

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**21-604**

**PHARMACOLOGY REVIEW**

**PHARMACOLOGY/TOXICOLOGY COVER SHEET**

NDA number: 21604

Review number: No.1

Sequence number/date/type of submission: Original submission/December 31, 2002

Information to sponsor: Yes ( ) No (x)

Sponsor and/or agent: Taro Pharmaceuticals USA Inc., Hawthorne, NY 10532

Manufacturer for drug substance: \_\_\_\_\_

Reviewer name: Conrad H. Chen, Ph.D.

Division name: Anti-inflammatory, Analgesic, and Ophthalmic Drug Products

HFD #: 550

Review completion date: August 8, 2003

Drug:

Trade name: Children's ElixSure™ IB (Ibuprofen) Oral Suspension, 100 mg/5 ml

Generic name (list alphabetically): Ibuprofen Oral Suspension, 100 mg/5 ml

Code name:

Chemical name: Benzeneacetic acid,  $\alpha$ -methyl-4-(2-methylpropyl), ( $\pm$ )-.

CAS registry number: 15687-27-1

Mole file number:

Molecular formula/molecular weight: C<sub>13</sub>H<sub>18</sub>O<sub>2</sub>/206.28

Structure:

Relevant INDs/NDAs/DMFs: IND 62832

Drug class: NSAID

Indication: For the reduction of fever and the temporary relief of minor aches and pains associated with a cold, flu, head ache, sore throat, \_\_\_\_\_ toothache.

Clinical formulation:

The components and composition of the drug product are presented below:

| Ingredient                               | Concentration (%w/w) | Concentration per 5ml (mg) |
|--|----------------------|----------------------------|
| Purified Water, USP                      |                      |                            |
| FD&C Yellow#6, TARO                      |                      |                            |
| Poloxamer 188, NF                        |                      |                            |
| Ibuprofen, USP                           |                      |                            |
| Sodium Hydroxide, NF                     |                      |                            |
| Carbomer 934P                            |                      |                            |
| Sorbitol (Crystalline), NF               |                      |                            |
| Propylene Glycol, USP                    |                      |                            |
| Butylparaben, USP                        |                      |                            |
| Glycerin, USP                            |                      |                            |
| _____                                    |                      |                            |
| _____                                    |                      |                            |
| Berry Flavour Natural & Artificial, TARO |                      |                            |
| Total                                    |                      |                            |

\_\_\_\_\_ The liquid concentrate is an intensely sweet aqueous solution that contain \_\_\_\_\_ at pH 1.1 and preserved with \_\_\_\_\_ te.

Route of administration: Oral

Proposed use: OTC

Disclaimer: Tabular and graphical information is from sponsor's submission.



## ***PHARMACOLOGY/TOXICOLOGY REVIEW***

### **Non-Clinical Pharmacology, Pharmacokinetic, and Toxicology Studies.**

Ibuprofen is a non-steroidal anti-inflammatory agent (NSAID) known to possess analgesic and antipyretic activities. Its mechanism of action is generally believed to be related to the inhibition of prostaglandin synthesis.

The information on animal pharmacology, pharmacokinetic, and toxicology for ibuprofen was obtained from the published literature. A summary of non-clinical studies was submitted in the NDA with the citation of literature sources.

### **DETAILED CONCLUSIONS AND RECOMMENDATIONS:**

Ibuprofen was approved in 1974 for prescription use and in 1984 for OTC use. Children's ibuprofen oral suspension for OTC use has been marketed since 1995. Ibuprofen belongs to the NSAID. In this submission, the sponsor submitted a summary of non-clinical pharmacology/toxicology information based on the published literature.

In this NDA, Taro Pharmaceuticals is seeking approval to market Children's ElixSure™ IB (Ibuprofen) Oral Suspension, 100 mg/5ml, as an OTC product. The drug product is a thick syrup and spill resistant from a spoon. The sponsor states that this product is an ideal delivery system for pediatric patients. All inactive ingredients in the drug formulation are GRAS components. Since the proposed labeling follows the format for OTC products, there is no non-clinical section.

The approval of this product for OTC use is recommended.

Conrad H. Chen, Ph.D.  
Review Pharmacologist

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

/s/

-----  
Conrad Chen  
8/19/03 02:06:13 PM  
PHARMACOLOGIST  
The approval of this NDA is recommended.  
You have seen the review.

Josie Yang  
8/19/03 03:36:59 PM  
PHARMACOLOGIST