending patent litigation in the U.S. District Court for the District of New Jersey.
clarithromycin extended-release tablets	Biaxin XL®	Tablets, 1000 mg	Jan 26		The 1000 mg generic formulation taken once daily is expected to have the same therapeutic effect as two tablets of the 500 mg dose of Biaxin XL taken once daily.
fentanyl	Duragesic®	Transdermal System, 25 mcg/hr, 50 mcg/hr, 75 mcg/hr	Jan 28	Jan 28	

DRUG SAFETY

Medication Errors Due to Zyprexa® (olanzapine) and Zyrtec® (cetirizine) Name Confusion[3] A MedWatch Alert was issued by Eli Lilly notifying healthcare professionals about reports of medication errors (dispensing or prescribing) between the atypical antipsychotic Zyprexa and the antihistamine Zyrtec. These dispensing or prescribing errors could lead to unnecessary adverse events or potential relapse in patients suffering from schizophrenia or bipolar disorder. Some of the measures that Lilly has taken or will be taking to help reduce the potential for future errors include: changes to the label on the Zyprexa 10 mg bottles from "ZYPREXA" to "ZyPREXA", for easier identification; launch awareness direct mail campaign to pharmacists; sponsor medication error prevention continuing education; and journal ads focusing on this dispensing error potential, with emphasis on good prescribing and good dispensing practices.

Saquinavir/ritonavir Drug Interaction with Rifampin[4] Roche Laboratories Inc. notified healthcare professionals about an important drug interaction warning. Drug-induced hepatitis with marked transaminase elevations has been observed in healthy volunteers receiving rifampin 600 mg once daily in combination with ritonavir 100 mg/saquinavir 1000 mg twice daily (ritonavir boosted saquinavir). Roche advises prescribers that rifampin should not be administered to patients also receiving saquinavir/ritonavir as part of combination antiretroviral therapy for HIV.

Agrylin® (anagrelide) Labeling Changes The FDA and Shire US Inc. notified healthcare professionals about changes to the *Contraindications* and *Warnings* sections of the Agrylin prescribing information.[5] Agrylin is indicated for the treatment of thrombocythemia secondary to myeloproliferative disorders to reduce the elevated platelet count and the risk of thrombosis. It is also used to ameliorate associated symptoms including thrombohemorrhagic events.[6] Labeling changes include the contraindication to the use of Agrylin in patients with severe hepatic impairment.[5] Changes to the *Warnings* section discusses the need for dosage reduction in patients with moderate hepatic impairment and the necessity of monitoring these patients carefully for cardiovascular effects.[5] New information has also been added to the *Clinical Pharmacology* and *Drug Interactions* sections regarding the use of Agrylin in renally impaired patients, and patients concomitantly taking aspirin, as well as information regarding the effect of food.[6]

Public Health Advisory for Adderall® (mixed amphetamine salts) and Adderall XR®[7] The FDA has issued a Public Health Advisory to notify healthcare professionals that Health Canada, the Canadian drug regulatory agency, has suspended sales of Adderall XR in the Canadian market. The Canadian action was based on U.S. post-marketing reports of sudden deaths in pediatric patients. Adderall XR is approved in the U.S. for the treatment of adults and pediatric patients six to twelve years of age and older with Attention Deficit Hyperactivity Disorder (ADHD). Adderall, the immediate-release formulation of the drug, is approved for pediatric patients with ADHD. The FDA is aware of these post-marketing reports and evaluated the risk of sudden death with Adderall prior to approving the drug for treatment of ADHD in adults last year. The FDA will continue to evaluate post-marketing reports of serious adverse events in children, adolescents, and adults being treated with Adderall and related products. At this time, the FDA has decided not to take any further regulatory action. However, because it appeared that patients with underlying heart defects might be at increased risk for sudden death, the labeling for Adderall XR was changed in August 2004. The new labeling includes a warning that these patients might be at particular risk and should ordinarily not be treated with Adderall products.

Methylin® (methylphenidate) Recall Expanded to All Lots[8] Alliant Pharmaceuticals, Inc., expanded its voluntary recall of Methylin to include all lots of the product. The nationwide recall now includes all 2.5 mg, 5 mg, and 10 mg dosage strengths of Methylin because some tablets may contain too much or too little active ingredient. Alliant's liquid form of the product, Methylin Oral Solution is not affected by the recall and is still available.

References

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4. U.S. Food and Drug Administration. MedWatch 2005 Safety Alert: Invirase (saquinavir mesylate tablets and capsules) and Fortovase (saquinavir soft gelatin capsules). Available at: http://www.fda.gov/medwatch/SAFETY/2005/Saquinavir-Rifampin_deardoc_Feb05.pdf. Accessed on: February 9, 2005.
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6. Agrylin® product information. Shire US Inc., December 2004.

7. U.S. Food and Drug Administration. Public Health Advisory for Adderall and Adderall XR. Available at:: http://www.fda.gov/cder/drug/advisory/adderall.htm. Accessed on: February 10, 2005.
8. U.S. Food and Drug Administration. MedWatch 2005; Recall- Form Press Release. Alliant Pharmaceuticals Expands its Voluntary Nationwide Recall of Methylin® CT, 2.5 mg, 5 mg, and 10 mg tablets. Available at: http://www.fda.gov/oc/po/firmrecalls/alliant02_05.html. Accessed on: February 11, 2005.