

# CENTER FOR DRUG EVALUATION AND RESEARCH

## Approval Package for:

### *APPLICATION NUMBER:*

**209449Orig1s000**

*Trade Name:* Nityr

*Generic or Proper Name:* nitisinone, tablets

*Sponsor:* Cycle Pharmaceuticals Ltd.

*Approval Date:* July 26, 2017

*Indication:* Treatment of hereditary tyrosinemia type 1 (HT) in combination with dietary restriction of tyrosine and phenylalanine.

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## 209449Orig1s000

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*APPLICATION NUMBER:*

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**APPROVAL LETTER**



NDA 209449

**NDA APPROVAL**

Cycle Pharmaceuticals Ltd.  
Attention: Fariha Butt  
U.S. Agent for Applicant  
2343 Alexandria Drive, Suite 100  
Lexington, Kentucky 40504

Dear Fariha Butt:

Please refer to your New Drug Application (NDA), dated September 26, 2016 and received September 26, 2016, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for NITYR (nitisinone) tablets, 2 mg, 5 mg, and 10 mg.

This new drug application provides for the use of NITYR (nitisinone) tablets for the treatment of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

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

**CONTENT OF LABELING**

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Content of labeling must be identical to the enclosed labeling (i.e., text for the Package Insert, Instructions for Use). Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As*, available at <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible via publicly available labeling repositories.

**CARTON AND IMMEDIATE CONTAINER LABELS**

We acknowledge your submission, dated July 7, 2017, containing final printed carton and container labels.

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that you have fulfilled the pediatric study(ies) requirement for all relevant pediatric age groups for this application.

### **POSTMARKETING COMMITMENTS NOT SUBJECT TO THE REPORTING REQUIREMENTS UNDER SECTION 506B**

We remind you of your post-marketing commitment as follows:

3245-1            To conduct assays of two pediatric preparations and report the assay results within two months post approval.

The timetable you submitted on July 7, 2017, states that you will conduct this study according to the following schedule:

Study/Trial Completion:	09/2017
Final Report Submission:	09/2017

Submit clinical protocols to your IND 121021 for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all postmarketing final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii) you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled **“Postmarketing Commitment Protocol,” “Postmarketing Commitment Final Report,”** or **“Postmarketing Commitment Correspondence.”**

### **PROMOTIONAL MATERIALS**

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert, Medication Guide, and patient PI (as applicable) to:

OPDP Regulatory Project Manager  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at: <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf> ).

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. Form FDA 2253 is available at: <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM083570.pdf>. Information and Instructions for completing the form can be found at: <http://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/Forms/UCM375154.pdf>. For more information about submission of promotional materials to the Office of Prescription Drug Promotion (OPDP), see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>.

## **REPORTING REQUIREMENTS**

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 LCDR Hong Vu, Regulatory Project Manager, at (301) 796 - 7401.

Sincerely,

*{See appended electronic signature page}*

Lisa M. Soule, M.D.  
Acting Associate Director  
Division of Gastroenterology and Inborn  
Errors Products  
Office of Drug Evaluation III  
Center for Drug Evaluation and Research

Enclosure(s):  
Content of Labeling  
Instructions for Use  
Carton and Container Labeling

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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.**  
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/s/  
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LISA M SOULE  
07/26/2017