CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210709Orig1s000

OTHER REVIEW(S)

DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS

Regulatory Project Manager Overview

I. GENERAL INFORMATION

NDA: 210709
Drug: aliskiren hemifumarate
Class: Direct Renin Inhibitor
Applicant: Noden Pharma DAC
Proposed Indications: The treatment of hypertension, to lower blood pressure
Date of User fee: May 5, 2017
PDUFA date: November 15, 2017
Target Action date: November 14, 2017

II. REVIEW TEAM

- **Office of New Drugs, Office of Drug Evaluation I:**

Division of Cardiovascular & Renal Product
Norman Stockbridge, MD, PhD, Director
Mary Ross Southworth, PharmD, Deputy Director for Safety
Michael Monteleone, MS, RAC, Assistant Director for Labeling
Aliza Thompson, MD, Cross Discipline Team Leader
Christine Garnett, PharmD, Clinical Reviewer
Thomas Papoian, PhD, Non-Clinical Supervisor
Gowra Jagadeesh, PhD, Non-Clinical Reviewer
Edward Fromm, RPh, RAC, Chief, Project Management Staff
Maryam Changi, PharmD, Regulatory Project Manager

- **Office of Pharmaceutical Quality:**

Wendy Wilson-Lee, PhD, Application Technical Lead
Grafton Adams, Regulatory Business Process Manager
Rao Kambhampati, PhD, Drug Product and Drug Substance Reviewer
Wu, Ta-Chin, PhD, Biopharmaceutical Team Leader
Qi Zhang, PhD, Biopharmaceutical Reviewer
Ruth Moore, PhD, Facility Team Leader
Wayne Seifert, PhD, Facility Reviewer
Peter Guerrieri, PhD, Process Team Leader
Yahong Wang, PhD, Process Reviewer

- **Office of Clinical Pharmacology:**

Sudharshan Hariharan, PhD, Clinical Pharmacology Team Leader

Martina Sahre, Clinical Pharmacology Reviewer

- **Office of Biostatistics, Division of Biometrics I:**
  Hsien Ming (Jim) Hung, PhD, Director
  Fanhui Kong, PhD, Statistician

- **Office of Surveillance and Epidemiology:**
  Darrel Lyons, RN, Safety Regulatory Project Manager
  Tu, Chi-Ming, PharmD, DMEPA Team Leader
  Rhiannon Leutner, PharmD, DMEPA Reviewer

- **Office of Prescription Drug Promotion:**
  Zarna Patel, PharmD, OPDP Reviewer
  James Dvorsky, OPDP Team Leader
  Barbara Fuller, RN, MSN, CWOCN, Patient Labeling Team Leader
  Susan Redwood, MPH, BSN, RN, Patient Labeling Reviewer

III. BACKGROUND

Noden Pharma submitted NDA 210709 to support marketing of a pediatric formulation for Tekturna (aliskiren) in response to a FDA pediatric written request. This product was initially submitted as a supplemental NDA (under NDA 021985) but was later reclassified as a new NDA due to the new dosage form classification. The sponsor submitted this supplement for Tekturna ® tablets to submit pediatric study reports required to fulfill the conditions of a Written Request under the Best Pharmaceuticals for Children's Act (BPCA), and to fulfill the "assessments" required under the Pediatric Research Equity Act (PREA).
The submission was granted **priority review** with a PDUFA date of November 15, 2017.

IV. APPLICATION REVIEW

1. User Fee

The User fee for this application was paid in full on May 15, 2017. User Fee I.D. Number for this application is PD3016758.

2. Pediatric Review Committee (PeRC)

This application is presenting new dosage form which triggered PREA. The Division met with PeRC on September 20, 2017. This application is also reviewed by Pediatric Exclusivity Board on September 12, 2017, in which the Board granted 6-months Pediatrics Exclusivity.

3. Advisory Committee

There was no Advisory Committee meeting for this NDA because it did not raise any significant safety or efficacy issues.

