CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

207844Orig1s000

OTHER REVIEWS

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: April 17, 2015

TO: Sumathi Nambiar, M.D.
Director
Division of Anti-Infective Products (DAIP)
Office of Antimicrobial Products (OAP)
Office of New Drugs (OND)

John Peters, M.D.
Director (Acting)
Office of Bioequivalence (OB)
Office of Generic Drugs (OGD)

FROM: Arindam Dasgupta, Ph.D.
Lead Pharmacologist
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

Himanshu Gupta, Ph.D.
Staff Fellow
Division of Generic Drug Bioequivalence Evaluation (DGDBE)
Office of Scientific Integrity & Surveillance (OSIS)

THROUGH: Charles Bonapace, Pharm.D.
Director (Acting)
Division of New Drug Bioequivalence Evaluation (DNDBE)
Office of Study Integrity and Surveillance (OSIS)

SUBJECT: Surveillance inspection of (b) (4) (b) (4) covering NDA 207-844 (Albendazole chewable tablets), (b) (4) (b) (4)

Summary:

At the request of the Division of Anti-infective Products (DAIP), Office of Antimicrobial Products (OAP) and the office of Bioequivalence(OB), Office of Generic Drugs (OGD), the Office of Study Integrity and Surveillance (OSIS) conducted an inspection of the analytical portion of the following bioequivalence studies conducted by [redacted] Two additional studies (including one from a recently submitted ANDA [redacted] were also selected as part of a surveillance approach to assess the firm's overall bioanalytical operations and capability to conduct bioequivalence studies. **Additional details including study conduct dates can be found in Attachment 1.**

Division of Anti-Infective Products, Office of Antimicrobial Products

Study #: [redacted]-13-187
Study Title: "A randomized, open label, balanced, two-treatment, three-period, three- sequence, single dose, reference replicated, crossover, bioequivalence study of albendazole chewable tablets, 200 mg of amedra pharmaceuticals llc, usa with albenza® (albendazole) tablets, 200 mg of amedra pharmaceuticals llc, usa in normal, healthy, adult, human subjects under fed condition."

[redacted]

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(b) (4)

Conclusion:

Following review of the inspectional findings, the data from the audited studies were found to be reliable. Therefore, we recommend that the data from the studies below be accepted for agency review:

NDA 207844
Study #: (b) (4)-13-187

(b) (4)

Arindam Dasgupta Ph.D.
Lead Pharmacologist
DNDBE, OSIS

Himanshu Gupta, Ph.D.
Staff Fellow
DGDBE, OSIS

Final Classification:

Analytical (b) (4)

NAI: (b) (4)

FEI (b) (4)

DARRTS CC:

OSIS/Taylor/Dejernett/Nkah/Fenty-Stewart/Johnson
OSIS/DGDBE/ Haidar/Bonapace/Skelly/Choi/Gupta
OSIS/DNDBE/Bonapace/Dasgupta/Cho
CDER/OND/OAP/DAIP/Nambiar
OGD/Peters

Draft: HG 3/24/2015 AD 04/17/2015
Edit:CB 4/19/2015

Edits:
OSI file#s:
File # BE6749 (NDA 207-844); (b) (4)
(b) (4)

ECMS: Cabinets/CDER_OC/OSI/Division of Bioequivalence & Good Laboratory Practice Compliance/INSPECTIONS/BE Program/Analytical Sites/ (b) (4)
(b) (4)

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/s/

ARINDAM DASGUPTA
04/22/2015

HIMANSHU GUPTA
04/22/2015

CHARLES R BONAPACE
04/22/2015

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: February 24, 2015

To: Gregory DiBernardo
Regulatory Project Manager
Division of Anti-Infective Products (DAIP)

From: Puja Shah
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: NDA 207844
ALBENZA® (albendazole) (b) (4) chewable tablet, for oral use

As requested in DAIP's consult dated October 16, 2014, OPDP has reviewed the draft PI and proposed "wallet card" for ALBENZA® (albendazole) (b) (4) chewable tablet, for oral use. OPDP reviewed the proposed substantially complete version of the draft PI accessed via the DAIP Sharepoint site on February 10, 2015. Our comments on the draft PI are included directly on the attached copy of the labeling.

OPDP has also reviewed the "wallet card" received via email from DAIP on February 10, 2015. OPDP has no comments on the proposed "wallet card" at this time.

OPDP appreciates the opportunity to provide comments on these materials. If you have any questions or concerns, please contact Puja Shah at 240-402-5040 or puja.shah@fda.hhs.gov

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/s/

PUJA J SHAH
02/24/2015

MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	November 21, 2014
Requesting Office or Division:	Division of Anti-Infective Products (DAIP)
Application Type and Number:	NDA 207844
Product Name and Strength:	Albenza (albendazole) Chewable Tablet, 200 mg
Submission Date:	November 12, 2014
Applicant/Sponsor Name:	Amedra Pharmaceuticals
OSE RCM #:	2014-1248-1
DMEPA Primary Reviewer:	Tingting Gao, PharmD
DMEPA Team Leader:	Chi-Ming (Alice) Tu, PharmD

1 PURPOSE OF MEMO

Division of Anti-Infective Products (DAIP) requested that we review the revised Albenza Chewable Tablet blister label, carton label, and wallet card label (Appendix A) to determine if it is acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[1]

2 CONCLUSIONS

The revised blister label, carton label, and wallet card label are acceptable from a medication error perspective. We have no additional recommendations at this time.

[1] Neupauer D. Label and Labeling Review for Albenza Chewable Tablet (NDA 207844) (b) (4) . Silver Spring (MD): Food and Drug Administration, Center for Drug Evaluation and Research, Office of Surveillance and Epidemiology, Division of Medication Error Prevention and Analysis (US); 2014 Oct 17. 20 p. OSE RCM No.: 2014-1248 and 2014-1805.

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/s/

TINGTING N GAO
11/21/2014

CHI-MING TU
11/21/2014

RPM FILING REVIEW

(Including Memo of Filing Meeting)

To be completed for all new NDAs, BLAs, and Efficacy Supplements [except SE8 (labeling change with clinical data) and SE9 (manufacturing change with clinical data]

Application Information		
NDA # **207844**	NDA Supplement #: **Not Applicable**	Efficacy Supplement Type: **Not Applicable**
Proprietary Name: **Albenza** Established/Proper Name: **(albendazole)** Dosage Form: **Chewable Tablet** Strengths: **200 mg**		
Applicant: **Amedra Pharmaceuticals LLC** Agent for Applicant: **Not Applicable**		
Date of Application: **June 19, 2014 (original) August 11, 2014 (user fee paid)** Date of Receipt: **June 19, 2014 (original) August 11, 2014 (user fee paid)** Date clock started after UN: **August 11, 2014**		
PDUFA Goal Date: **June 11, 2015**	Action Goal Date (if different): **April 19, 2015**	
Filing Date: **October 10, 2014**	Date of Filing Meeting: **July 29, 2014**	
Chemical Classification: (1,2,3 etc.) (original NDAs only) **3**		
Proposed indications: **Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*, and cystic hydatid disease of the liver, lung, and peritoneum caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.** Proposed change: **Change in dosage form from tablet to chewable tablet**		
Type of Original NDA: AND (if applicable) Type of NDA Supplement: ***If 505(b)(2): Draft the "505(b)(2) Assessment" review found at:*** ***http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/ImmediateOffice/UCM027499.***		☒ **505(b)(1)** ☐ 505(b)(2) ☐ 505(b)(1) ☐ 505(b)(2)
Type of BLA ***If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team***		☐ 351(a) ☐ 351(k)
Review Classification: ***If the application includes a complete response to pediatric WR, review classification is Priority.*** ***If a tropical disease priority review voucher or pediatric rare disease priority review voucher was submitted, review classification is Priority.***		☒ **Standard** ☐ Priority ☐ Tropical Disease Priority Review Voucher submitted ☐ Pediatric Rare Disease Priority Review Voucher submitted
Resubmission after withdrawal? ☐		Resubmission after refuse to file? ☐
Part 3 Combination Product? ☐ ***If yes, contact the Office of Combination Products (OCP) and copy them on all Inter-Center consults***		☐ Convenience kit/Co-package ☐ Pre-filled drug delivery device/system (syringe, patch, etc.) ☐ Pre-filled biologic delivery device/system (syringe, patch, etc.) ☐ Device coated/impregnated/combined with drug ☐ Device coated/impregnated/combined with biologic ☐ Separate products requiring cross-labeling

