

(1) Although the "descriptive" first paragraphs of the old and new FPL begin with the latter phrase (notably it is in quotes, "antirheumatic"), and end with "rheumatic disorders," this information refers only to the "generic" capacity of the drug and is clearly not an approved broad indication for such "generic" use of Indocin.

(2) The forced association in the physician's mind with aspirin and its use in rheumatic fever, acute rheumatic arthritis and "carditis," etc., is at least potentially misleading.

Recommend: Prompt and vigorous regulatory action, with serious consideration being given to the advisability of a forced "remedial" letter designed to correct the above misconceptions.

R. S. McCLEERY, M.D.

[U.S. Government Memorandum]

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE,
FOOD AND DRUG ADMINISTRATION,
November 4, 1966.

To: Herbert L. Ley, Jr., M.D., Director, Bureau of Medicine.

Through: John J. Jennings, M.D., Acting Associate Director/ODS.

From: Marvin Seife, M.D., Acting Deputy Director/DSR.

Subject: Indocin (indomethacin)—NDA 16-059

A revised indomethacin package insert, #6176404, dated August, 1966, submitted on September 2, 1966, contained most of the changes suggested by the Bureau of Medicine at a meeting with M.S.D. on July 15, 1966. Nevertheless, additional revision of the proposed insert is considered mandatory.

A. A drug warning statement must appear at the beginning of the insert as follows:

IMPORTANT WARNING

"Indocin, brand of indomethacin, cannot be considered a simple analgesic and should never be administered casually. Each patient should be carefully evaluated before treatment is started and should remain constantly under the close supervision of the physician. The drug should not be used in children because safe conditions for use have not been established and severe reactions, including fatalities, have been reported."

B. The following misleading words, phrases and unsupported material should be deleted from the package insert introductory section, (paragraphs one and two).

1. Paragraph one, sentence one—omit the word "antirheumatic".
2. Paragraph one, sentence three—eliminate the entire sentence—"Unlike corticosteroids, it has no effect on pituitary or adrenal function."
3. Paragraph two, sentence one—omit the phrase "of all ages".
4. Paragraph two, sentence two—omit the phrase "in patients with rheumatic disorders".

C. Indications:

1. The first sentence should be changed from "INDOCIN (indomethacin) has been effective in the treatment of:" to "INDOCIN (indomethacin) has been found effective in the symptomatic treatment of".
2. Eliminate the sentence following the listing of the indications: ("In these conditions indomethacin may often replace other commonly used agents such as corticosteroids, salicylates, phenylbutazone—like compounds, and colchicine.")
3. Rheumatoid Arthritis Section: Eliminate the last sentence of paragraph one—"Treatment should be continued for at least a month before concluding that it has not produced significant benefit"—unless M.S.D. can substantiate the recommendation contained therein.

D. Contraindications:

1. Eliminate sentences four and five from paragraph one.
2. The third sentence of paragraph one should be changed from "For these reasons it should not be given to patients with active peptic ulcer, gastritis, or ulcerative colitis, and should be used with caution if there is a history of these disorders." to "For these reasons it should not be given to patients with active peptic ulcer, gastritis, regional enteritis, or ulcerative colitis, and should be used with caution if there is a history of these disorders."