4. Trade name

Per the July 26, 2017 proprietary name submission, Noden has obtained the trademark Tekturna, The proposed proprietary name is acceptable.

5. Facilities Inspections

The Office of Process and Facilities has recommended overall approval for the Manufacturing facilities (refer to OPQ review dated October 11, 2017).

6. Regulatory Timeline

FDA User fee Received Date: May 15, 2017
Filing date: July 14, 2017
Exclusivity Board Meeting: September 12, 2017
PeRC Meeting: September 20, 2017
Pediatric exclusivity grant date: October 3, 2017
Send Labeling/PMC-PMR to Sponsor: September 15, 2017
PDUFA Date: November 15, 2017 (Priority)
Approval letter: November 14, 2017

7. Reviews

a) Divisional Memorandum – *November 14, 2017*

Dr. Stockbridge indicated his concurrence on Dr. Thompson's CDTL memo.

b) Cross-Discipline Team Leader Review – *November 14, 2017*

Dr. Thompson recommends approval. Her review summarizes each disciplines findings including consults. She also provided a detailed regulatory history.

c) Clinical Pharmacology Review – *October 12, 2017*

The Office of Clinical Pharmacology has reviewed the submission for quality and accuracy of the submitted material and to support the labeling statements in Sections 2 and 12.3. The sponsor has conducted a relative bioequivalence study (A2109), a pharmacokinetics and pharmacodynamics study (A2256) and a pivotal efficacy study (A2365, A2365E1) to support this submission. Dr. Sahre had a joint review with Dr. Garnett (Clinical Reviewer).

d) Pharmacology & Toxicology Review – *September 14, 2017*

Dr. Jagadeesh recommended approval. In his review he concluded that the findings in very young rats, which accounted for the observed morbidity and mortality, are considered to be of great safety concern with regard to dosing of aliskiren in neonates and infants. The results strongly suggest that there is a distinct agedependent relationship between dose, exposure, and toxicity in aliskiren-treated neonates. The substantial aliskiren exposure increase in very young juvenile rats correlates with the process of maturation of the drug transporters involved in aliskiren absorption and disposition. Immaturity of MDR1 appears to be the most important mechanism responsible for the high exposure following oral aliskiren administration to very young rats.

e) Office of Pharmaceutical Quality Review – *October 11, 2017*

Dr. Wilson-Lee recommended approval of NDA 210709 on behalf of Office of Pharmaceutical Quality for Tekturna (aliskiren) Oral Pellets, 37.5 mg along with the comparability protocol to support a drug product manufacturing site change post-approval.

f) Office of Biostatistics, Division of Biometrics I – *September 22, 2017*

Dr. Kong recommended approval. In his review he concluded:
With a total of 265 patients in the FAS1 population, the primary efficacy analysis in Phase 1 of the pivotal study (SPP100A2365) yielded a slope estimate of -0.17 (mmHg per unit increase in dose ratio) for the dose-response curve for the change from baseline to the end of Phase 1 in msSBP. The negative slope estimate was statistically different from zero ($p<0.001$), indicating a significant dose-response. According to the study design, this result provided the evidence supporting the effectiveness of aliskiren in the treatment of hypertension in pediatric patients 6- 17 years of age. The analyses of the LSM change of msSBP in Phase 2 gave a numerical difference in favor of the aliskiren high dose group compared to the corresponding placebo group. The numerical difference was not statistical significant therefore was not strong supporting evidence for the efficacy of aliskiren in hypertensive pediatric patients. Strictly speaking, the study sample size did not meet the terms of the WR. However, given the study results can be viewed as interpretable, the Agency considers the study as being conducted fairly in response to the WR.

8. Consults

Please see the following reviews and their corresponding dates:

- OSE/DMEPA: October 10, 2017 and October 20, 2017 (Proprietary Name)
- OPDP: October 17, 2017 and October 18, 2017
- Patient Labeling (Instructions for Use): October 18, 2017
- DPMH: N/A

9. Labeling

Labeling discussions occurred with the applicant. The final agreed-upon labeling will be attached to the approval letter.