	☐ Drug/Biologic ☐ Possible combination based on cross-labeling of separate products ☐ Other (drug/device/biological product)
☐ Fast Track Designation ☐ Breakthrough Therapy Designation ***(set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager)*** ☐ Rolling Review ☒ **Orphan Designation (PENDING)** ☐ Rx-to-OTC switch, Full ☐ Rx-to-OTC switch, Partial ☐ Direct-to-OTC Other:	☐ PMC response ☐ PMR response: ☐ FDAAA [505(o)] ☐ PREA deferred pediatric studies [21 CFR 314.55(b)/21 CFR 601.27(b)] ☐ Accelerated approval confirmatory studies (21 CFR 314.510/21 CFR 601.41) ☐ Animal rule postmarketing studies to verify clinical benefit and safety (21 CFR 314.610/21 CFR 601.42)
Collaborative Review Division (*if OTC product*): **Not Applicable**	
List referenced IND Number(s):	

Goal Dates/Product Names/Classification Properties	**YES**	**NO**	**NA**	**Comment**
PDUFA and Action Goal dates correct in tracking system? ***If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.***	☒	☐		
Are the proprietary, established/proper, and applicant names correct in tracking system? ***If no, ask the document room staff to make the corrections. Also, ask the document room staff to add the established/proper name to the supporting IND(s) if not already entered into tracking system.***	☒	☐		
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, 505(b)(2), orphan drug)? ***For NDAs/NDA supplements, check the New Application and New Supplement Notification Checklists for a list of all classifications/properties at:*** ***http://inside.fda.gov:9003/CDER/OfficeofBusinessProcessSupport/ucm163969.htm*** ***If no, ask the document room staff to make the appropriate entries.***	☒	☐	☐	
Application Integrity Policy	**YES**	**NO**	**NA**	**Comment**
Is the application affected by the Application Integrity Policy (AIP)? ***Check the AIP list at:*** ***http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm***	☐	☒		**Verified on 6/20/14**
If yes, explain in comment column.				
If affected by AIP, has OC/OMPQ been notified of the submission? **If yes,** date notified:	☐	☐		

User Fees	YES	NO	NA	Comment
Is Form 3397 (User Fee Cover Sheet) included with authorized signature?	☒	☐		**Product Granted Orphan Designation 1/1996 when owned by SmithKline Beecham. Transfer of Orphan Designation to Amedra [new owner] PENDING.**

User Fee Status ***If a user fee is required and it has not been paid (and it is not exempted or waived), the application is unacceptable for filing following a 5-day grace period. Review stops. Send Unacceptable for Filing (UN) letter and contact user fee staff.***	Payment for this application: ☒ Paid ☐ Exempt (orphan, government) Note: Orphan Status **PENDING** ☐ Waived (e.g., small business, public health) ☐ Not required
If the firm is in arrears for other fees (regardless of whether a user fee has been paid for this application), the application is unacceptable for filing (5-day grace period does not apply). Review stops. Send UN letter and contact the user fee staff.	Payment of other user fees: ☒ **Not in arrears** ☐ In arrears

505(b)(2) **(NDAs/NDA Efficacy Supplements only)**	YES	NO	NA	Comment
Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?	☐	☐	☒	
Is the application for a duplicate of a listed drug whose only difference is that the extent to which the active ingredient(s) is absorbed or otherwise made available to the site of action is less than that of the reference listed drug (RLD)? **[see 21 CFR 314.54(b)(1)].**	☐	☐	☒	
Is the application for a duplicate of a listed drug whose only difference is that the rate at which the proposed product's active ingredient(s) is absorbed or made available to the site of action is unintentionally less than that of the listed drug **[see 21 CFR 314.54(b)(2)]?** ***If you answered yes to any of the above questions, the application may be refused for filing under 21 CFR 314.101(d)(9). Contact the 505(b)(2) review staff in the Immediate Office of New Drugs***	☐	☐	☒	
Is there unexpired exclusivity on any drug product containing the active moiety (e.g., 5-year, 3-year, orphan, or pediatric exclusivity)? ***Check the Electronic Orange Book at:*** ***http://www.accessdata.fda.gov/scripts/cder/ob/default.cfm*** **If yes**, please list below:	☐	☐	☒	

Application No.	Drug Name	Exclusivity Code	Exclusivity Expiration

If there is unexpired, 5-year exclusivity remaining on the active moiety for the proposed drug product, a 505(b)(2) application cannot be submitted until the period of exclusivity expires (unless the applicant provides paragraph IV patent certification; then an application can be submitted four years after the date of approval.) Pediatric exclusivity will extend both of the timeframes in this provision by 6 months. 21 CFR 314.108(b)(2). Unexpired, 3-year exclusivity may block the approval but not the submission of a 505(b)(2) application.

Exclusivity	YES	NO	NA	Comment
Does another product (same active moiety) have orphan exclusivity for the same indication? ***Check the Orphan Drug Designations and Approvals list at:*** ***http://www.accessdata.fda.gov/scripts/opdlisting/oopd/index.cfm***	☒	☐		**Albenza Tablets 200mg, Same Applicant.**
If another product has orphan exclusivity, is the product considered to be the same product according to the orphan drug definition of sameness **[see 21 CFR 316.3(b)(13)]**? ***If yes, consult the Director, Division of Regulatory Policy II, Office of Regulatory Policy***	☒	☐	☐	**Product is from same Applicant, for same drug but different dosage form.**
Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity? ***(NDAs/NDA efficacy supplements only)*** **If yes**, # years requested: ***Note:*** *An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	☐	☒	☐	
Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use (***NDAs only***)?	☐	☒	☐	
If yes, did the applicant: (a) elect to have the single enantiomer (contained as an active ingredient) not be considered the same active ingredient as that contained in an already approved racemic drug, and/or (b): request exclusivity pursuant to section 505(u) of the Act (per FDAAA Section 1113)? ***If yes, contact the Orange Book Staff (CDER-Orange Book Staff).***	☐	☐	☒	
For BLAs: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? ***If yes, notify Marlene Schultz-DePalo, OBP Biosimilars RPM*** ***Note****: Exclusivity requests may be made for an original BLA submitted under Section 351(a) of the PHS Act (i.e., a biological reference product). A request may be located in Module 1.3.5.3 and/or other sections of the BLA and may be included in a supplement (or other correspondence) if exclusivity has not been previously requested in the original 351(a) BLA. An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*	☐	☐	☒	

