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Gardasil® Designated for Priority Review for New Age Indication

Merck and Co., Inc. has announced that the FDA has accepted, and designated for priority review, its supplemental Biologics License Application (sBLA) for Gardasil®, its Human Papillomavirus Vaccine, for possible use in women 27 through 45 years of age. This vaccine is currently indicated for girls and women nine through 26 years of age for the prevention of cervical cancer, precancerous or dysplastic lesions, and genital warts caused by human papillomavirus (HPV) types 6, 11, 16 and 18. The vaccine is given as three injections over six months. Women remain at risk for acquiring HPV infections and developing HPV-related disease throughout their lifetime; therefore, an unmet medical need exists for this additional age group of women. The goal of the FDA will be to review and act on this submission within six months.

Neupro® Patch Recalled

Neupro® (rotigotine transdermal system) will be recalled at the end of April, 2008. Patients must be gradually down titrated with current supplies. Recall by Schwarz Pharma is due to formation of rotigotine crystals in the patches and resultant incomplete absorption.

Sources:

www.fda.gov
www.thomsonhc.com
www.medscape.com
www.PTCommunity.com
www.ashp.org
www.biotechnologyhealthcare.com

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Drug Information Highlights

- **Erythropoiesis-stimulating agents (ESAs): Darbepoetin alfa (Aranesp®) and Epoetin alfa (Epogen®, Procrit®):** The FDA has approved an updated boxed warning for these ESAs stating that they shortened overall survival and/or time-to-tumor progression in clinical studies in patients with breast, non-small cell lung, head and neck, lymphoid and cervical cancer when dosed to a target hemoglobin of ≥ 12 g/dL. This updated labeling approval follows updated labeling information in November, 2007, which addressed both the risks of these agents to patients with cancer and to patients with chronic kidney failure. For chronic kidney failure patients, maintaining hemoglobin levels higher than 10-12 g/dL increased the risk of death and serious cardiovascular events. On March 13, 2008, the FDA's Oncologic Drugs Advisory Committee voted that these agents should stay on the market but with narrowed indications. Their labels should state that they are not indicated for patients undergoing curative treatment, those with metastatic breast cancer, or those with metastatic head and neck cancer. The FDA has not yet responded to the Advisory Committee's recommendations.

- **Tiotropium (Spiriva® HandiHaler):** Boehringer Ingelheim and the FDA have notified healthcare professionals of a possible increased risk of stroke in patients taking Spiriva® as identified by ongoing safety monitoring. This drug is used to treat bronchospasm associated with chronic obstructive pulmonary disease (COPD). This risk has been determined by pooled analyses which have inherent limitations; therefore, further research is required to confirm any interpretation of these analyses.

- **Oseltamivir (Tamiflu®):** Roche and the FDA informed healthcare professionals of neuropsychiatric events associated with the use of Tamiflu® in patients with influenza. The post-marketing reports, mostly from Japan, include delirium and abnormal behavior leading to injury, and in some cases, resulting in fatal outcomes. These events were reported primarily among pediatric patients and often had abrupt onset and rapid resolution.

- **Darunavir (Prezista®):** Healthcare professionals are being notifed by the FDA and Tibotec Therapeutics of changes to the WARNINGS section of the prescribing information for Prezista® tablets regarding risk of hepatotoxicity. Drug-induced hepatitis has been reported in clinical trials and post-marketing experience in patients receiving combination therapy with Prezista®/ritonavir. It is recommended that appropriate laboratory testing be done prior to therapy initiation and that monitoring be done during treatment.

- **Etanercept (Enbrel®):** Prescribing information (PI) now contains a boxed warning (previously the PI had a bolded warning) related to risk of infections and tuberculosis (TB). Additional language is added to recommend screening and monitoring of patients for TB, even those having tested negative for latent TB. TB has been observed in patients receiving TNF-blockers, including Enbrel®, and may be due either to reactivation of latent TB or new infection. The risk of TB reactivation is lower with Enbrel® than with other agents in its class; however, post-marketing cases of TB have been reported with Enbrel®.

- **Cetuximab (Erbitux®):** Researchers funded by the National Institute of Allergy and Infectious Diseases (NIAID) have discovered, that pre-existing IgE antibodies to a specific sugar molecule present on cetuximab, have caused previously unexplained severe and rapid adverse reaction, including anaphylaxis, to this drug in some patients. The finding was prompted by research into the unusual geographic distribution of patients who experienced severe reactions to the drug, even as a result of the first exposure. Researchers are intrigued by their findings and seek further detail which is cause for further related research.

- **Hydrocodone/ chlorpheniramine Cough Suspension (Tussionex® Pennkinetic Extended-Release Suspension):** Adverse events, including death, have been reported related to misuse and inappropriate use of this potent cough medicine containing a narcotic ingredient and an antihistamine. The side effects have been due to doses greater than those that are recommended or to taking the medication more often than every 12 hours as recommended due to its extended-release formulation. Tussionex® should not be used in patients less than six years of age and the dose should be accurately measured and taken only as prescribed.