V. CONCLUSION

The review team recommended approval.

An approval Letter was signed by Dr. Norman Stockbridge on November 14, 2017.

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/s/

MARYAM K CHANGI
11/14/2017

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Medical Policy

PATIENT LABELING REVIEW

Date:	October 18, 2017
To:	Norman Stockbridge, MD Director **Division of Cardiovascular and Renal Products (DCaRP)**
Through:	LaShawn Griffiths, MSHS-PH, BSN, RN Associate Director for Patient Labeling **Division of Medical Policy Programs (DMPP)** Barbara Fuller, RN, MSN, CWOCN Team Leader, Patient Labeling **Division of Medical Policy Programs (DMPP)**
From:	Susan Redwood, MPH, BSN, RN Patient Labeling Reviewer **Division of Medical Policy Programs (DMPP)** Zarna Patel, PharmD Regulatory Review Officer **Office of Prescription Drug Promotion (OPDP)**
Subject:	Review of Patient Labeling: Patient Package Insert (PPI) and Instructions for Use (IFU)
Drug Name (established name), Dosage Form and Route:	TEKTURNA (aliskiren) tablets and TEKTURNA Oral Pellets, for oral use
Application Type/Number:	NDA 210709
Applicant:	Noden Pharma DAC c/o Quintiles IMS

1 INTRODUCTION

On April 6, 2017 Noden Pharma DAC c/o of Quintiles IMS submitted a Prior Approval Supplement (PAS) to their New Drug Application (NDA) 021985/S-033. On May 15, 2017, Noden Pharma DAC c/o Quintiles IMS, resubmitted the Application as an original New Drug Application (NDA) 210709 for TEKTURNA (aliskiren) tablets, for oral use and TEKTURNA (aliskiren) Oral Pellets, for oral use in response to an Agency request advising the Applicant to reclassify the PAS submission to NDA 210709. The proposed indication for TEKTURNA (aliskiren) tablets and Oral Pellets is for the treatment of hypertension in adults and children.

This collaborative review is written by the Division of Medical Policy Programs (DMPP) and the Office of Prescription Drug Promotion (OPDP) in response to a request by the Division of Cardiovascular and Renal Products (DCaRP) on April 13, 2017, for DMPP and OPDP on April 10, 2017, to review the Applicant's proposed Patient Package Insert (PPI) and Instructions for Use (IFU) for TEKTURNA (aliskiren).

DMPP conferred with the Division of Medication Error, Prevention, and Analysis (DMEPA) and DMEPA and a separate review of the IFU was completed on October 10, 2017.

2 MATERIAL REVIEWED

- Draft TEKTURNA (aliskiren) PPI and IFU received on May 15, 2017 revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 10, 2017.
- Draft TEKTURNA (aliskiren) Prescribing Information (PI) received on May 15, 2017 revised by the Review Division throughout the review cycle, and received by DMPP and OPDP on October 10, 2017.
- Approved TEKTURNA (aliskiren) labeling dated November 4, 2016.

3 REVIEW METHODS

To enhance patient comprehension, materials should be written at a 6th to 8th grade reading level, and have a reading ease score of at least 60%. A reading ease score of 60% corresponds to an 8th grade reading level.

Additionally, in 2008 the American Society of Consultant Pharmacists Foundation (ASCP) in collaboration with the American Foundation for the Blind (AFB) published *Guidelines for Prescription Labeling and Consumer Medication Information for People with Vision Loss*. The ASCP and AFB recommended using fonts such as Verdana, Arial or APHont to make medical information more accessible for patients with vision loss. We reformatted the PPI and IFU document using the Arial font, size 10.

In our collaborative review of the PPI and IFU we:

- simplified wording and clarified concepts where possible

- ensured that the PPI are IFU are consistent with the Prescribing Information (PI)
- removed unnecessary or redundant information
- ensured that the PPI and IFU are free of promotional language or suggested revisions to ensure that it is free of promotional language
- ensured that the PPI and IFU meet the criteria as specified in FDA's Guidance for Useful Written Consumer Medication Information (published July 2006)
- ensured that the PPI and IFU are consistent with the approved labeling where applicable.