Format and Content				
Do not check mixed submission if the only electronic component is the content of labeling (COL).	☐ All paper (except for COL) ☒ **All electronic** ☐ Mixed (paper/electronic) ☐ CTD ☐ Non-CTD ☐ Mixed (CTD/non-CTD)			
If mixed (paper/electronic) submission, which parts of the application are submitted in electronic format?				
Overall Format/Content	**YES**	**NO**	**NA**	**Comment**
If electronic submission, does it follow the eCTD guidance?[1] **If not,** explain (e.g., waiver granted).	☒	☐	☐	
Index: Does the submission contain an accurate comprehensive index?	☒	☐		
Is the submission complete as required under 21 CFR 314.50 (*NDAs/NDA efficacy supplements*) or under 21 CFR 601.2 (*BLAs/BLA efficacy supplements*) including: ☒ legible ☒ English (or translated into English) ☒ pagination ☒ navigable hyperlinks (electronic submissions only) **If no**, explain.	☒	☐		
BLAs only: Companion application received if a shared or divided manufacturing arrangement? **If yes**, BLA #	☐	☐	☒	
Forms and Certifications				
***Electronic** forms and certifications with electronic signatures (scanned, digital, or electronic – similar to DARRTS, e.g., /s/) are acceptable. Otherwise, **paper** forms and certifications with hand-written signatures must be included. **Forms** include: user fee cover sheet (3397), application form (356h), patent information (3542a), financial disclosure (3454/3455), and clinical trials (3674); **Certifications** include: debarment certification, patent certification(s), field copy certification, and pediatric certification.*				
Application Form	**YES**	**NO**	**NA**	**Comment**
Is form FDA 356h included with authorized signature per 21 CFR 314.50(a)? ***If foreign applicant, a U.S. agent must sign the form [see 21 CFR***	☒	☐		

[1] http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm072349.pdf

314.50(a)(5)].				
Are all establishments and their registration numbers listed on the form/attached to the form?	☒	☐	☐	
Patent Information (NDAs/NDA efficacy supplements only)	**YES**	**NO**	**NA**	**Comment**
Is patent information submitted on form FDA 3542a per 21 CFR 314.53(c)?	☒	☐	☐	**Form submitted on 8/11/14.**
Financial Disclosure	**YES**	**NO**	**NA**	**Comment**
Are financial disclosure forms FDA 3454 and/or 3455 included with authorized signature per 21 CFR 54.4(a)(1) and (3)? ***Forms must be signed by the APPLICANT, not an Agent [see 21 CFR 54.2(g)].*** ***Note:*** *Financial disclosure is required for bioequivalence studies that are the basis for approval.*	☒	☐		
Clinical Trials Database	**YES**	**NO**	**NA**	**Comment**
Is form FDA 3674 included with authorized signature? ***If yes, ensure that the application is also coded with the supporting document category, "Form 3674."*** ***If no, ensure that language requesting submission of the form is included in the acknowledgement letter sent to the applicant***	☒	☐		
Debarment Certification	**YES**	**NO**	**NA**	**Comment**
Is a correctly worded Debarment Certification included with authorized signature? ***Certification is not required for supplements if submitted in the original application; If foreign applicant, <u>both</u> the applicant and the U.S. Agent must sign the certification [per Guidance for Industry: Submitting Debarment Certifications].*** ***Note:*** *Debarment Certification should use wording in FD&C Act Section 306(k)(1) i.e., "[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application." Applicant may not use wording such as, "To the best of my knowledge…"*	☒	☐	☐	
Field Copy Certification (NDAs/NDA efficacy supplements only)	**YES**	**NO**	**NA**	**Comment**
For paper submissions only: Is a Field Copy Certification (that it is a true copy of the CMC technical section) included? ***Field Copy Certification is not needed if there is no CMC technical section or if this is an electronic submission (the Field Office has access to the EDR)*** ***If maroon field copy jackets from foreign applicants are received,***	☐	☐	☒	**Electronic Submission- Electronic Archival Copy available to FDA.**

return them to CDR for delivery to the appropriate field office.				
Controlled Substance/Product with Abuse Potential	**YES**	**NO**	**NA**	**Comment**
For NMEs: Is an Abuse Liability Assessment, including a proposal for scheduling, submitted per 21 CFR 314.50(d)(5)(vii)? ***If yes,*** *date consult sent to the Controlled Substance Staff:* For non-NMEs: *Date of consult sent to Controlled Substance Staff*:	☐	☐	☒	
Pediatrics	**YES**	**NO**	**NA**	**Comment**
PREA Does the application trigger PREA? ***If yes, notify PeRC RPM (PeRC meeting is required)***[2] ***Note****: NDAs/BLAs/efficacy supplements for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration trigger PREA. All waiver & deferral requests, pediatric plans, and pediatric assessment studies must be reviewed by PeRC prior to approval of the application/supplement.*	☒	☐		**Yes, until the Orphan Disease Designation Granted 1/1996 to SmithKlineBeecham. Transfers to Amedra; transfer is PENDING.**
If the application triggers PREA, are the required pediatric assessment studies or a full waiver of pediatric studies included?	☐	☒	☐	See note above.
If studies or full waiver not included, is a request for full waiver of pediatric studies OR a request for partial waiver and/or deferral with a pediatric plan included? ***If no, request in 74-day letter***	☐	☒	☐	See note above and a Comment on PREA Requirements was included in 74-day letter
If a request for full waiver/partial waiver/deferral is included, does the application contain the certification(s) required by FDCA Section 505B(a)(3) and (4)? ***If no, request in 74-day letter***	☐	☐	☒	A full waiver/partial waiver/deferral was not included
BPCA (NDAs/NDA efficacy supplements only): Is this submission a complete response to a pediatric Written Request? ***If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required)***[3]	☐	☒		
Proprietary Name	**YES**	**NO**	**NA**	**Comment**
Is a proposed proprietary name submitted? ***If yes, ensure that the application is also coded with the***	☒	☐	☐	**Proprietary Name submitted on 9/5/14**

[2] http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/ucm027829.htm
[3] http://inside.fda.gov:9003/CDER/OfficeofNewDrugs/PediatricandMaternalHealthStaff/ucm027837.htm

supporting document category, "Proprietary Name/Request for Review."				
REMS	**YES**	**NO**	**NA**	**Comment**
Is a REMS submitted? ***If yes, send consult to OSE/DRISK and notify OC/ OSI/DSC/PMSB via the CDER OSI RMP mailbox***	☐	☒	☐	
Prescription Labeling	☐ **Not applicable**			
Check all types of labeling submitted.	☒ **Package Insert (PI)** ☐ Patient Package Insert (PPI) ☐ Instructions for Use (IFU) ☐ Medication Guide (MedGuide) ☒ **Carton labels** ☒ **Immediate container labels** ☐ Diluent ☒ **Other (specify): Wallet Card**			
	YES	**NO**	**NA**	**Comment**
Is Electronic Content of Labeling (COL) submitted in SPL format? ***If no, request applicant to submit SPL before the filing date.***	☒	☐		
Is the PI submitted in PLR format?[4]	☒	☐		
If PI not submitted in PLR format, was a waiver or deferral requested before the application was received or in the submission? **If requested before application was submitted**, what is the status of the request? ***If no waiver or deferral, request applicant to submit labeling in PLR format before the filing date.***	☐	☐	☒	
All labeling (PI, PPI, MedGuide, IFU, carton and immediate container labels) consulted to OPDP?	☒	☐	☐	
MedGuide, PPI, IFU (plus PI) consulted to OSE/DRISK? (*send WORD version if available*)	☐	☐	☒	
Carton and immediate container labels, PI, PPI sent to OSE/DMEPA and appropriate CMC review office (OBP or ONDQA)?	☒	☐	☐	
OTC Labeling	☒ **Not Applicable**			
Other Consults	**YES**	**NO**	**NA**	**Comment**
Are additional consults needed? (e.g., IFU to CDRH; QT study report to QT Interdisciplinary Review Team) ***If yes, specify consult(s) and date(s) sent:*** **OSI: Biopharmaceutical Inspections: Foreign Site**	☒	☐	☐	

