DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-286/S-001

Sankyo Pharma, Inc.
Attention: Mr. Albert S. Yehaskel
780 Third Avenue, 47th Floor
New York, New York 10017

Dear Mr. Yehaskel:

Please refer to your supplemental new drug application dated April 30, 2002, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Benicar (olmesartan medoxomil) Tablets, 5, 20 and 40 mg.

We acknowledge receipt of your submissions dated April 30, May 3, and October 3, 2002.

This supplemental new drug application provides for final printed labeling revised as follows:

1. Under **ADVERSE REACTIONS**, 3rd paragraph, the adverse events of "inflicted injury" and "upper respiratory tract infection" have been deleted.

2. Under **ADVERSE REACTIONS**, the listing of "other (potentially important) adverse events…in controlled or open-label trials" has been changed to:

   Body as a Whole: chest pain, peripheral edema
   Central and Peripheral Nervous System: vertigo
   Gastrointestinal: abdominal pain, dyspepsia, gastroenteritis, nausea
   Heart Rate and Rhythm Disorders: tachycardia
   Metabolic and Nutritional Disorders: hypercholesterolemia, hyperlipemia, hyperuricemia
   Musculoskeletal: arthralgia, arthritis, myalgia
   Skin and Appendages: rash

3. Under **PRECAUTIONS**, **Carcinogenesis, Mutagenesis, Impairment of Fertility**, the phrase "for DNA damage in the rat kidney (comet assay)" has been deleted from the second paragraph of this subsection.

4. Under **OVERDOSAGE**, the second paragraph, which makes reference to studies in mice, rats, and dogs, has been deleted.

5. Under **WARNINGS, Fetal/Neonatal Morbidity and Mortality**, the next to the last sentence of the 7th paragraph, which had mentioned "delays in developmental milestones" has been expanded to list the specific *developmental milestones* that were delayed. This sentence now reads as follows:

   In rats, significant decreases in pup birth weight and weight gain were observed at doses $\geq$ 1.6 mg/kg/day, and delays in developmental milestones (delayed separation of ear auricula, eruption of lower incisors,

appearance of abdominal hair, descent of testes, and separation of eyelids) and dose-dependent increases in the incidence of dilation of the renal pelvis were observed at doses $\geq$ 8 mg/kg/day.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted final printed labeling (package insert included in your submission of April 30, 2002). Accordingly, the supplemental application is approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Edward Fromm
Regulatory Health Project Manager
(301) 594-5332

Sincerely,

{See appended electronic signature page}

Douglas C.Throckmorton M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Doug Throckmorton

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