4 CONCLUSIONS

The PPI and IFU are acceptable with our recommended changes.

5 RECOMMENDATIONS

- Please send these comments to the Applicant and copy DMPP and OPDP on the correspondence.
- Our collaborative review of the PPI and IFU are appended to this memorandum. Consult DMPP and OPDP regarding any additional revisions made to the PI to determine if corresponding revisions need to be made to the PPI and IFU.

Please let us know if you have any questions.

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/s/

SUSAN W REDWOOD
10/18/2017

ZARNA PATEL
10/18/2017

LASHAWN M GRIFFITHS
10/18/2017

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

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

Memorandum

Date: October 17, 2017

To: Maryam Changi, PharmD
Regulatory Project Manager
Division of Cardiovascular and Renal Products (DCRP)

Michael Monteleone, Associate Director for Labeling (DCRP)

From: Zarna Patel, PharmD
Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

CC: James Dvorsky, Team Leader, OPDP

Subject: OPDP Labeling Comments for TEKTURNA® (aliskirent) tablets and TEKTURNA® Oral Pellets, for oral use

NDA/BLA: 210709

In response to DCRP's consult request dated April 10, 2017, OPDP has reviewed the proposed product labeling (PI), patient package insert (PPI), Instructions for Use (IFU), and carton and container labeling for the original NDA for TEKTURNA® (aliskiren) tablets and TEKTURNA® Oral Pellets.

PI and PPI/IFU: OPDP's comments on the proposed labeling are based on the draft PI received by electronic mail from DCRP on October 10, 2017, and are provided below.

A combined OPDP and Division of Medical Policy Programs (DMPP) review will be completed, and comments on the proposed PPI and IFU will be sent under separate cover.

Carton and Container Labeling: OPDP has reviewed the attached proposed carton and container labeling submitted by the Sponsor to the electronic document room on September 29, 2017, and June 5, 2017, and we do not have any comments.

Thank you for your consult. If you have any questions, please contact Zarna Patel at (301) 796-3822 or zarna.patel@fda.hhs.gov.

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/s/

ZARNA PATEL
10/17/2017

LABEL AND LABELING REVIEW 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:	10 October 2017
Requesting Office or Division:	Division of Cardiovascular and Renal Products (DCRP)
Application Type and Number:	NDA 210709
Product Name and Strength:	Tekturna (Aliskiren) Oral Pellets, 37.5 mg
Product Type:	Single Ingredient
Rx or OTC:	Rx
Applicant/Sponsor Name:	Noden Pharma
Submission Date:	5 June 2017 and 29 September 2017
OSE RCM #:	2017-1024
DMEPA Pediatric Medication Safety Advisor:	Rhiannon Leutner, PharmD, MPH, MBA
DMEPA Team Leader:	Alice Tu, PharmD, BCPS

1 REASON FOR REVIEW

The Division of Cardiovascular and Renal Products (DCRP) requested that we review the Prescribing Information, Instructions for Use, and carton and container labels submitted for Tekturna (NDA 210709) to determine if they are acceptable from a medication error perspective.

1.1 REGULATORY HISTORY

Tekturna (Aliskiren) Tablets, 150 mg and 300 mg, were approved on 5 March 2007 for the treatment hypertension in adult patients under NDA 021985.

On 6 April 2017, Noden Pharma proposed the new pediatric dosage form Tekturna (Aliskiren) Oral Pellets, 37.5 mg, for the treatment of hypertension in children 6-17 years of age under NDA 210709. This new pediatric dosage form is to fulfill the conditions of a Written Request under the Best Pharmaceuticals for Children's Act (BPCA), and to fulfill the "assessments" required under the Pediatric Research Equity Act (PREA).

