

## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

[Docket No. FDA-2008-N-0174]

#### Identification of Drug and Biological Products Deemed to Have Risk Evaluation and Mitigation Strategies for Purposes of the Food and Drug Administration Amendments Act of 2007

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

**SUMMARY:** The Food and Drug Administration (FDA) is issuing this notice to notify holders of certain prescription new drug and biological license applications that they will be deemed to have in effect an approved risk evaluation and mitigation strategy (REMS) under the Food and Drug Administration Amendments Act of 2007 (FDAAA). Holders of applications deemed to have in effect an approved REMS are required to submit a proposed REMS to FDA.

**DATES:** Submit proposed REMSs to FDA by September 21, 2008.

**ADDRESSES:** Written communications regarding the applicability of this notice to a specific product should be identified with Docket Number FDA-2008-N-0174 and submitted to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic communications to <http://www.regulations.gov>. Information about FDA implementation of FDAAA is available on the Internet at <http://www.fda.gov/oc/initiatives/advance/fdaaa.html>.

#### FOR FURTHER INFORMATION CONTACT:

Mary Dempsey, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, rm. 4326, Silver Spring, MD 20993-0002, 301-796-0147.

#### SUPPLEMENTARY INFORMATION:

##### I. Introduction

On September 27, 2007, the President signed into law FDAAA (Public Law 110-85). Title IX, subtitle A, section 901

of FDAAA created new section 505-1 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 355-1). Section 505-1(a) of the act authorizes FDA to require persons submitting certain applications<sup>1</sup> to submit and implement a REMS if FDA determines that a REMS is necessary to ensure that the benefits of a drug outweigh the risks of the drug and informs the holder of the application for the drug of the determination. Section 909 of FDAAA provides that Title IX, subtitle A takes effect 180 days after its enactment, which is March 25, 2008.

FDAAA also contains REMS requirements for drug and biological products approved before the effective date of Title IX, subtitle A. Section 909(b)(1) of FDAAA specifies that a “drug that was approved before the effective date of this Act is \* \* \* deemed to have in effect an approved risk evaluation and mitigation strategy under section 505-1 of the Federal Food, Drug, and Cosmetic Act \* \* \* if there are in effect on the effective date of this Act elements to assure safe use— (A) required under section 314.520 or section 601.42 of title 21, Code of Federal Regulations; or (B) otherwise agreed to by the applicant and the Secretary [of Health and Human Services] for such drug.”

Section 909(b)(3) of FDAAA states: “Not later than 180 days after the effective date of this Act, the holder of an approved application for which a risk evaluation and mitigation strategy is deemed to be in effect \* \* \* shall submit to the Secretary a proposed risk evaluation and mitigation strategy. Such proposed strategy is subject to section 505-1 of the Act as if included in such application at the time of submission of the application to the Secretary.”<sup>2</sup>

Section 909(b)(2) of FDAAA states that a REMS for a drug deemed to have a REMS consists of the timetable required under section 505-1(d) of the act and any additional elements under section 505-1(e) and (f) of the act in effect for the drug on the effective date of FDAAA.

The purpose of this notice is to identify those drugs that FDA has determined will be deemed to have in effect an approved REMS and to notify holders of applications for such drugs that they are required to submit a proposed REMS by September 21, 2008.

FDA is developing guidance on the preferred content and format of a proposed REMS required to be submitted under section 909(b) of FDAAA and will issue it as soon as possible.

##### II. List of Drug and Biological Products Deemed to Have a REMS

Drug and biological products deemed to have in effect an approved REMS are those that on March 25, 2008 (the effective date of Title IX, subtitle A of FDAAA), had in effect “elements to assure safe use.” “Elements to assure safe use” include the following: (1) Health care providers who prescribe the drug have particular training or experience, or are specially certified; (2) pharmacies, practitioners, or health care settings that dispense the drug are specially certified; (3) the drug is dispensed to patients only in certain health care settings, such as hospitals; (4) the drug is dispensed to patients with evidence or other documentation of safe use conditions, such as laboratory test results; (5) each patient using the drug is subject to certain monitoring; or (6) each patient using the drug is enrolled in a registry (see section 505-1(f)(3) of the act).

Some applications approved before the effective date of FDAAA Title IX, subtitle A contain these elements to assure safe use.<sup>3</sup> Some of these applications were approved under § 314.520 (21 CFR 314.520) or § 601.42 (21 CFR 601.42). Others were not approved under part 314, subpart H or part 601, subpart E, but still contain elements to assure safe use that were agreed to by the applicant and the Secretary for such drug. Since 2005, these elements typically appeared in approved risk minimization action plans (RiskMAPs) (see the guidance for industry entitled “Development and Use of Risk Minimization Action Plans” (70 FR 15866, March 29, 2005)).

FDA has reviewed its records to identify applications that were approved before the effective date of Title IX of FDAAA with elements to assure safe use and has identified the drug and biological products listed in table 1 of this document as those that will be deemed to have in effect an approved REMS.

