

New FDA regulations for sunscreens

IN A MOVE that could ultimately prevent some cases of skin cancer, the FDA has issued new regulations for the testing and labeling of sunscreens to help consumers choose products that offer the best protection against skin damage caused by excessive sun exposure.

The final rule establishes a standard test for over-the-counter (OTC) sunscreen products that will determine which such products can be labeled “broad spectrum.” This designation indicates that the particular sunscreen provides protection against both ultraviolet A (UVA) and ultraviolet B (UVB) radiation, both of which can cause skin cancer as well as sunburn and premature aging of the skin. (UVC rays are also dangerous, but they are absorbed by the ozone layer before reaching the ground.) Approximately 65% to 90% of melanomas alone are caused by exposure to UV light (www.cdc.gov/cancer/skin/basic_info/index.htm).

The FDA Division of Non-prescription Regulation Development has been developing and testing labeling requirements for sunscreen products for decades, but only recently have the data become sufficient to establish an accurate and reliable test for broad-spectrum UV protection.



Sunscreen products that protect against all types of sun-induced skin damage will be labeled not only broad spectrum but also SPF 15 (or higher). In combination with the broad-spectrum properties and other sun-protection measures, an item with a Sun Protection Factor of 15 or higher can reduce the risks of skin cancer and premature skin aging (wrinkling). A sunscreen that is not designated broad spectrum or that has an SPF value of 14 or lower has only been shown to help prevent sunburn, not skin cancer or early skin aging. A warning on the packaging will warn consumers of this.

Under the final rule, manufacturers will no longer be allowed to claim that their products are waterproof or sweatproof, or are a sunblock, because these claims

Sunscreen should be reapplied every 2 hours.

overstate their effectiveness, according to the FDA. Sunscreen packaging also will not be able to claim to provide sun protection for more than 2 hours without reapplication or to provide protection immediately after application without submitting data to support these claims and obtaining FDA approval.

The final rule will take effect by June 2012 for most manufacturers (those with annual sales less than \$25,000 will have 2 years to comply), but the agency expects that some sunscreen labels will change sooner.

The FDA also released three additional regulatory documents along with the final rule:

- A proposed rule that limits the maximum SPF value on sunscreen labels to 50+ because no sufficient data show that products with higher SPF values provide greater protection for users than products with SPF values of 50
- An advanced notice of proposed rulemaking for dosage forms that allocates a period of time for the public to submit requested data addressing the effectiveness and the safety of sunscreen sprays and to comment on possible directions and warnings for sprays
- A draft enforcement guidance for industry that outlines information to help sunscreen product manufacturers understand how to label and test their products in light of the new final rule and other regulatory initiatives. ■

A sunscreen that is not designated broad spectrum or that is SPF 14 or lower has only been shown to help prevent sunburn, not skin cancer or early skin aging.

FDA Update

The FDA reports that the **Chantix (varenicline)** drug label now contains updated efficacy and safety information. In addition to updated information on using varenicline in stable cardiovascular disease and information on using varenicline in patients with chronic obstructive pulmonary disease (COPD), the new label includes alternative directions for patients to select a quit smoking date. The alternative instructions tell patients to begin taking the drug, and then select a target quit date between day 8 and day 35 of treatment.

The FDA is continuing to evaluate whether use of **oral bisphosphonate drugs** is associated with an increased risk of esophageal cancer. The agency is reviewing data from published studies, which have reported conflicting findings on this risk. However, FDA believes at this time that the benefits of these drugs in reducing the risk of serious fractures in people with osteoporosis continue to outweigh their potential risks.

The FDA approved **Zytiga (abiraterone acetate)** in combination with prednisone (a corticosteroid) to treat patients with late-stage (metastatic) castration-resistant prostate cancer who have received prior docetaxel (chemotherapy).

New licensing deal for palliative constipation drug

THE RIGHTS to methylal-trexone bromide (Relistor)—a treatment for opioid-induced constipation—were licensed by Salix Pharmaceuticals, Ltd (Raleigh, North Carolina), in an exclusive worldwide agreement (with the exception of Japan) with Progenics Pharmaceuticals, Inc (Tarrytown, New York).