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
Previous DMEPA Reviews	B – N/A
Human Factors Study	C – N/A
ISMP Newsletters	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Labels and Labeling	G

N/A=not applicable for this review
*We do not typically search FAERS for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

Noden Pharma submitted NDA 210709 to seek marketing approval of Tekturna (Aliskiren) Oral Pellets, 37.5 mg, for treatment of hypertension in children 6-17 years of age. Tekturna Oral Pellets will be packaged in a “dispensing” capsule containing 12 oral pellets. Per the submission, these capsules should not be swallowed whole. The proposed labeling states that capsules must be opened. The oral pellets inside the capsule should be poured onto a spoonful

of soft food (e.g. vanilla pudding, vanilla ice cream), or directly into the mouth for swallowing without chewing.

Capsules are common dosage form for many oral drug products where the capsule itself may be swallowed whole. We typically recommend that drug products should not be packaged in a container/closure system that implies or affords a type of administration other than the route or technique intended, unless there are no other options available, because this practice has led to medication errors.[1] Since the capsule carrying Tekturna oral pellets is not intended to be swallowed whole, we are concerned that this design may lead to administration errors where the capsule may be swallowed.

We brought our concern for wrong technique in administration errors associated with this capsule packaging to the Tekturna Review Team's attention. The Review Team discussed other packaging options such as packaging the oral pellets inside a pouch, sachet, stick pack, etc. or to reformulate the oral pellets into an oral solution. In addition, the Review Team considered the following:

- Per the applicant, the estimated number of pediatric patients that may be expected to use Tekturna oral pellets is 25 per year.[2]
- The potential choking hazard for incorrect whole capsule ingestion was considered and there appears to be minimal risk for choking.
- There appears to be other approved comparable products for the treatment of hypertension in children aged 6-17 years. For example, angiotensin-converting-enzyme inhibitors, angiotensin II receptor antagonists, long-acting calcium channel blockers, and thiazide diuretics. According to the clinical team, Aliskiren is not expected to have any advantage over the aforementioned agents, however, it does offer an additional option for the management of pediatric hypertension.
- The clinical consequence of inadvertently swallowing a capsule may result in lower therapeutic response due to the capsule dissolution time, but it is unknown if this difference is likely to have a profound clinical effect.

Following internal discussion, and considering the totality of the aforementioned information, the Review Team agreed that the residual risk of wrong technique in administration errors for the proposed Tekturna oral pellet product may be mitigated via labels and labeling. We note that the proposed carton labeling and Instructions for Use (IFU) provide pictograms and instructions to the end user for opening the capsules before administration. Additionally, the "dispensing" capsule is imprinted with arrows to indicate that the capsule should be opened prior to administration. However, we find that additional labeling interventions in the

[1] See Guidance for Industry – Safety Considerations Safety Considerations for Product Design to Minimize Medication Errors, April 2016. Available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM331810.pdf

[2] \\cdsesub1\evsprod\nda210709\0009\m1\us\info-amend-2017-aug-25.pdf

Prescribing Information (PI), and on the carton labeling and container label may help to further reduce the risk of wrong technique in administration errors.

4 CONCLUSION & RECOMMENDATIONS

We conclude that the proposed labels and labeling for Tekturna oral pellets may be improved to promote the safe use of the product. We provide recommendations in Section 4.1 and Section 4.2 below.

4.1 RECOMMENDATIONS FOR THE DIVISION

A. General
    1. We recommend that prominent statements that recommend against swallowing capsules whole remain in the Prescribing Information and Patient Information to mitigate the risk of wrong technique of administration medication errors unless adequate data supports that the proposed product may be swallowed without profound clinical effects.

B. Prescribing Information
    1. See Appendix H for our recommendations for the proposed PI.

C. Patient Information
    1. Remove the duplicate instructions concerning what to do in the event of a missed dose or overdose under the header "How should I take Tekturna oral pellets?".

