

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPROVAL PACKAGE FOR:**

**APPLICATION NUMBER**

**NDA 21-516**

**Approval Letter(s)**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville, MD 20857

NDA 21-516

Senju Pharmaceutical Co., Ltd.  
c/o Ista Pharmaceuticals, Inc.  
Attention: Marvin J. Garrett  
Vice President  
15279 Alton Parkway, Suite 100  
Irvine, California 92618

Dear Mr. Garrett:

Please refer to your new drug application (NDA) dated September 25, 2002, received September 26, 2002, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Istalol (timolol maleate ophthalmic solution) 0.5%.

We acknowledge receipt of your submissions dated July 29, September 30, and December 6, 12, and 15, 2003, and February 18, March 12 (two), 16, 18, and 19, April 2, 13, 20, and 22, May 4, 5, 6, 7, and 11 (two), and June 4, 2004.

The December 15, 2003, submission constituted a complete response to our July 25, 2003, action letter.

This new drug application provides for the use of Istalol (timolol maleate ophthalmic solution) 0.5% for the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed draft labeling (package insert submitted May 11, 2004, and immediate container and carton labels submitted May 6, 2004). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

The electronic labeling rule published December 11, 2003, (68 FR 69009) requires submission of labeling content in electronic format effective June 8, 2004. For additional information, consult the following guidances for industry regarding electronic submissions: *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999) and *Providing Regulatory Submissions in Electronic Format - Content of Labeling* (February 2004). The guidances specify that labeling should

be submitted in *pdf* format. To assist in our review, we request that labeling also be submitted in MS Word format. If formatted copies of all labeling pieces (i.e., package insert, patient package insert, container labels, and carton labels) are submitted electronically, labeling does not need to be submitted in paper. For administrative purposes, designate this submission "**FPL for approved NDA 21-516.**" Approval of this submission by FDA is not required before the labeling is used.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,  
and Communications, HFD-42  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Michael Puglisi, Project Manager, at (301) 827-2090.

Sincerely,

*{See appended electronic signature page}*

Wiley A. Chambers, M.D.  
Deputy Director  
Division of Anti-Inflammatory, Analgesic  
and Ophthalmic Drug Products, HFD-550  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

Enclosure

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

/s/

-----  
Wiley Chambers  
6/4/04 06:54:37 PM