[BFAD BUREAU CIRCULAR NO. 11, S. 2005, June 07, 2005]

REVISED LABELING OF SELECTIVE COX-2 INHIBITOR DRUGS AND NSAIDS

For guidance and information of all concerned, BFAD has decided to defer the implementation of PSD Memos 05-2005 and 06-2005.

The Bureau of Food and Drugs is requesting manufacturers to revise the labels (PACKAGE INSERTS) of all marketed selective Cyclooxygenase-2 (COX-2) inhibitor drugs like Celebrex and Arcoxia as well as prescription and over-the-counter (OTC) non-prescription nonsteroidal anti-inflammatory drugs (NSAIDs). Such label changes shall include boxed warnings, highlighting potential for risk of cardiovascular events and the well-described serious potential life-threatening gastrointestinal (GI) bleeding associated with their use. The black box warning shall be placed on the first page of the insert, after posology/dosing statements.

BFAD would like to emphasize in our request to the manufacturers of OTC nonprescription NSAIDs to revise their labeling to provide more specific information about aforementioned risks of individual products and remind patients of limited dose and duration of treatment of these products according to package instructions. Although, aspirin (ASA) is an NSAID, it is exempted from this directive. ASA is a platelet inhibitor. In clinical studies, ASA has been shown to reduce the risk of cardiovascular (CV) events like heart attack and stroke. Likewise, Paracetamol is not included since it is used as antipyretic and analgesic for mild to moderate pain.

With respect to Celebrex and Arcoxia, we advise the manufacturers to implement the following actions:

1. Include black boxed warning and contraindications about CV and GI risks. Please refer to Bureau Circular No. 8 s. 2005

2. Inform practitioners to use lowest effective dose for shortest duration consistent with individual patient treatment objectives

3. Commit to conduct a long-term study and monitoring to assess the safety of Celebrex and Arcoxia

4. Mandatory Patient Leaflet Information

As to the prescription nonselective NSAIDs, the manufacturers are advised the following product labeling changes

1. Boxed warning about potential CV events and potentially serious GI adverse events

2. Contraindications for use in Coronary Artery Bypass Graft (CABG) operations

3. Instructions to patients to discuss with their doctors the risks and benefits of using NSAIDs and the importance of using the lowest effective dose for the shortest duration possible if treatment for NSAID is required.

For OTC NSAIDs, the available data do not suggest increased risk of serious CV events for short-term and low dosage use of NSAIDs. Such products are to be allowed in the market provided package insert revisions are instituted, which include the following:

1. More specific information about potential CV and GI risks

2. Stronger warnings about limiting dose and duration of treatments according to package instructions

3. Warning about potential skin reactions and to stop treatment once itchiness or rashes occur.

4. Public information through posters in drugstores.

Posters and leaflets about these products shall be made available in drug outlets.

Illustrative examples are provided in the following annexes.

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(SGD.) PROF. LETICIA BARBARA B. GUTIERREZ, MS
Director

ANNEX A

1. For Selective COX-2 Inhibitors like Celecoxib and Etoricoxib the black box warning should contain:

Absolute contraindications:

Not to be given to those patients who have history of:

- Stroke : Cerebrovascular accident, CVA
- Heart attack: Myocardial infarction, MI
- Coronary artery bypass graft: CABG
- Congestive heart failure (CHF) NYHA II - IV

2. We advise that above warning be placed right after "Dosage and Administrator", preferably in the first page of the insert.

3. Under CAUTION/WARNING statement: