CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

208082Orig1s000

OTHER REVIEW(S)

`505(b)(2) ASSESSMENT

Application Information		
NDA # 208082	NDA Supplement #: S-	Efficacy Supplement Type SE-
Proprietary Name: Austedo Established/Proper Name: deutetrabenazine Dosage Form: Oral Tablets Strengths: 6 mg, 9 mg, and 12 mg		
Applicant: Teva Pharmaceuticals		
Date of Receipt: 10/3/16		
PDUFA Goal Date: 4/3/17	Action Goal Date (if different):	
RPM: Stacy Metz, PharmD		
Proposed Indication(s): Treatment of chorea associated with Huntington's disease		

GENERAL INFORMATION

1) Is this application for a recombinant or biologically-derived product and/or protein or peptide product *OR* is the applicant relying on a recombinant or biologically-derived product and/or protein or peptide product to support approval of the proposed product?

YES ☐ NO ☒

*If "**YES** "contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

INFORMATION PROVIDED VIA RELIANCE (LISTED DRUG OR LITERATURE)

2) List the information essential to the approval of the proposed drug that is provided by reliance on our previous finding of safety and efficacy for a listed drug by reliance on published literature, or by reliance on a final OTC monograph. *(If not clearly identified by the applicant, this information can usually be derived from annotated labeling.)*

Source of information* (e.g., published literature, name of listed drug(s), OTC final drug monograph)	Information relied-upon (e.g., specific sections of the application or labeling)
Xenazine (tetrabenazine) tablets, 12.5 mg and 25 mg (NDA 21894)	Clinical studies information. Clinical Pharmacology information. Non-Clinical Toxicology information. Post-marketing data

3) The bridge in a 505(b)(2) application is information to demonstrate sufficient similarity between the proposed product and the listed drug(s) or to justify reliance on information described in published literature for approval of the 505(b)(2) product. Describe in detail how the applicant bridged the proposed product to the listed drug(s) and/or published literature[1]. See also Guidance for Industry Providing Clinical Evidence of Effectiveness for Human Drug and Biological Products.

The sponsor's reliance on FDA's finding of safety and effectiveness for Xenazine is for nonclinical chronic toxicity, carcinogenicity, and reproductive toxicology information, and some clinical pharmacology information referenced in the Xenazine label such as additional in vitro drug-drug interactions. The Sponsor was unable to obtain the listed drug, Xenazine, to complete BA/BE studies that directly compared SD-809 to Xenazine. The Sponsor's bridging strategy compared human PK data from patients enrolled in clinical study SD-809-C-16. Patients entered the study taking a stable dose of Xenazine. PK samples were drawn at baseline while they were on a stable dose of Xenazine on the day before switching to SD-809, and a second set of PK samples were drawn after switching patients to an equivalent, stable dose of SD-809 expected to be similar to their prior Xenazine dose. The Cmax of the active α-HTBZ and β-HTBZ metabolites from SD-809 were below the Cmax of the active metabolites from Xenazine. Additionally in this study, efficacy was evaluated using the Unified Huntington Disease Rating Scale (UHDRS) Total Maximal Chorea (TMC) score. Patients who switched overnight from Xenazine to SD-809 experienced no loss in control of chorea compared to Xenazine, as assessed by the mean UHDRS TMC score, through Week 1.

The SD-809 NDA included additional clinical pharmacology information typically required for a 505(b)(1) NDA including a Mass Balance Recovery Study in healthy volunteers, in vitro and in vivo Drug-Drug interaction studies of SD-809 and several of its' metabolites.

RELIANCE ON PUBLISHED LITERATURE

[1]For 505(b)(2) applications that rely on a listed drug(s), bridging studies are often BA/BE studies comparing the proposed product to the listed drug(s) Other examples include: comparative physicochemical tests and bioassay; preclinical data (which may include bridging toxicology studies); pharmacokinetic/pharmacodynamic (PK/PD) data; and clinical data (which may

4) (a) Regardless of whether the applicant has explicitly stated a reliance on published literature to support their application, is reliance on published literature necessary to support the approval of the proposed drug product (i.e., the application *cannot* be approved as labeled without the published literature)?

YES ☐ NO ☒

*If "**NO**," proceed to question #5.*

(b) Does any of the published literature necessary to support approval identify a specific (e.g., brand name) *listed* drug product?

YES ☐ NO ☐

*If "**NO**", proceed to question #5.*

*If "**YES**", list the listed drug(s) identified by name and answer question #4(c).*

(c) Are the drug product(s) listed in (b) identified by the applicant as the listed drug(s)?

YES ☐ NO ☐

[1]For 505(b)(2) applications that rely on a listed drug(s), bridging studies are often BA/BE studies comparing the proposed product to the listed drug(s) Other examples include: comparative physicochemical tests and bioassay; preclinical data (which may include bridging toxicology studies); pharmacokinetic/pharmacodynamic (PK/PD) data; and clinical data (which may

RELIANCE ON LISTED DRUG(S)

Reliance on published literature which identifies a specific approved (listed) drug constitutes reliance on that listed drug. Please answer questions #5-9 accordingly.

5) Regardless of whether the applicant has explicitly cited reliance on listed drug(s), does the application **rely** on the finding of safety and effectiveness for one or more listed drugs (approved drugs) to support the approval of the proposed drug product (i.e., the application cannot be approved without this reliance)?

YES ☒ NO ☐

*If "**NO**," proceed to question #10.*

6) Name of listed drug(s) relied upon, and the NDA #(s). Please indicate if the applicant explicitly identified the product as being relied upon (see note below):

Name of Listed Drug	NDA #	Did applicant specify reliance on the product? (Y/N)
Xenazine (tetrabenazine) tablets, 12.5 mg and 25 mg	21894	Y

Applicants should specify reliance on the 356h, in the cover letter, and/or with their patent certification/statement. If you believe there is reliance on a listed product that has not been explicitly identified as such by the applicant, please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.

7) If this is a (b)(2) supplement to an original (b)(2) application, does the supplement rely upon the same listed drug(s) as the original (b)(2) application?

N/A ☒ YES ☐ NO ☐

*If this application is a (b)(2) supplement to an original (b)(1) application or not a supplemental application, answer **"N/A"**.*

*If "**NO**", please contact the (b)(2) review staff in the Immediate Office, Office of New Drugs.*

8) Were any of the listed drug(s) relied upon for this application:

a) Approved in a 505(b)(2) application?

YES ☐ NO ☒

*If "**YES**", please list which drug(s).*

Name of drug(s) approved in a 505(b)(2) application:

b) Approved by the DESI process?

YES ☐ NO ☒

*If "**YES**", please list which drug(s).*

Name of drug(s) approved via the DESI process:

c) Described in a final OTC drug monograph?

YES ☐ NO ☒

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