FDA Approved New Molecular Entities (NMEs), Biologic Products (BLAs)/Orphan Drugs and New Indications/New Formulations for Existing Products

Generic Name	Trade Name	Description	Applicant	FDA Status
Lamivudine	Epivir®	Nucleoside reverse transcriptase inhibitor indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection and now available in a tablet dosage form of 150 mg for pediatric patients.	GlaxoSmithKline	FDA approved new tablet dosage strength 02-01-2008
Bevacizumab	Avastin®	Recombinant humanized monoclonal IgG1 antibody, now approved, in combination with paclitaxel chemotherapy, for treatment of patients chemotherapy-naïve for their metastatic HER2 (Human Epidermal growth factor Receptor 2)-negative breast cancer.	Genentech, Inc.	FDA approved new indication 02-22-2008
Adalimumab	Humira®	Tumor necrosis factor inhibitor now approved as a treatment to reduce signs and symptoms of moderately to severely active polyarticular juvenile idiopathic arthritis (JIA) in patients four years of age and older. JIA is also referred to as juvenile rheumatoid arthritis (JRA).	Abbott	FDA approved new indication 02-22-2008
Rilonacept	Arcalyst™	Targeted inhibitor of interleukin-1 (IL-1), the key driver of inflammation in cryopyrin-associated periodic syndromes (CAPS), for treatment of familial cold autoinflammatory syndrome and Muckle-Wells syndrome, both cryopyrin-associated periodic syndromes, in patients 12 years of age and older. These conditions affect about 300 people in the United States. Rilonacept acts as a decoy receptor that binds IL-1 beta and then blocks IL-1 beta signaling, thereby preventing its interaction with cell surface receptors. Rilonacept is an injectable product, supplied as a lyophilized powder for reconstitution, which must be stored under refrigeration and protection from light, and used within three hours of reconstitution.	Regeneron Pharmaceuticals, Inc.	FDA approved BLA 02-27-2008
Esomeprazole	Nexium®	Proton pump inhibitor (PPI) now approved for short-term use in children ages one to eleven years of age for treatment of gastroesophageal reflux disease (GERD). Both the delayed-release capsule and the liquid formulation are approved for this age and indication.	AstraZeneca	FDA approved new age indication 02-28-2008
Fluvoxamine maleate	Luvox CR®	Selective serotonin reuptake inhibitor (SSRI) now approved in an extended-release capsule formulation and for the treatment of social anxiety disorder (SAD) and obsessive-compulsive disorder (OCD) in adults.	Jazz Pharmaceuticals, Inc.	FDA approved new dosage form and indication 02-28-2008
Desvenlafaxine succinate	Pristiq®	Serotonin-norepinephrine reuptake inhibitor (SNRI), administered once daily, for treatment of major depressive disorder (MDD) in adult patients. Wyeth expects to begin shipment second quarter of 2008.	Wyeth Pharmaceuticals, Inc.	FDA approved NME 02-29-2008
Palonosetron	Aloxi®	Receptor antagonist of 5-hydroxytryptamine-3 (5-HT3), available in an injectable formulation, and now approved for prevention of postoperative nausea and vomiting for up to 24 hours following surgery.	MGI Pharma, Inc.	FDA approved new indication 02-29-2008
Oxymorphone extended-release	Opana ER®	Extended-release opioid analgesic now approved in strengths of 7.5, 15, and 30 mg tablets for treatment of moderate to severe pain requiring continuous, around-the-clock relief for an extended period of time.	Endo Pharmaceuticals	FDA approved new dosage strengths 02-29-2008
Levoleucovorin for Injection		Single-isomer version of the folate analog leucovorin approved for use as rescue therapy in patients with osteosarcoma treated with high-dose methotrexate and to diminish the toxicity and counteract the effects of impaired methotrexate elimination and of inadvertent overdosage of folic acid antagonists.	Spectrum Pharmaceuticals, Inc.	FDA approved new drug 03-07-2008
Dextroamphetamine sulfate	Liquadd®	An amphetamine, now approved in an oral solution (5 mg/5 ml), for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). This product is to be launched during the second quarter of 2008.	Auriga Laboratories, Inc.	FDA approved new dosage formulation 03-10-2008
Insulin aspart rDNA	Novolog®	Rapid action and short duration of action insulin analogue now approved for patients aged four to eighteen years of age for administration via insulin pump.	Novo Nordisk	FDA approved new pediatric use 03-18-2008
Bendamustine	Treanda®	Nitrogen mustard alkylating agent approved for first and second-line treatment of chronic lymphocytic leukemia.	Cephalon	FDA approved new drug 03-20-2008