APPLICATION NUMBER:

206099Orig1s000

OTHER ACTION LETTERS
Avanir Pharmaceuticals  
Attention: Arthur Rosenthal, R.A.C.  
Senior Director, Regulatory Affairs & Quality  
30 Enterprise, Suite 400  
Aliso Viejo, CA 92656

Dear Mr. Rosenthal:


We acknowledge receipt of your amendment(s) dated:

March 10, 2013  
April 18, 2014  
April 30, 2014  
May 5, 2014  
June 25, 2014  
July 8, 2014  
July 11, 2014  
July 18, 2014  
July 25, 2014  
July 25, 2014  
August 13, 2014  
August 28, 2014  
September 19, 2014  
October 1, 2014  
October 28, 2014  
November 3, 2014  
November 24, 2014  
November 25, 2014

We have completed our review of this application, and have determined that we cannot approve this application in its present form. We have described our reasons for this action below and, where possible, our recommendations to address these issues.

Human Factors:

The human factors validation study does not support that the intended population will be able to use the product safely and effectively. Of the twenty-seven participants, only fourteen were able to successfully complete the delivery of a full treatment dose, i.e., two administrations (one to each nostril). Of the remaining thirteen participants who did not deliver a full treatment dose, seven were able to administer one nosepiece to one nostril, and four failed to simulate administering any treatment. Of these, one did not pierce the capsule of either of the two nosepieces, two blew into the device and then pierced the drug capsule, and one kept the button depressed while blowing into the device during the delivery step. The remaining two participants used more than two nosepieces to simulate administration of a total dose. One of these end-users used three nosepieces despite understanding that the correct dose was two nosepieces, and the other used four nosepieces.
We are also concerned with your proposal that patients will be able ascertain whether or not the piercing process was successful through visualization alone, as this was not validated in your study.

Most of the task failures noted in the study would result in patients receiving either an underdose or not receiving the medication at all, resulting in possible treatment failures or reduced efficacy. Thus, we recommend you further evaluate the root cause(s) of the failures seen in your study, and implement additional mitigations to address the failures and concerns described above. We request that you conduct an updated use-related risk analysis, and validate all user interface changes (including labeling, IFU, training, and/or device) in another human factors validation study with at least fifteen (15) representative users, to demonstrate that the changes are effective and that they do not introduce any new risks.

**PRESCRIBING INFORMATION**

We reserve comment on the proposed labeling until the application is otherwise adequate. We encourage you to review the labeling review resources on the PLR Requirements for Prescribing Information website including regulations and related guidance documents and the Selected Requirements for Prescribing Information (SRPI) – a checklist of 42 important format items from labeling regulations and guidances.

If you revise labeling, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances. Your response must include updated content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm.

**PROPRIETARY NAME**

Please refer to correspondence dated, July 28, 2014, which addresses the proposed proprietary name, Onzetra. This name was found acceptable pending approval of the application in the current review cycle. Please resubmit the proposed proprietary name when you respond to the application deficiencies.

**OTHER**

Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65. You may also request an extension of time in which to resubmit the application. A resubmission must fully address all the deficiencies listed. A partial response to this letter will not be processed as a resubmission and will not start a new review cycle.
Under 21 CFR 314.102(d), you may request a meeting or telephone conference with us to discuss what steps you need to take before the application may be approved. If you wish to have such a meeting, submit your meeting request as described in the FDA Guidance for Industry, “Formal Meetings Between the FDA and Sponsors or Applicants,” May 2009 at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM153222.pdf.

The drug product may not be legally marketed until you have been notified in writing that this application is approved.

If you have any questions, call Vandna Kishore, Regulatory Project Manager, at (301) 796-4193.

Sincerely,

{See appended electronic signature page}

Eric Bastings, MD
Deputy Director
Division of Neurology Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

ERIC P BASTINGS
11/26/2014