4.2 RECOMMENDATIONS FOR NODEN PHARMA

We recommend the following be implemented prior to approval of this NDA:

A. Container Label and Carton labeling
    1. The container labels and carton labeling should bear prominent warning statements to prevent accidental ingestion of whole capsules. Revise the container label to include the statement "Open capsule to administer" on each blister cell. Revise the carton labeling to include the prominent statement "Capsules must be opened prior to administration. See the Instructions for Use for the proper way to take Tekturna Oral Pellets" on the principal display panel.
    2. Provide the actual NDC numbers proposed for review in lieu of the placeholder (XXXXX-XXXX-XX) currently depicted on the container labels and carton labeling.

B. Container Labels
    1. As currently presented, the NDC number is located in the bottom or the middle of each blister cell. Revise the location of the NDC number to the top third of each blister cell in accordance with 21 CFR 207.35(b)(3)(i).

C. Carton Labeling
    1. Revise the font color of the 37.5 mg strength statement to a non-purple color so that the strength appears in its own unique color (b) (4)

(b) (4)

2. Revise the back and side panel dosing and administration instructions to ensure consistency with final approved product labeling. For example, dosing vehicles described on the back panel of carton labeling should reflect the final approved language in Section 2.3 of the Prescribing Information. Additionally, and the side panel pictograms and accompanying instructions should reflect the final approved language in the Instructions for Use (IFU).

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Tekturna (Aliskiren) that Noden Pharma submitted on 5 June 2017.

Table 2. Relevant Product Information for Tekturna (Aliskiren) Oral Pellets	
Initial Approval Date	N/A
Active Ingredient	aliskiren hemifumarate
Indication	treatment of hypertension in children 6-17 years of age
Route of Administration	oral
Dosage Form	Oral Pellets
Strength	37.5 mg
Dose and Frequency	*20 to 49 kg:* (b) (4) a starting dose of 75 mg may be used. 150 mg max dose. *50 kg and up*: 150 mg once daily starting dose. 300 mg max dose.
How Supplied	Blister packages of 48 capsules (8 strips of 6 capsules)
Storage	Store at 25ºC (77ºF); excursions permitted to 15ºC to 30ºC (59 ºF to 86ºF)
Container Closure	child-resistant / senior friendly unit-dose blister packages

Table 3 presents relevant product information for Tekturna (Aliskiren) tablets.[3]

Table 3. Relevant Product Information for Tekturna (Aliskiren) tablets (NDA 021985)	
Initial Approval Date	5 March 2007
Active Ingredient	aliskiren hemifumarate
Indication	treatment of hypertension in adults
Route of Administration	oral
Dosage Form	tablet
Strength	150 mg, 300 mg
Dose and Frequency	150 mg once daily with a routine pattern with regard to meals; if blood pressure remains uncontrolled titrate up to 300 mg daily
How Supplied	Bottles of 90 tablets; Bottles of 30 tablets; unit-dose blister packages 100 tablets (10 strips of 10 tablets)
Storage	Store at 25ºC (77ºF); excursions permitted to 15ºC to 30ºC (59 ºF

[3] Accessed 28 July 2017; https://www.accessdata.fda.gov/spl/data/c3d6f2d0-6154-49c1-8758-a87cbf88f59d/c3d6f2d0-6154-49c1-8758-a87cbf88f59d.xml

	to 86ºF)
Container Closure	[redacted] (b) (4) blister packaging

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

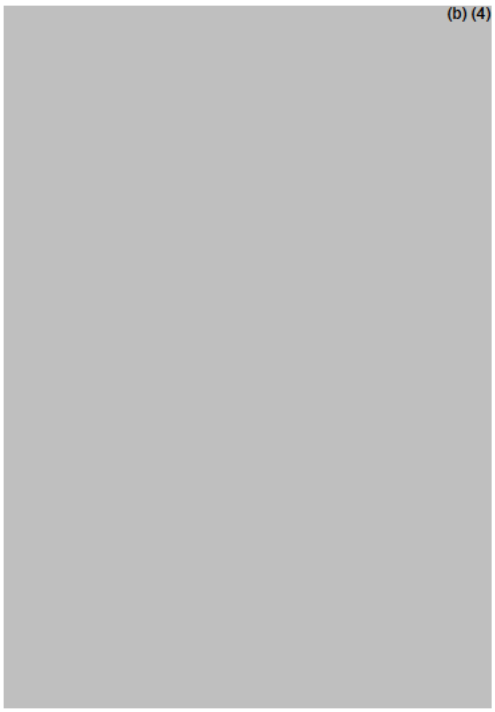
Using the principles of human factors and Failure Mode and Effects Analysis,[4] along with postmarket medication error data, we reviewed the following Tekturna labels and labeling submitted by Noden Pharma.

