CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-100

OTHER REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

REQUEST FOR CONSULTATION

TO *(Office/Division)*: OMP/DDMAC Attn: Lisa Hubbard, PharmD			FROM *(Name, Office/Division, and Phone Number of Requestor)*:	
DATE January 18, 2007	IND NO. 70,410	NDA NO. 22-100	TYPE OF DOCUMENT Labeling	DATE OF DOCUMENT November 27, 2006
NAME OF DRUG AZOR (amlodipine besylate and olmesartan medoxomil)	PRIORITY CONSIDERATION S		CLASSIFICATION OF DRUG Fixed dose combination CCB/ARB	DESIRED COMPLETION DATE April 18, 2007

NAME OF FIRM: Daiichi Sankyo Inc.

REASON FOR REQUEST

I. GENERAL

- ☐ NEW PROTOCOL
- ☐ PROGRESS REPORT
- ☐ NEW CORRESPONDENCE
- ☐ DRUG ADVERTISING
- ☐ ADVERSE REACTION REPORT
- ☐ MANUFACTURING CHANGE / ADDITION
- ☐ MEETING PLANNED BY
- ☐ PRE-NDA MEETING
- ☐ END-OF-PHASE 2a MEETING
- ☐ END-OF-PHASE 2 MEETING
- ☐ RESUBMISSION
- ☐ SAFETY / EFFICACY
- ☐ PAPER NDA
- ☐ CONTROL SUPPLEMENT
- ☐ RESPONSE TO DEFICIENCY LETTER
- ☐ FINAL PRINTED LABELING
- ☐ LABELING REVISION
- ☐ ORIGINAL NEW CORRESPONDENCE
- ☐ FORMULATIVE REVIEW
- ☒ OTHER *(SPECIFY BELOW)*:

II. BIOMETRICS

- ☐ PRIORITY P NDA REVIEW
- ☐ END-OF-PHASE 2 MEETING
- ☐ CONTROLLED STUDIES
- ☐ PROTOCOL REVIEW
- ☐ OTHER (SPECIFY BELOW):
- ☐ CHEMISTRY REVIEW
- ☐ PHARMACOLOGY
- ☐ BIOPHARMACEUTICS
- ☐ OTHER (SPECIFY BELOW):

III. BIOPHARMACEUTICS

- ☐ DISSOLUTION
- ☐ BIOAVAILABILTY STUDIES
- ☐ PHASE 4 STUDIES
- ☐ DEFICIENCY LETTER RESPONSE
- ☐ PROTOCOL - BIOPHARMACEUTICS
- ☐ IN-VIVO WAIVER REQUEST

IV. DRUG SAFETY

- ☐ PHASE 4 SURVEILLANCE/EPIDEMIOLOGY PROTOCOL
- ☐ DRUG USE, e.g., POPULATION EXPOSURE, ASSOCIATED DIAGNOSES
- ☐ CASE REPORTS OF SPECIFIC REACTIONS (List below)
- ☐ COMPARATIVE RISK ASSESSMENT ON GENERIC DRUG GROUP
- ☐ REVIEW OF MARKETING EXPERIENCE, DRUG USE AND SAFETY
- ☐ SUMMARY OF ADVERSE EXPERIENCE
- ☐ POISON RISK ANALYSIS

V. SCIENTIFIC INVESTIGATIONS

- ☐ CLINICAL
- ☐ NONCLINICAL

COMMENTS / SPECIAL INSTRUCTIONS: Daiichi-Sankyo submitted this 505(b)2 application electronically for approval of the proposed fixed dose combination of Pfizer's product, Norvasc (amlodipine besylate) 2.5, 5, and 10 mg Tablets and their product, Benicar (olmesartan medoxomil) 5, 20, and 40 mg Tablets. The sponsor provided paragraph II and III certifications for the two patents listed by Pfizer for Norvasc, as the application relies on reports of investigations in NDA 19-787. The application also relies on the Agency's previous finding of safety and efficacy for information in NDA 21-286 for Benicar.

Please review the proposed labeling for this immediate release, fixed-dose combination film-coated drug product formulated as a once a day tablet available in four dose combinations of 5/20 mg, 5/40 mg, 10/20 mg, and 10/40 mg with the following proposed indications:

- Indicated either alone or in combination with other antihypertensive agents for the treatment of hypertension
- Indicated for initial therapy in patients with hypertension requiring a blood pressure reduction

The labeling was submitted in SPL and PLR format and is available in the EDR. I will provide you with a hard copy for your review.

SIGNATURE OF REQUESTOR	METHOD OF DELIVERY (Check one)
Denise M. Hinton for Akinwole Williams, MD	☒ DFS ☐ EMAIL ☐ MAIL ☒ HAND
PRINTED NAME AND SIGNATURE OF RECEIVER	PRINTED NAME AND SIGNATURE OF DELIVERER

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/s/

Denise Hinton
1/18/2007 02:26:49 PM

MEMORANDUM

To: Denise M. Hinton, RHPM for
Akinwole Williams, MD
Division of Cardiovascular and Renal Products, HFD-110

From: Lisa Hubbard, R.Ph., Regulatory Review Officer
DDMAC, HFD-42

Date: April 25, 2007

Re: Comments on draft labeling:
NDA 22-100
Azor (amlodipine besylate and olmesartan medoxomil)

DDMAC has reviewed the annotated version of the proposed label for NDA 22-100 Azor (amlodipine besylate and olmesartan medoxomil) and offers the following comments with regard to promotional considerations. Proposed wording from the insert is presented in *Italics,* followed by DDMAC comment.

Section 1: INDICATIONS AND USAGE

The proposed PI presents the following statement,

b(4)

The proposed indication is promotional in tone. The phrase may be confused with the JNC7 In addition, as written the proposed indication may unintentionally overstate the efficacy of the product.

Please also consider clarifying the b(4)
term in order to prevent unsubstantiated efficacy claims in promotional materials. DDMAC notes that a similar statement is found in the last paragraph in section 2 of the proposed label. We recommend that this statement be revised as well.

Section 12.3: Pharmacokinetics/Geriatric

The proposed PI presents the following language prior to a risk statement related to creatinine clearance,

b(4)

The proposed statement appears to minimize the risks associated with olmesartan therapy. DDMAC recommends eliminating the language.

Section 14: CLINICAL STUDIES

The proposed PI presents paragraphs that begin as b(4)

The proposed paragraphs in their entirety are highly promotional in tone.

The language does not appear in either the Norvasc label or the Benicar label. The language may be used to support misleading promotion by the sponsor.

As stated b(4)
during the recent advisory committee meeting, such guidelines are subject to change. DDMAC recommends deleting the first two paragraphs of this section of the label. We also recommend deleting the within the Clinical Trials section of the label and reference section of the label. Because of the overall tone of this proposed section of the PI and in light of recent enforcement activity, DDMAC recommends that the firm use caution with regard to promotional considerations for this product. Specifically, the JNC7 guidelines are not indicative of substantial evidence or substantial clinical experience with regard to the PI or promotional materials and considerations.

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/s/

Lisa Hubbard
4/30/2007 04:17:00 PM
DDMAC REVIEWER