[4] http://inside fda.gov:9003/CDER/OfficeofNewDrugs/StudyEndpointsandLabelingDevelopmentTeam/ucm025576.htm

requested 8/18/14.				
Meeting Minutes/SPAs	**YES**	**NO**	**NA**	**Comment**
End-of Phase 2 meeting(s)? **Date(s):** ***If yes, distribute minutes before filing meeting***	☐	☒		
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? **Date(s):** ***If yes, distribute minutes before filing meeting***	☐	☒		
Any Special Protocol Assessments (SPAs)? **Date(s):** ***If yes, distribute letter and/or relevant minutes before filing meeting***	☐	☒		

ATTACHMENT

MEMO OF FILING MEETING

DATE: July 29, 2014

NDA #: 207844

PROPRIETARY NAME: Albenza

ESTABLISHED/PROPER NAME: (albendazole)

DOSAGE FORM/STRENGTH: Chewable Tablet 200 mg

APPLICANT: Amedra Pharmaceuticals LLC

PROPOSED INDICATIONS: Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*, and cystic hydatid disease of the liver, lung, and peritoneum caused by the larval form of the dog tapeworm, *Echinococcus granulosus.*

PROPOSED CHANGE: Change in dosage form to chewable tablet

BACKGROUND: This submission is for Albenza (albendazole) Chewable Tablets 200 mg.

The NDA 20666 for Albenza Tablets 200 mg was approved in 1996. Albenza is indicated for the treatment of parenchymal neurocysticerosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium* and cystic hydatid disease of the liver lung and peritoneum caused by larval form of the dog tapeworm, *Echinococcus granulosus*.

On August 7, 2014, DAIP was informed that Amedra Pharmaceuticals was not listed as the holder of the Orphan Drug designation granted for both indications in 1996 for albendazole. The Orphan Designation was still assigned to SmithKlineBeecham. At present time a transfer to Amedra Pharmaceuticals LLC from SmithKlineBeecham is **PENDING**. The Orphan indications remain unchanged so no pediatric assessment is required as PREA will not apply once the transfer [expected shortly] of Orphan Designation to Amedra occurs. Amedra purchased the product from SmithKlineBeecham.

On August 8, 2014, FDA issued an Unacceptable for Filing letter to Amedra Pharmaceuticals because of the unpaid user fee for NDA 207844. On August 11, 2014, Amedra Pharmaceuticals submitted the User Fee. A new PDUFA goal date of June 11, 2014, was established with User Fee payment.

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Gregory DiBernardo Carmen DeBellas	N Y
	CPMS:	Maureen Dillon-Parker	N
Cross-Discipline Team Leader (CDTL)	Angelica Dorantes		N
Clinical	Reviewer:	Kimberly Martin	Y
	TL:	Shirmant Mishra	Y
Social Scientist Review (*for OTC products*)	Reviewer:	Not Applicable	
	TL:		
OTC Labeling Review (*for OTC products*)	Reviewer:	Not Applicable	
	TL:		
Clinical Microbiology (*for antimicrobial products*)	Reviewer:	Lynette Berkeley	Y
	TL:	Kerry Snow	Y
Clinical Pharmacology	Reviewer:	Dakshina Chilukuri	Y
	TL:	Philip Colangelo	Y
Biostatistics	Reviewer:	Cheryl Dixon	Y
	TL:	Karen Higgins	N
Nonclinical (Pharmacology/Toxicology)	Reviewer:	Wendelyn Schmidt	N
	TL:	Wendelyn Schmidt Terry Miller (Acting)	N Y
Statistics (carcinogenicity)	Reviewer:	Not Applicable	
	TL:		
Product Quality (CMC): Biopharmacuetics	Reviewer:	Okpo Eradiri	Y
	TL:	Angela Dorantes	N
Product Quality (CMC)	Reviewer:	Caroline Strasinger	N

	TL:	Dorota Matecka	Y
Quality Microbiology *(for sterile products)*	Reviewer:	Erika Pfeiler	Y
	TL:	Stephen Langille	N
CMC Labeling Review	Reviewer:		
	TL:		
Facility Review/Inspection	Reviewer:	Steve Hertz	Y
	TL:		
OSE/DMEPA (proprietary name)	Reviewer:	Danielle Neupauer	Y
	TL:	Tingting Gao	Y
OSE/DRISK (REMS)	Reviewer:		
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:		
	TL:		
Bioresearch Monitoring (OSI)	Reviewer:	Not Applicable	
	TL:		
Controlled Substance Staff (CSS)	Reviewer:	Not Applicable	
	TL:		
Other reviewers			
Other attendees	Division Director Sumathi Nambiar (Acting) Deputy Director for Safety Dmitri Iarikov		Y Y

FILING MEETING DISCUSSION:

GENERAL	
• 505(b)(2) filing issues: ○ Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?	☒ **Not Applicable** ☐ YES ☐ NO

○ Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the referenced product(s)/published literature? Describe the scientific bridge (e.g., BA/BE studies):	☐ YES ☐ NO
• Per reviewers, are all parts in English or English translation? **If no**, explain:	☒ **YES** ☐ NO
• Electronic Submission comments **List comments**:	☒ **Not Applicable**
CLINICAL **Comments**: Will provide comments for letter	☐ Not Applicable ☒ **FILE** ☐ REFUSE TO FILE ☒ **Review issues for 74-day letter**
• Clinical study site(s) inspections(s) needed? **If no,** explain: **No clinical studies conducted.**	☐ YES ☒ **NO**
• Advisory Committee Meeting needed? **Comments**: ***If no, for an NME NDA or original BLA , include the reason. For example:*** ○ ***this drug/biologic is not the first in its class*** ○ ***the clinical study design was acceptable*** ○ ***the application did not raise significant safety or efficacy issues*** ○ ***the application did not raise significant public health questions on the role of the drug/biologic in the diagnosis, cure, mitigation, treatment or prevention of a disease***	☐ YES Date if known: ☒ **NO** ☐ To be determined Reason:
• Abuse Liability/Potential **Comments**:	☒ **Not Applicable** ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• If the application is affected by the AIP, has the division made a recommendation regarding whether	☒ **Not Applicable** ☐ YES

or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? **Comments**:	☐ NO
CLINICAL MICROBIOLOGY **Comments**: Will provide comments for the label.	☐ Not Applicable ☒ **FILE** ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL PHARMACOLOGY **Comments**:	☐ Not Applicable ☒ **FILE** ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical pharmacology study site(s) inspections(s) needed?	☐ YES ☒ **NO**
BIOSTATISTICS **Comments**:	☐ Not Applicable ☒ **FILE** ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
NONCLINICAL (PHARMACOLOGY/TOXICOLOGY) **Comments**:	☐ Not Applicable ☒ **FILE** ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
IMMUNOGENICITY (BLAs/BLA efficacy supplements only) **Comments**:	☒ **Not Applicable** ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC) **Comments**:	☐ Not Applicable ☒ **FILE** ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
PRODUCT QUALITY (CMC) Biopharmaceutics	☐ Not Applicable ☒ **FILE** ☐ REFUSE TO FILE