- Prescribing Information submitted 29 September 2017
- Instructions for Use submitted 5 June 2017
- Container label submitted 5 June 2017
- Carton labeling submitted 29 September 2017
- Capsule Image

G.2 Label and Labeling Images

Container Labels

(b) (4)



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

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RHIANNON LEUTNER
10/10/2017

CHI-MING TU
10/10/2017

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

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

Application: NDA 210709

Application Type: New NDA

Drug Name(s)/Dosage Form(s): Tekturna® (aliskiren Tablets)

Applicant: Noden Pharma DAC

Receipt Date: 06/05/17 (User-fee received 05/15/2017)

Goal Date: 11/15/2017

1. Regulatory History and Applicant's Main Proposals

We received a new efficacy supplement for Tukturna ® (aliskiren)(sNDA 21985/033) on April 6, 2017. The sponsor submitted this supplement for Tekturna ® tablets to submit pediatric study reports required to fulfill the conditions of a Written Request under the Best Pharmaceuticals for Children's Act (BPCA), and to fulfill the "assessments" required under the Pediatric Research Equity Act (PREA).
In this submission, the sponsor proposed new Pediatrics formulation. After consult with CMC folks, it was determined that this is also a New Dosage Form, which requires new NDA. We later contacted the sponsor to pay the required User-fee to fulfill NDA user fee requirement.
The user fee has been paid in full on May 15, 2017, which is the start of the new regulatory clock for this application.

Noden is referring to WR letter that was issued on May 13, 2008, and the following amendments dated March 13, 2009, August 6, 2012, and August 9, 2016. The sponsor provided data to response to a PMC under PREA and a WR. In alignment with the PMC required under PREA and the WR, the sponsor conducted three studies under IND 62976.
This application submitted in response to a Written Request under the Best Pharmaceuticals for Children Act, Noden Pharma is requesting priority review and seeking approval of the following revised indication for Tekturna*: treatment of hypertension, to lower blood pressure in adults and children 6 to 17 years of age.*

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 of Prescribing Information (SRPI)" checklist (see Section 4 of this review).

3. Conclusions/Recommendations

SRPI format deficiencies were identified in the review of this PI. For a list of these deficiencies, see Section 4 of this review.

All SRPI format deficiencies of the PI and other labeling issues identified above will be conveyed to the applicant in the 74-day letter. The applicant will be asked to correct these deficiencies and resubmit the PI in Word format by July 10, 2017. The resubmitted PI will be used for further labeling review.

4. Selected Requirements of Prescribing Information

The Selected Requirement of Prescribing Information (SRPI) is a 41-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 for a sample tool illustrating Highlights format.

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:

NO 3. A horizontal line must separate:

- HL from the Table of Contents (TOC), **and**
- TOC from the Full Prescribing Information (FPI).

Comment: *No horizontal line \between TOC and FPI*

NO 4. All headings in HL (from Recent Major Changes to Use in Specific Populations) must be **bolded** and presented in the center of a horizontal line. (Each horizontal line should extend over the entire width of the column.) The HL headings (from Recent Major Changes to Use in Specific Populations) should be in UPPER CASE letters. See Appendix for HL format.

Comment: *The horizontal lines are not all extended over the entire width of the column.*

NO 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 for HL format.

Comment: *There is a white space between the product title and Initial U.S. Approval.*

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. Headings in HL must be presented in the following order:

Heading	Required/Optional
• **Highlights Heading**	Required
• **Highlights Limitation Statement**	Required
• **Product Title**	Required
• **Initial U.S. Approval**	Required
• **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 five labeling sections in the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS.

