



NDA 204078/S-004

SUPPLEMENT APPROVAL

Éclat Pharmaceuticals LLC
c/o The Weinberg Group, Inc.
1129 Twentieth St. NW, Suite 600
Washington DC 20036

Attention: Marla Scarola, MS
Senior Consultant

Dear Ms. Scarola:

Please refer to your Supplemental New Drug Application (sNDA) dated and received April 2, 2014, submitted pursuant to Section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Bloxiverz (neostigmine methylsulfate injection).

We acknowledge receipt of your amendment dated October 13, 2014.

This “Prior Approval” supplemental new drug application proposes changes to the **NONCLINICAL TOXICOLOGY** section of the package insert, to include the results of the nonclinical studies ECL-13-001 and ECL-13-002, to fulfill the following Postmarketing Requirements listed in the approval letter dated May 31, 2013.

- 2046-1 Conduct an in vitro chromosomal aberration assay using Chinese hamster ovary cells to evaluate the potential for neostigmine to produce chromosomal damage.
- 2046-2 Conduct an in vivo mouse micronucleus assay for chromosomal damage for neostigmine methylsulfate.

We have completed our review of this supplemental application, as amended. 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(1)] 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 (text for the package insert), with the

addition of any labeling changes in pending “Changes Being Effected” (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eList may be found in the guidance for industry titled *SPL Standard for Content of Labeling Technical Qs and As*, available at <http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf>

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that includes labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

FULFILLMENT OF POSTMARKETING REQUIREMENT S

Your April 2, 2014, submission contains the final study reports for the following postmarketing requirements listed in the May 31, 2013, approval letter.

- 2046-1 Conduct an in vitro chromosomal aberration assay using Chinese hamster ovary cells to evaluate the potential for neostigmine to produce chromosomal damage.
- 2046-2 Conduct an in vivo mouse micronucleus assay for chromosomal damage for neostigmine methylsulfate.

We have reviewed your submission and conclude that the above requirements were fulfilled.

We remind you that there are additional postmarketing requirements listed in the May 31, 2013, approval letter that have not been fulfilled.

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 Allison Meyer, Regulatory Project Manager, at (301) 796-1258.

Sincerely,

{See appended electronic signature page}

Sharon Hertz, MD
Acting Director
Division of Anesthesia, Analgesia, and
Addiction Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

ENCLOSURE(S):
Content of Labeling

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

/s/

SHARON H HERTZ
12/11/2014