<sup>1</sup> Section 505(p)(1) of the act (21 U.S.C. 355(p)(1)) states that section 505-1 of the act applies to applications for prescription drugs approved under section 505(b) or (j) of the act and applications approved under section 351 of the Public Health Service Act (42 U.S.C. 262).

<sup>2</sup> Title IX, subtitle A of FDAAA, which includes section 909, takes effect March 25, 2008; 180 days after that date is September 21, 2008.

<sup>3</sup> These plans sometimes contain other elements to minimize risk such as a Medication Guide (21 CFR part 208) or a communication/educational plan

for health care providers or patients. A drug will not be deemed to have a REMS if it has only a Medication Guide, patient package insert, and/or communication plan (see section 505-1(e)(2) and (e)(3) of the act).

TABLE 1.—PRODUCTS DEEMED TO HAVE IN EFFECT AN APPROVED REMS

| Generic or Proper Name             | Brand Name                        | Application Number <sup>1</sup> | Date of Approval <sup>2</sup> |
|------------------------------------|-----------------------------------|---------------------------------|-------------------------------|
| Abarelix                           | Plenaxis <sup>3</sup>             | NDA 21–320                      | 11/25/2003                    |
| Alosetron                          | Lotronex                          | NDA 21–107                      | 02/09/2000                    |
| Ambrisentan                        | Letairis                          | NDA 22–081                      | 06/15/2007                    |
| Bosentan                           | Tracleer                          | NDA 21–290                      | 11/20/2001                    |
| Clozapine                          | Clozaril                          | NDA 19–758                      | 09/26/1989                    |
|                                    |                                   | ANDA 74–949                     | 11/26/97                      |
| ANDA 75–417                        |                                   | 5/27/99                         |                               |
| ANDA 75–713                        |                                   | 11/15/02                        |                               |
| ANDA 75–162                        |                                   | 4/26/05                         |                               |
| ANDA 76–809                        |                                   | 12/16/05                        |                               |
|                                    | Fazaclo ODT                       | NDA 21–590                      | 02/09/2004                    |
| Dofetilide                         | Tikosyn                           | NDA 20–931                      | 10/01/1999                    |
| Eculizumab                         | Soliris                           | BLA 125166                      | 03/16/2007                    |
| Fentanyl PCA                       | lonsys <sup>3</sup>               | NDA 21–338                      | 05/22/2006                    |
| Fentanyl citrate                   | Actiq                             | NDA 20–747                      | 11/04/1998                    |
| Isotretinoin                       | Accutane<br>Amnesteem<br>Claravis | NDA 18–662                      | 05/07/1982                    |
|                                    |                                   | ANDA 75–945                     | 11/2002                       |
|                                    |                                   | ANDA 76–135                     | 04/2003                       |
|                                    |                                   | ANDA 76–356                     | 04/2003                       |
|                                    |                                   | ANDA 76–041                     | 12/2002                       |
|                                    | Sotret                            | ANDA 76–503                     | 06/2003                       |
| Lenalidomide                       | Revlimid                          | NDA 21–880                      | 12/27/2005                    |
| Mifepristone                       | Mifeprex                          | NDA 20–687                      | 09/28/2000                    |
| Natalizumab                        | Tysabri                           | BLA 125104                      | 11/23/2004                    |
| Small pox (Vaccinia) Vaccine, Live | ACAM2000                          | BLA 125158                      | 08/31/2007                    |
| Sodium oxybate                     | Xyrem                             | NDA 21–196                      | 07/17/2002                    |
| Thalidomide                        | Thalomid                          | NDA 20–785<br>NDA 21–430        | 07/16/1998                    |

<sup>1</sup> New drug application (NDA), abbreviated new drug application (ANDA), biologics license application (BLA).

<sup>2</sup> The original date of approval of the drug. FDA may have required elements to assure safe use at a later date.

<sup>3</sup> Product is not currently marketed in the United States.

FDA is further asking members of the public to please notify the agency if they are aware of applications that have not been identified in this document and that they believe should be deemed to have in effect an approved REMS. Please provide the information to Mary Dempsey, Risk Management Coordinator (see the **FOR FURTHER INFORMATION CONTACT** section of this document).

Any application holder that believes its product identified in this notice should not be on the list of drug or biological products that will be deemed to have in effect an approved REMS should submit a letter identified with Docket Number FDA–2008–N–0174 to the Division of Dockets Management (see **ADDRESSES**) stating why the application holder believes its product was improperly identified in this notice.

FDA will notify the application holder within 30 days of receipt of the letter of its determination.

Dated: March 19, 2008.

**Jeffrey Shuren,**

*Associate Commissioner for Policy and Planning.*

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## DEPARTMENT OF HEALTH AND HUMAN SERVICES

### Food and Drug Administration

#### Joint Meeting of the Anesthetic and Life Support Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee; Notice of Meeting

**AGENCY:** Food and Drug Administration, HHS.

**ACTION:** Notice.

This notice announces a forthcoming of a public advisory committee of the Food and Drug Administration (FDA). The meeting will be open to the public.

*Name of Committees:* Anesthetic and Life Support Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee.