CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
22-362

SUMMARY REVIEW
# Summary Review for Regulatory Action

<table>
<thead>
<tr>
<th>Date</th>
<th>June 25, 2009</th>
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<tbody>
<tr>
<td>From</td>
<td>Eric Colman, MD</td>
</tr>
<tr>
<td>Subject</td>
<td>Deputy Division Director Summary Review</td>
</tr>
<tr>
<td>NDA#</td>
<td>22-362</td>
</tr>
<tr>
<td>Applicant Name</td>
<td>Daiichi Sankyo Pharma</td>
</tr>
<tr>
<td>Date of Submission</td>
<td>August 15, 2008</td>
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<tr>
<td>PDUFA Goal Date</td>
<td>June 15, 2009</td>
</tr>
<tr>
<td>Proprietary Name / Established (USAN) Name</td>
<td>Welchol for Oral Solution/Colesevelam</td>
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<tr>
<td>Dosage Forms / Strength</td>
<td>3.75 gram packet once daily or 1.875 gram twice daily</td>
</tr>
<tr>
<td>Proposed Indication(s)</td>
<td>Primary Hyperlipidemia and Type 2 Diabetes Mellitus</td>
</tr>
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<td>Recommended Action for NME:</td>
<td>Approve</td>
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## Material Reviewed/Consulted

**OND Action Package, including:**

- **Medical Officer Review**: Eileen Craig, MD
- **Statistical Review**: Not Applicable
- **Pharmacology Toxicology Review**: Not Applicable
- **CMC Review/OBP Review**: Elsbeth Chikhale, PhD
- **Microbiology Review**: Not Applicable
- **Clinical Pharmacology Review**: Jaya Vaidyanathan, PhD
- **DDMAC**: Not Applicable
- **DSI**: Not Applicable
- **CDTL Review**: Not Applicable
- **OSE/DMEPA**: Deveonne Hamilton-Stokes, RN
- **OSE/DDRE**: Not Applicable
- **OSE/DSRCS**: Not Applicable
- **Thorough QT Consult**: Not Applicable

OND=Office of New Drugs  
DDMAC=Division of Drug Marketing, Advertising and Communication  
OSE=Office of Surveillance and Epidemiology  
DMEPA=Division of Medication Error Prevention and Analysis  
DSI=Division of Scientific Investigations  
DDRE=Division of Drug Risk Evaluation  
DSRCS=Division of Surveillance, Research, and Communication Support  
CDTL=Cross-Discipline Team Leader
1. Introduction

This memorandum summarizes the relevant data and information related to the evaluation of Welchol for Oral Solution (pre-administered powder), an alternative dosage form of colesevelam tablet and capsule formulations, approved under NDAs 21-176 and 21-141, respectively.

2. Background

Colesevelam tablets and capsules are non-absorbed, bile-acid resins approved for the treatment of primary hyperlipidemia and type 2 diabetes mellitus. Data from an in-vitro bioequivalence study form the basis of approval for Welchol for Oral Solution. No clinical efficacy or safety studies were deemed necessary for submission or approval of this NDA.

3. CMC

I concur with the conclusions reached by the chemistry reviewer regarding the acceptability of the manufacturing of the drug product and drug substance.

4. Nonclinical Pharmacology/Toxicology

Because Welchol for Oral Solution is an alternative dosage form of currently approved Welchol capsules and tablets, nonclinical pharmacology and toxicology data were not considered necessary for this NDA. Reference is made to the nonclinical pharmacology and toxicology assessments for Welchol tablets and capsules.

5. Clinical Pharmacology

Following review of the pivotal in-vitro data, Dr. Vaidyanathan concluded that Welchol for Oral Solution has similar bile-acid binding characteristics compared with Welchol tablets. Specifically, the ratios of the average percent of each bile acid (glycocholic acid, glycochenodeoxycholic acid, and taurodeoxycholic acid) bound to Welchol for Oral Solution and Welchol tables were 0.97, 0.96, and 0.98, respectively.

6. Clinical Microbiology

Not applicable.
7. Clinical/Statistical-Efficacy

Clinical efficacy data were not considered necessary for this NDA. Reference is made to the clinical efficacy assessment for Welchol tablets and capsules.

8. Safety

Clinical safety data were not considered necessary for this NDA. Reference is made to the clinical safety assessments for Welchol tablets and capsules.

9. Advisory Committee Meeting

An advisory committee meeting was not considered necessary for this NDA.

10. Pediatrics

The sponsor received a Written Request to conduct a clinical study of Welchol tablets in patients aged 10 – 17 years with heterozygous familial hypercholesterolemia (HeFH). This study was completed and the sponsor received pediatric exclusivity. The Welchol labeling has been updated to reflect the results from this pediatric study. Pediatric studies for the hyperlipidemia indication with the Welchol for Oral Solution formulation have been waived.

Regarding the indication for the treatment of type 2 diabetes mellitus, studies in children aged 0 – 9 years were waived. The sponsor is required to conduct a study in pediatric patients with type 2 diabetes and aged 10 – 17 years. Welchol for Oral Solution will be used in this study. The final study report is to be submitted no later than November 2015.

11. Other Relevant Regulatory Issues

None

12. Labeling

There are no outstanding labeling issues.

13. Decision
Approve
<table>
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<tr>
<th>Application Type/Number</th>
<th>Submission Type/Number</th>
<th>Submitter Name</th>
<th>Product Name</th>
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<tr>
<td>NDA-22362</td>
<td>ORIG-1</td>
<td>DAIICHI SANKYO INC</td>
<td>WELCHOL POWDER FOR ORAL SUSPENSION</td>
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This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC C COLMAN
01/27/2010