Comments: Will provide comments for letter on the BE/BA studies completed, Biopharmaceutical Inspections to be requested.	☒ **Review issues for 74-day letter**
Environmental Assessment • Categorical exclusion for environmental assessment (EA) requested? **If no**, was a complete EA submitted? **If EA submitted**, consulted to EA officer (OPS)? **Comments**:	☒ **YES** ☐ NO ☐ YES ☐ NO ☐ YES ☐ NO
Quality Microbiology (for sterile products) • Was the Microbiology Team consulted for validation of sterilization? (**NDAs/NDA supplements only**) **Comments**: **Information request will be sent to Applicant for more information to support their proposal to waive microbial limits testing.**	☐ Not Applicable ☒ **YES** ☐ NO ☒ **Review issues for 74-day letter**
Facility Inspection • Establishment(s) ready for inspection? ▪ Establishment Evaluation Request (EER/TBP-EER) submitted to OMPQ? **Comments**:	☐ Not Applicable ☒ **YES** ☐ NO ☒ **YES** ☐ NO
Facility/Microbiology Review (BLAs only) **Comments**:	☒ **Not Applicable** ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CMC Labeling Review **Comments**:	☐ Review issues for 74-day letter

APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs)	☒ **N/A**
• Were there agreements made at the application's pre-submission meeting (and documented in the minutes) regarding certain late submission components that could be submitted within 30 days after receipt of the original application?	☐ YES ☐ NO
• If so, were the late submission components all submitted within 30 days?	☐ YES ☐ NO
• What late submission components, if any, arrived after 30 days?	
• Was the application otherwise complete upon submission, including those applications where there were no agreements regarding late submission components?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all clinical sites included or referenced in the application?	☐ YES ☐ NO
• Is a comprehensive and readily located list of all manufacturing facilities included or referenced in the application?	☐ YES ☐ NO

REGULATORY PROJECT MANAGEMENT

Signatory Authority: Sumathi Nambiar, Division Director

Date of Mid-Cycle Meeting (for NME NDAs/BLAs in "the Program" PDUFA V): **Not Applicable**

21st Century Review Milestones (see attached) (listing review milestones in this document is optional): **Not Applicable**

Comments:

REGULATORY CONCLUSIONS/DEFICIENCIES

☐	The application is unsuitable for filing. Explain why:
☒	The application, on its face, appears to be suitable for filing.

	Review Issues: ☐ No review issues have been identified for the 74-day letter. ☒ **Review issues have been identified for the 74-day letter.** Review Classification: ☒ **Standard Review** ☐ Priority Review
	ACTIONS ITEMS
☒	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into tracking system (e.g., chemical classification, combination product classification, 505(b)(2), orphan drug).
☐	If RTF, notify everybody who already received a consult request, OSE PM, and Product Quality PM (to cancel EER/TBP-EER).
☐	If filed, and the application is under AIP, prepare a letter either granting (for signature by Center Director) or denying (for signature by ODE Director) an exception for review.
☐	BLA/BLA supplements: If filed, send 60-day filing letter
☐	If priority review: • notify sponsor in writing by day 60 (For BLAs/BLA supplements: include in 60-day filing letter; For NDAs/NDA supplements: see CST for choices) • notify OMPQ (so facility inspections can be scheduled earlier)
☒	Send review issues/no review issues by day 74
☒	Conduct a PLR format labeling review and include labeling issues in the 74-day letter
☐	Update the PDUFA V DARRTS page (for NME NDAs in the Program)
☐	BLA/BLA supplements: Send the Product Information Sheet to the product reviewer and the Facility Information Sheet to the facility reviewer for completion. Ensure that the completed forms are forwarded to the CDER RMS-BLA Superuser for data entry into RMS-BLA one month prior to taking an action [These sheets may be found in the CST eRoom at: http://eroom.fda.gov/eRoom/CDER2/CDERStandardLettersCommittee/0_1685f]
☒	Other: **Verify with Office of Orphan Product Designation that Transfer of Orphan Designation to Amedra Pharmaceuticals occurs.**

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

/s/

GREGORY F DIBERNARDO
10/29/2014

MAUREEN P DILLON PARKER
10/30/2014

REGULATORY PROJECT MANAGER
PHYSICIAN'S LABELING RULE (PLR) FORMAT REVIEW
OF THE PRESCRIBING INFORMATION

Complete for all new NDAs, BLAs, Efficacy Supplements, and PLR Conversion Labeling Supplements

Application: 207844

Application Type: New NDA

Name of Drug/Dosage Form: ALBENZA (albendazole) Chewable Tablets, 200 mg

Applicant: Amedra Pharmacueticals, LLC

Receipt Date: August 11, 2014

Goal Date: June 11, 2015

1. Regulatory History and Applicant's Main Proposals

The Applicant has submitted a new dosage form (chewable tablet) in NDA 207844. The Applicant is including information from the previously approved Package Insert (PI) for the tablet formulation (NDA 20666) and now is updating the PI to the PLR format and including new information on the chewable tablet.

2. Review of the Prescribing Information

This review is based on the applicant's submitted Word format of the prescribing information (PI). The applicant's proposed PI was reviewed in accordance with the labeling format requirements listed in the "Selected Requirements for Prescribing Information (SRPI)" checklist (see the Appendix).

Note to RPM: See the *SEALD intranet site* for additional PI information including the Labeling Review Tool, labeling regulations and guidances, and the OND labeling review process.

3. Conclusions/Recommendations

No SRPI format deficiencies were identified in the review of this PI.

Appendix

The Selected Requirement of Prescribing Information (SRPI) is a 42-item, drop-down checklist of important format elements of the prescribing information (PI) based on labeling regulations (21 CFR 201.56 and 201.57) and guidances.

Highlights

See Appendix A for a sample tool illustrating the format for the Highlights.

HIGHLIGHTS GENERAL FORMAT

YES 1. Highlights (HL) must be in a minimum of 8-point font and should be in two-column format, with ½ inch margins on all sides and between columns.

Comment:

YES 2. The length of HL must be one-half page or less unless a waiver has been granted in a previous submission. The HL Boxed Warning does not count against the one-half page requirement. Instructions to complete this item: If the length of the HL is one-half page or less, select "YES" in the drop-down menu because this item meets the requirement. However, if HL is longer than one-half page, select "NO" unless a waiver has been granted.

Comment:

YES 3. A horizontal line must separate HL from the Table of Contents (TOC). A horizontal line must separate the TOC from the FPI.

Comment:

YES 4. All headings in HL must be **bolded** and presented in the center of a horizontal line (each horizontal line should extend over the entire width of the column as shown in Appendix A). The headings should be in UPPER CASE letters.

Comment:

YES 5. White space should be present before each major heading in HL. There must be no white space between the HL Heading and HL Limitation Statement. There must be no white space between the product title and Initial U.S. Approval. See Appendix A for a sample tool illustrating white space in HL.

Comment:

YES 6. Each summarized statement or topic in HL must reference the section(s) or subsection(s) of the Full Prescribing Information (FPI) that contain more detailed information. The preferred format is the numerical identifier in parenthesis [e.g., (1.1)] at the end of each summarized statement or topic.