The peripherally acting mu-opioid receptor antagonist counteracts the constipating effects of opioid pain medications in the gastrointestinal tract without affecting the ability of those agents to relieve pain. Relistor subcutaneous injection is indicated for persons with advanced illness who are receiving palliative care and have an insufficient response to laxative therapy.

Methylnaltrexone bromide, which was cleared for use in the United States in 2008, is the first approved medication to



Relistor is indicated for patients with advanced illness who have an insufficient response to laxative therapy.

specifically target the underlying cause of opioid-induced constipation in patients in palliative care who are receiving opioid therapy for pain. (The use of the drug beyond 4 months has not been studied.) Single-use, prefilled syringes were approved in the United States, Canada, and the European Union in 2010. The Salix license includes intellectual property from the University of Chicago, Progenics Pharmaceuticals, and Wyeth Pharmaceuticals (now owned by Pfizer, Inc), including patents and applications with expiration dates ranging from 2017 through 2031.

An oral formulation of the drug to address opioid-induced constipation in patients with chronic, noncancer pain is in phase III development (www.progenics.com/releasedetail.cfm?ReleaseID=547932). ■

Potential Signals of Serious Risks/New Safety Information Identified by the Adverse Event Reporting System (AERS) January-March 2011

Product name	Potential signal of a serious risk/new safety information	Additional information as of May 31, 2011
Azathioprine (Imuran)	Acute febrile neutrophilic dermatosis (Sweet syndrome)	The Adverse Reactions section of the labeling for azathioprine was updated May 2011, to include Sweet syndrome.
Cetuximab (Erbixux)	<ul style="list-style-type: none"> • Corneal infection • Skin necrosis • Ulcerative keratitis 	FDA is continuing to evaluate these issues to determine the need for any regulatory action.
Mercaptopurine (Purinethol)	Hepatosplenic T-cell lymphoma	FDA is continuing to evaluate this issue to determine the need for any regulatory action.
Rituximab (Rituxan)	Hypogammaglobulinemia	FDA is continuing to evaluate this issue to determine the need for any regulatory action.

FDA group stands against bevacuzimab for breast cancer

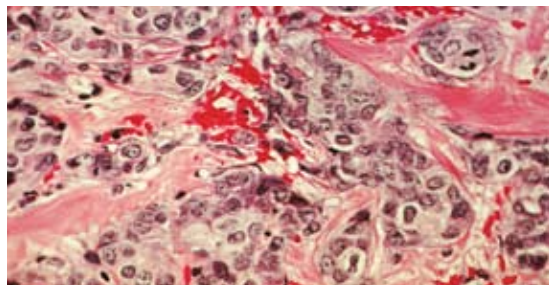
THE FDA'S Oncologic Drug Advisory Committee (ODAC) recommended on June 29, 2011, that the agency withdraw its approval of bevacizumab (Avastin) in combination with paclitaxel chemotherapy for first-line HER2-negative metastatic breast cancer. However, the docket remained open for public comment until July 28, 2011—the due date for additional written submissions from bevacizumab manufacturer Genentech as well as the Center for Drug Evaluation and Research, the FDA office that proposed in December 2010 to withdraw approval of the breast cancer indication.

The bevacizumab/paclitaxel regimen was approved in February 2008 under the FDA's accelerated approval program based on the results of a clinical trial known as "E2100." In July 2010, an independent advisory committee composed primarily of

oncologists voted 12-1 to remove the breast cancer indication from the bevacizumab label. According to the FDA, studies failed to confirm the survival benefit observed in the original trial, but demonstrated serious side effects.

ODAC's recommendation is not the final decision of the FDA. Agency commissioner Joan Hamburg is expected to make her final decision sometime after the docket closes. Any decision will affect the use of bevacizumab only in relation to breast cancer; the drug is also indicated for use in the treatment of colon, lung, kidney, and brain cancers (www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm193900.htm).

"We are very disappointed by the committee's recommendation and hope the commissioner does not decide to remove this



Histologic slide of cancer cells (blue) in breast tissue.

important medicine for women with an incurable disease who already have too few treatment options," commented Hal Barron, MD, the chief medical officer of Genentech and head of global product development for the company, in a statement issued by Genentech (www.gene.com/gene/news/press-releases/display.do?method=detail&id=13528). "We remain ready to collaborate with the FDA to find a solution that is in the best interest of patients who need Avastin." ■