Colleen M. Johns
Head of Regulatory Affairs
Alpha Cognition USA, Inc.
1645 Palm Beach Lakes Blvd., Suite 1200
West Palm Beach, FL 33401

May 27, 2021

Re: Docket No. FDA-2020-P-2301

Dear Ms. Johns:

This letter responds to your citizen petition received on December 10, 2020 (Petition), requesting that the Food and Drug Administration (FDA or Agency) designate an additional reference standard for Galantamine Hydrobromide oral tablets, Equivalent (Eq) 4 milligrams (mg) Base, approved under new drug application (NDA) 021169, in the *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).[1]

We have carefully considered the Petition. For the reasons described below, your Petition is granted in that we have selected a new reference standard. FDA will select abbreviated new drug application (ANDA) 077604 held by Yabao Pharmaceutical Co. Ltd. Beijing (Yabao), as the new reference standard for this drug product.

I. BACKGROUND

Section 505(j) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355(j)) allows the submission of an ANDA to market a generic version of a previously approved drug product. To obtain approval, the ANDA applicant must show, among other things, that the generic drug product: (1) has the same active ingredient(s), dosage form, route of administration, strength, conditions of use, and, with certain exceptions, labeling as the listed drug; and (2) is bioequivalent to the listed drug.

A *listed drug* is a new drug product: (1) that has been approved under section 505(c) of the FD&C Act for safety and effectiveness or under section 505(j) of the FD&C Act; (2) whose approval has not been withdrawn or suspended under section 505(e)(1) through (e)(5) or (j)(6) of the FD&C Act; and (3) that has not been withdrawn from sale for what FDA has determined are reasons of safety or effectiveness.[2] Listed drug status is evidenced by the drug product's identification in the current edition of FDA's Orange Book as an approved drug.[3] A *reference listed drug* (RLD) is the listed drug identified by FDA as the drug product on which an applicant

[1] The Orange Book is available at http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm.

[2] § 314.3(b) (21 CFR 314.3(b)).

[3] Id.

relies in seeking approval of its ANDA.[4] Generally, an RLD is a drug product approved in an NDA under section 505(c) of the FD&C Act.

A *reference standard* is the drug product selected by FDA that an applicant seeking approval of an ANDA must use in conducting an in vivo bioequivalence study required for approval.[5] FDA generally selects a single reference standard that ANDA applicants must use in any in vivo bioequivalence testing required for approval. A single reference standard ensures the greatest level of consistency between a generic drug and its RLD and among generic drugs. Generally, the RLD will be the drug product selected by the Agency as the reference standard for conducting in vivo bioequivalence testing.[6] In certain circumstances, however, the Agency may select a generic drug product as the reference standard for bioequivalence testing. For instance, if the RLD has been discontinued from marketing, FDA may select a therapeutically equivalent[7] generic drug product as the reference standard.[8]

II. DISCUSSION

In the Petition, you request that FDA designate an additional reference standard for Galantamine Hydrobromide oral tablets (Petition at 1). You state that the current reference standard, which is Razadyne (galantamine hydrobromide) oral tablets, Eq) 4 mg base, held by Janssen Pharmaceuticals, Inc. (Janssen) under NDA 021169, is unavailable in the market and that Janssen has discontinued their product (Petition at 2).

We have examined the information in the docket, regulatory filings for the current reference standard, and third-party commercial data regarding Galantamine Hydrobromide oral tablets, Eq 4 mg base. Based on this information, FDA concludes that the current reference standard, Razadyne (galantamine hydrobromide) oral tablets, Eq 4 mg base, drug product is unavailable in the market. Therefore, we agree that you have stated grounds for selecting a new reference standard.[9]

In this instance, we have determined that it is appropriate to select ANDA 077604 held by Yabao as the new reference standard for Galantamine Hydrobromide oral tablets, Eq 4 mg base. It is

[4] Id.

[5] Id.

[6] § 314.94(a)(3) (21 CFR 314.94(a)(3)).

[7] "Therapeutic equivalents are approved drug products that are pharmaceutical equivalents for which bioequivalence has been demonstrated, and that can be expected to have the same clinical effect and safety profile when administered to patients under the conditions specified in the labeling" (§ 314.3(b)).

[8] See preamble to the final rule, "Abbreviated New Drug Applications and 505(b)(2) Applications," 81 FR 69580 at 69619 (Oct. 6, 2016).

[9] See 81 FR at 69619.

therapeutically equivalent to the RLD, and it is the current market leader as determined by FDA based on commercial data.[10]

III. CONCLUSION

For the reasons described in this response, the Petition is granted in that FDA will identify ANDA 077604 for Galantamine Hydrobromide oral tablets, EQ 4 mg base, held by Yabao, as the new reference standard in the Orange Book.

Sincerely,

Douglas C. Throckmorton -S

Digitally signed by Douglas C. Throckmorton -S
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Date: 2021.05.27 11:57:52 -04'00'

Patrizia Cavazzoni, M.D.
Director
Center for Drug Evaluation and Research

[10] We note that FDA will not approve any ANDA that uses the reference standard to demonstrate bioequivalence until FDA determines that the RLD was not withdrawn from sale for reasons of safety or effectiveness. See § 314.161 (21 CFR 314.161) and § 314.122 (21 CFR 314.122).