Comment:

YES 7. Section headings must be presented in the following order in HL:

Section	Required/Optional
• **Highlights Heading**	Required
• **Highlights Limitation Statement**	Required
• **Product Title**	Required
• **Initial U.S. Approval**	Required

Selected Requirements of Prescribing Information

• **Boxed Warning**	Required if a BOXED WARNING is in the FPI
• **Recent Major Changes**	Required for only certain changes to PI*
• **Indications and Usage**	Required
• **Dosage and Administration**	Required
• **Dosage Forms and Strengths**	Required
• **Contraindications**	Required (if no contraindications must state "None.")
• **Warnings and Precautions**	Not required by regulation, but should be present
• **Adverse Reactions**	Required
• **Drug Interactions**	Optional
• **Use in Specific Populations**	Optional
• **Patient Counseling Information Statement**	Required
• **Revision Date**	Required

* RMC only applies to the BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS sections.

Comment:

HIGHLIGHTS DETAILS

Highlights Heading

YES 8. At the beginning of HL, the following heading must be **bolded** and should appear in all UPPER CASE letters: **"HIGHLIGHTS OF PRESCRIBING INFORMATION"**.

Comment:

Highlights Limitation Statement

ES 9. The **bolded** HL Limitation Statement must include the following verbatim statement: "**These highlights do not include all the information needed to use (insert name of drug product) safely and effectively. See full prescribing information for (insert name of drug product).**" The name of drug product should appear in UPPER CASE letters.

Comment:

Product Title in Highlights

YES 10. Product title must be **bolded**.

Comment:

Initial U.S. Approval in Highlights

YES 11. Initial U.S. Approval in HL must be **bolded**, and include the verbatim statement "**Initial U.S. Approval:**" followed by the **4-digit year**.

Comment:

Boxed Warning (BW) in Highlights

N/A 12. All text in the BW must be **bolded**.

Comment:

N/A 13. The BW must have a heading in UPPER CASE, containing the word "**WARNING**" (even if more than one warning, the term, "**WARNING**" and not "**WARNINGS**" should be used) and other words to identify the subject of the warning (e.g., "**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**"). The BW heading should be centered.

Comment:

N/A 14. The BW must always have the verbatim statement "***See full prescribing information for complete boxed warning***." This statement should be centered immediately beneath the heading and appear in *italics*.

Comment:

N/A 15. The BW must be limited in length to 20 lines (this includes white space but does not include the BW heading and the statement "***See full prescribing information for complete boxed warning.***").

Comment:

Recent Major Changes (RMC) in Highlights

N/A 16. RMC pertains to only the following five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. RMC must be listed in the same order in HL as the modified text appears in FPI.

Comment:

N/A 17. The RMC must include the section heading(s) and, if appropriate, subsection heading(s) affected by the recent major change, together with each section's identifying number and date (month/year format) on which the change was incorporated in the PI (supplement approval date). For example, "Warnings and Precautions, Acute Liver Failure (5.1) --- 9/2013".

Comment:

N/A 18. The RMC must list changes for at least one year after the supplement is approved and must be removed at the first printing subsequent to one year (e.g., no listing should be one year older than revision date).

Comment:

Indications and Usage in Highlights

N/A 19. If a product belongs to an established pharmacologic class, the following statement is required under the Indications and Usage heading in HL: "(Product) is a (name of established pharmacologic class) indicated for (indication)".

Comment:

Dosage Forms and Strengths in Highlights

YES 20. For a product that has several dosage forms (e.g., capsules, tablets, and injection), bulleted subheadings or tabular presentations of information should be used under the Dosage Forms and Strengths heading.

Comment:

Contraindications in Highlights

YES

21. All contraindications listed in the FPI must also be listed in HL or must include the statement "None" if no contraindications are known. Each contraindication should be bulleted when there is more than one contraindication.

Comment:

Adverse Reactions in Highlights

YES 22. For drug products other than vaccines, the verbatim **bolded** statement must be present: "**To report SUSPECTED ADVERSE REACTIONS, contact (insert name of manufacturer) at (insert manufacturer's U.S. phone number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch**".

Comment:

Patient Counseling Information Statement in Highlights

YES 23. The Patient Counseling Information statement must include one of the following three **bolded** verbatim statements that is most applicable:

If a product **does not** have FDA-approved patient labeling:

- **"See 17 for PATIENT COUNSELING INFORMATION"**

If a product **has** FDA-approved patient labeling:

- **"See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling"**
- **"See 17 for PATIENT COUNSELING INFORMATION and Medication Guide"**

Comment:

Revision Date in Highlights

YES 24. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., "**Revised: 9/2013**").

Comment:

Contents: Table of Contents (TOC)

See Appendix A for a sample tool illustrating the format for the Table of Contents.

YES 25. The TOC should be in a two-column format.

Comment:

YES 26. The following heading must appear at the beginning of the TOC: **"FULL PRESCRIBING INFORMATION: CONTENTS"**. This heading should be in all UPPER CASE letters and **bolded**.

Comment:

N/A 27. The same heading for the BW that appears in HL and the FPI must also appear at the beginning of the TOC in UPPER CASE letters and **bolded**.

Comment:

YES 28. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.

Comment:

YES 29. In the TOC, all subsection headings must be indented and not bolded. The headings should be in title case [first letter of all words are capitalized except first letter of prepositions (through), articles (a, an, and the), or conjunctions (for, and)].

Comment:

ES 30. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.

Comment:

YES 31. In the TOC, when a section or subsection is omitted, the numbering must not change. If a section or subsection from 201.56(d)(1) is omitted from the FPI and TOC, the heading "FULL PRESCRIBING INFORMATION: CONTENTS" must be followed by an asterisk and the following statement must appear at the end of TOC: "*Sections or subsections omitted from the full prescribing information are not listed."

Comment:

Full Prescribing Information (FPI)

FULL PRESCRIBING INFORMATION: GENERAL FORMAT

YES 32. The **bolded** section and subsection headings in the FPI must be named and numbered in accordance with 21 CFR 201.56(d)(1) as noted below (section and subsection headings should be in UPPER CASE and title case, respectively). If a section/subsection required by regulation is omitted, the numbering must not change. Additional subsection headings (i.e., those not named by regulation) must also be **bolded** and numbered.

BOXED WARNING
1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
6 ADVERSE REACTIONS
7 DRUG INTERACTIONS
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.2 Labor and Delivery
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
9 DRUG ABUSE AND DEPENDENCE
9.1 Controlled Substance
9.2 Abuse
9.3 Dependence
10 OVERDOSAGE
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.2 Pharmacodynamics
12.3 Pharmacokinetics
12.4 Microbiology (by guidance)
12.5 Pharmacogenomics (by guidance)
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
13.2 Animal Toxicology and/or Pharmacology
14 CLINICAL STUDIES
15 REFERENCES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION

Comment:

YES 33. The preferred presentation for cross-references in the FPI is the section (not subsection) heading followed by the numerical identifier. The entire cross-reference should be in *italics* and enclosed within brackets. For example, *"[see Warnings and Precautions (5.2)]"* or *"[see Warnings and Precautions (5.2)]"*.

Comment:

/A 34. If RMCs are listed in HL, the corresponding new or modified text in the FPI sections or

subsections must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

YES 35. The following heading must be **bolded** and appear at the beginning of the FPI: "**FULL PRESCRIBING INFORMATION**". This heading should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

N/A 36. In the BW, all text should be **bolded**.

Comment:

N/A 37. The BW must have a heading in UPPER CASE, containing the word "**WARNING**" (even if more than one Warning, the term, "**WARNING**" and not "**WARNINGS**" should be used) and other words to identify the subject of the Warning (e.g., "**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**").

Comment:

CONTRAINDICATIONS Section in the FPI

N/A 38. If no Contraindications are known, this section must state "None."

Comment:

ADVERSE REACTIONS Section in the FPI

YES 39. When clinical trials adverse reactions data are included (typically in the "Clinical Trials Experience" subsection of ADVERSE REACTIONS), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

"Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice."

Comment:

YES 40. When postmarketing adverse reaction data are included (typically in the "Postmarketing Experience" subsection of ADVERSE REACTIONS), the following verbatim statement or appropriate modification should precede the presentation of adverse reactions:

"The following adverse reactions have been identified during post-approval use of (insert drug name). Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure."

Comment:

PATIENT COUNSELING INFORMATION Section in the FPI

N/A 41. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION section). The reference should appear at the beginning of Section 17 and

include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Medication Guide, Instructions for Use).

Comment:

N/A 42. FDA-approved patient labeling (e.g., Medication Guide, Patient Information, or Instructions for Use) must not be included as a subsection under section 17 (PATIENT COUNSELING INFORMATION). All FDA-approved patient labeling must appear at the end of the PI upon approval.

Comment:

Appendix A: Format of the Highlights and Table of Contents

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use [DRUG NAME] safely and effectively. See full prescribing information for [DRUG NAME].

[DRUG NAME (nonproprietary name) dosage form, route of administration, controlled substance symbol]
Initial U.S. Approval: [year]

WARNING: [SUBJECT OF WARNING]
See full prescribing information for complete boxed warning.

- **[text]**
- **[text]**

----------RECENT MAJOR CHANGES----------
[section (X.X)] [m/year]
[section (X.X)] [m/year]

----------INDICATIONS AND USAGE----------
[DRUG NAME] is a [name of pharmacologic class] indicated for [text]

----------DOSAGE AND ADMINISTRATION----------
- [text]
- [text]

----------DOSAGE FORMS AND STRENGTHS----------
[text]

----------CONTRAINDICATIONS----------
- [text]
- [text]

----------WARNINGS AND PRECAUTIONS----------
- [text]
- [text]

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence = x%) are [text].

To report SUSPECTED ADVERSE REACTIONS, contact [name of manufacturer] at [phone #] or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

----------DRUG INTERACTIONS----------
- [text]
- [text]

----------USE IN SPECIFIC POPULATIONS----------
- [text]
- [text]

See 17 for PATIENT COUNSELING INFORMATION [and FDA-approved patient labeling OR and Medication Guide].

Revised: [m/year]

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed.

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

/s/

GREGORY F DIBERNARDO
10/22/2014
Initial RPM SRPI Review

LABEL AND LABELING REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	October 17, 2014
Requesting Office or Division:	Division of Anti-Infective Products (DAIP)
Application Type and Number:	Albenza (albendazole) chewable tablet, 200 mg
Product Name and Strength:	NDA 207844 Albenza (albendazole) tablet, (b) (4) (b) (4)
Product Type:	Single ingredient product
Rx or OTC:	Rx
Applicant/Sponsor Name:	Amedra Pharmaceuticals
Submission Date:	June 19, 2014 and August 5, 2014
OSE RCM #:	2014-1248 and 2014-1805
DMEPA Primary Reviewer:	Danielle Neupauer, RPh
DMEPA Acting Team Leader:	Tingting Gao, PharmD

1 REASON FOR REVIEW

Amedra Pharmaceuticals submitted NDA 207844 to propose a new, chewable formulation for Albenza in a 200 mg strength. (b) (4)

Albenza Tablets (NDA 20666) is currently marketed as 200 mg tablets, which will remain on the market.

The Division of Anti-Infective Products (DAIP) requested that we review the submitted labels and labeling for Albenza Chewable Tablets 200 mg (b) (4) for areas of vulnerability that could lead to medication errors.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Label and Labeling Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
FDA Adverse Event Reporting System (FAERS)	B
Previous DMEPA Reviews	C- N/A
Human Factors Study	D- N/A
ISMP Newsletters	E
Other	F- N/A
Labels and Labeling	G

N/A=not applicable for this review

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

3.1 OVERALL ASSESSMENT FOR BOTH ALBENZA CHEWABLE TABLETS, 200 MG (NDA 207844) (b) (4)

(b) (4)

(b) (4)

(b) (4)

3.2 ALBENZA CHEWABLE TABLETS, 200 MG (NDA 207844)

The new formulation (chewable tablets) will be the same strength (200 mg) as the current marketed formulation (tablets). The marketed tablet and the proposed chewable tablet share the same active ingredient, same indication, dose and strength. The current and proposed formulations differ in dosage form. We acknowledge that this may lead to possible medication errors where one formulation may be dispensed for the other and may result in an adverse event. However, we evaluated the approved Prescribing Information (PI) for the current marketed formulation (tablets), and noted that it states "in young children, the tablets should be crushed or chewed and swallowed with a drink of water". Since the current marketed formulation (tablets) may also be chewed, we have no concerns with the proposed new chewable tablet formulation from a medication error perspective.

We evaluate the proposed Prescribing Information (PI) and we note the use of error prone symbols in the PI. We recommend replacing the symbols with the corresponding words for clarity.

We evaluate the carton labeling and note that the net quantity is located in a prominent location on the principal display panel, and can be mistaken for strength. We also recommend presenting the product strength, "200MG" to read "200 mg" to improve readability and for consistency with the strength presentation in the PI. For the wallet card, we note the presentation of the strength on the principal display panel of the wallet card is confusing and may be interpreted by patients to mean that (b) (4) We recommend revising the presentation of the strength and adding a net quantity statement on the principal display panel of the wallet card to minimize the risk of confusion that could lead to incorrect dosing errors.

We note Amedra is proposing to supply the Albenza chewable tablets in a package size of 2 tablets (1 dose or ½ day) and 12 tablets (6 doses or 3 days). Since the dose for Albenza for patients weighting 60 kg or greater is 400 mg twice daily with treatment duration of 8 – 30 days, we requested the rationale for package size quantity. Amedra responded on September 26, 2014 and stated, "The current Albenza 200 mg tablet is marketed in both a 2-count and 28-count package size. Notwithstanding the labeled dosing of the product, the majority of the unit sales volume of the current 200 mg product is in the 2-count size and a vast majority of prescriptions are for twelve (12) tablets or less. A carton containing 12 tablets configured in blister cards provides greater flexibility for dispensing the prescribed amount of product by

allowing the pharmacist to dispense any amount of 12 tablets or less as needed." Therefore, we have no concerns with the proposed packaging size.

Additionally, we requested and received a sample of the wallet card packaging for Albenza chewable tablets 200 mg 2 tablets to evaluate the ease of use and ability to open the package to retrieve Albenza. We determined that the directions to open the package are sufficient and the blister card technology that offers (b) (4) is acceptable.

4 CONCLUSION & RECOMMENDATIONS

Our evaluation determined that the chewable tablet formulation can be safely introduced to the market and that the proposed packaging size is acceptable. However, we conclude that the proposed label and labeling for Albenza chewable tablets 200 mg (b) (4) may be improved to promote the safe use of the product as described in Section 4.1 and Section 4.2.

4.1 RECOMMENDATIONS FOR DIVISION

DMEPA provides the following comments for the Division consideration:

1. Albenza Chewable Tablets, 200 mg, (NDA 207844)

    a. Dosage and Administration section, Highlights of Prescribing Information

        i. We note the use of dangerous symbols in the dosage and administration section in the Highlights of prescribing information. Consider replacing the symbols with the corresponding words, such as "≥" to read "greater than or equal to" and "<" to read "less than", for clarity.[1]

4.2 RECOMMENDATIONS FOR AMEDRA PHARMACEUTICALS

DMEPA provides the following comments for the sponsor consideration:

1. **General recommendations for the carton labeling for Albenza Chewable Tablets, 200 mg, (NDA 207844)** (b) (4)

    a. (b) (4)

2. **Albenza Chewable Tablets, 200 mg, (NDA 207844)**

    a. Blister Card (6 tablets)

        i. We note that the product strength is presented with no space between numerical dose and unit of measure, and that the unit of measure "MG" is capitalized. Since lower case letters are more commonly used in metric unit abbreviations and that the Dosage Forms and Strengths section of

[1] ISMP's List of Error-Prone Abbreviations, Symbols, and Dose Designations [Internet]. Horsham (PA): Institute for Safe Medication Practices. 2013 [cited 2014 Aug 19]. Available from: http://www.ismp.org/tools/errorproneabbreviations.pdf

the PI presents the strength as “200 mg” (with lower case ‘mg’), consider revising the product strength “200MG” to read “200 mg” to improve readability and for consistency with the strength presentation in the PI.

b. Carton Labeling for 2 blister cards (12 tablets)

   i. See 2.a.i.

   ii. The strength presentation is located next to the proprietary name which may cause the strength to be misinterpreted as part of the proprietary name. Consider relocating the strength below the proprietary and established names to minimize the risk of the strength being overlooked.

   iii. The net quantity (12 tablets) on the carton labeling could be mistaken as strength. Relocate away from the proprietary name, established name, and strength for less prominence (e.g. lower right corner).[2]

c. Wallet Card (b) (4) tablet)

   i. See 2.a.i. and 2.b.ii.

   ii. There is (b) (4) on the wallet card. Include net quantity (2 tablets) and ensure this net quantity is located away from product strength as described in 2.c.

   iii. Consider revising the strength statement to “200 mg per chewable tablet” on the principal display panel to avoid misinterpretation of (b) (4) (b) (4) This may be achieved by removing the picture of 2 tablets on the principal display panel.

(b) (4)

[2] Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. Food and Drug Administration. 2013. Available from http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf

[3] Guidance for Industry: Safety Considerations for Container Labels and Carton Labeling Design to Minimize Medication Errors. Food and Drug Administration. 2013. Available from http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM349009.pdf

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Albenza that Amedra Pharmaceuticals submitted on June 19, 2014.

Table 2. Relevant Product Information for Albenza

Product	Albenza Tablet (NDA 020666)	Albenza Chewable Tablet (NDA 207844)
Initial Approval Date	June 11, 1996	Currently under review
Active Ingredient	Albendazole	Albendazole
Indication	Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*. Treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.	Treatment of parenchymal neurocysticercosis due to active lesions caused by larval forms of the pork tapeworm, *Taenia solium*. Treatment of cystic hydatid disease of the liver, lung, and peritoneum, caused by the larval form of the dog tapeworm, *Echinococcus granulosus*.
Route of Administration	Oral	Oral
Dosage Form	**Tablets**	**Chewable tablets**
Strength	(b) (4) Currently marketed: 200 mg	200 mg
Dose and Frequency	Patients ≥ 60 kg, 400 mg twice daily; < 60 kg, 15 mg/kg/day in divided doses twice daily (maximum total daily dose 800 mg).	Patients ≥ 60 kg, 400 mg twice daily; < 60 kg, 15 mg/kg/day in divided doses twice daily (maximum total daily dose 800 mg).
How Supplied	(b) (4) **Currently marketed:** **Bottles of 2 tablets** **Bottles of 28 tablets**	**2 Tablets in 1 Blister card (configured as a Wallet Card)** **6 Tablets in 1 Blister card; 2 Blister cards in 1 Carton**
Storage	Store at room temperature, 20° to	Store at room temperature, 20° to

	25°C (68° to 77°F)	25°C (68° to 77°F)
Container Closure	(b) (4) 200 mg – bottle	Each (b) (4) foil laminate blister has a peel-push or a push-through blister foil lid and contains one tablet.

APPENDIX B. FDA ADVERSE EVENT REPORTING SYSTEM (FAERS)

B.1 Methods

We searched the FDA Adverse Event Reporting System (FAERS) on July 11, 2014 using the criteria in Table 3, and then individually reviewed each case. We limited our analysis to cases that described errors possibly associated with the label and labeling. We used the NCC MERP Taxonomy of Medication Errors to code the type and factors contributing to the errors when sufficient information was provided by the reporter.[2]

Table 3: FAERS Search Strategy	
Date Range	**Searched to September 1, 2014**
Product	**Albendazole** [active ingredient] **Albenza** [product name]
Event (MedDRA Terms)	**Medication Errors** [HLGT] **Product Packaging Issues** [HLT] **Product Label Issues** [HLT] **Product Quality Issues** (NEC)[HLT]

B.2 Results

Our search identified 14 cases, of which none described errors relevant for this review.

We excluded all 14 cases for the following reasons:

- Adverse event not related to medication error (n=8)
- Wrong drug selection due to name confusion (n=1)
- Insufficient information to determine medication error (n=1)
- Overdose not related to label and labeling (n=1)

B.3 List of FAERS Case Numbers

N/A

B.4 Description of FAERS

The FDA Adverse Event Reporting System (FAERS) is a database that contains information on adverse event and medication error reports submitted to FDA. The database is designed to support the FDA's postmarket safety surveillance program for drug and therapeutic biologic products. The informatic structure of the FAERS database adheres to the international safety

[2] The National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) Taxonomy of Medication Errors. Website http://www.nccmerp.org/pdf/taxo2001-07-31.pdf.

reporting guidance issued by the International Conference on Harmonisation. FDA's Office of Surveillance and Epidemiology codes adverse events and medication errors to terms in the Medical Dictionary for Regulatory Activities (MedDRA) terminology. Product names are coded using the FAERS Product Dictionary. More information about FAERS can be found at: http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

APPENDIX C. PREVIOUS DMEPA REVIEWS

C.1 Methods

We searched the L:Drive on July 14, 2014 using the terms Albenza and albendazole to identify reviews previously performed by DMEPA.

C.2 Results

Our search identified no previous reviews.

APPENDIX E. ISMP NEWSLETTERS

E.1 Methods

We searched the Institute for Safe Medication Practices (ISMP) newsletters on July 14, 2014 using the criteria below, and then individually reviewed each newsletter for medication error cases related to Albenza. We limited our analysis to cases that described medication errors or actions possibly associated with the label and labeling of Albenza.

ISMP Newsletters Search Strategy	
ISMP Newletter(s)	Acute Care, Community, Nursing
Search Strategy and Terms	Match Exact Word or Phrase: Albenza

E.2 Results

There were no relevant cases related to Albenza.

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[4] along with postmarket medication error data, we reviewed the followings:

Proposed label and labeling for Albenza Chewable Tablets, 200 mg (NDA 207844), submitted by Amedra Pharmaceuticals on June 19, 2014 and September 26, 2014:

- Blister card label
- Carton labeling
- Wallet card labeling

(b) (4)

(b) (4)

Current marketed label and labeling for Albenza Tablets, 200 mg (NDA 20666), submitted by Amedra Pharmaceuticals on August 5, 2014

- Container label

G.2 Label and Labeling Images

(b) (4)

[4] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

6 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

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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.

/s/

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10/17/2014