Comment:

HIGHLIGHTS DETAILS

Highlights Heading

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

Comment:

Highlights Limitation Statement

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

Comment:

Boxed Warning (BW) in Highlights

YES 12. All text in the BW must be **bolded**.

Comment:

YES 13. The BW must have a title in UPPER CASE, following the word "**WARNING**" and other words to identify the subject of the warning. Even if there is more than one warning, the term "**WARNING**" and not "**WARNINGS**" should be used. For example: "**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**". If there is more than one warning in the BW title, the word "and" in lower case can separate the warnings. The BW title should be centered.

Comment:

YES 14. The BW must always have the verbatim statement "***See full prescribing information for complete boxed warning***." This statement must be placed immediately beneath the BW title, and should be centered and appear in *italics*.

Comment:

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

Comment:

Recent Major Changes (RMC) in Highlights

YES 16. RMC pertains to only five sections of the FPI: BOXED WARNING, INDICATIONS AND USAGE, DOSAGE AND ADMINISTRATION, CONTRAINDICATIONS, and WARNINGS AND PRECAUTIONS. Labeling sections for RMC must be listed in the same order in HL as they appear in the FPI.

Comment:

YES 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) --- 8/2015."

Comment:

YES 18. A changed section must be listed under the RMC heading for at least one year after the date of the labeling change and must be removed at the first printing subsequent to the one year period. (No listing should be one year older than the revision date.)

Comment:

Dosage Forms and Strengths in Highlights

NO 19. For a product that has more than one dosage form (e.g., capsules, tablets, injection), bulleted headings should be used.

Comment: *bulleted heading is not used*

Contraindications in Highlights

NO 20. All contraindications listed in the FPI must also be listed in HL. If there is more than one contraindication, each contraindication should be bulleted. If no contraindications are known, must include the word "None."

Comment: *each contraindication is not bulleted*

Adverse Reactions in Highlights

YES 21. 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 which should be a toll-free number) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**"

Comment:

Patient Counseling Information Statement in Highlights

YES 22. 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 (or will have)** 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 23. The revision date must be at the end of HL, and should be **bolded** and right justified (e.g., "**Revised: 8/2015** ").

Comment:

Contents: Table of Contents (TOC)

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

YES 24. The TOC should be in a two-column format.

Comment:

YES 25. 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:

YES 26. The same title 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 27. In the TOC, all section headings must be **bolded** and should be in UPPER CASE.

Comment:

YES 28. 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 (for, of, to) and articles (a, an, the), or conjunctions (or, and)].

Comment:

YES 29. The section and subsection headings in the TOC must match the section and subsection headings in the FPI.

Comment:

YES 30. If a section or subsection required by regulation [21 CFR 201.56(d)(1)] is omitted from the FPI, the numbering in the TOC must not change. The heading "**FULL PRESCRIBING INFORMATION: CONTENTS***" must be followed by an asterisk and the following statement must appear at the end of the TOC: "*Sections or subsections omitted from the full prescribing information are not listed."

Comment:

Full Prescribing Information (FPI)

FULL PRESCRIBING INFORMATION: GENERAL FORMAT

YES 31. 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 Lactation (if not required to be in Pregnancy and Lactation Labeling Rule (PLLR) format, use "**Labor and Delivery**")
8.3 Females and Males of Reproductive Potential (if not required to be in PLLR format, use "**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 32. 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)]*."

Comment:

YES 33. For each RMC listed in HL, the corresponding new or modified text in the FPI must be marked with a vertical line on the left edge.

Comment:

FULL PRESCRIBING INFORMATION DETAILS

FPI Heading

YES 34. The following heading "**FULL PRESCRIBING INFORMATION"** must be **bolded,** must appear at the beginning of the FPI, and should be in UPPER CASE.

Comment:

BOXED WARNING Section in the FPI

YES 35. All text in the BW should be **bolded**.

Comment:

YES 36. The BW must have a title in UPPER CASE, following the word "**WARNING**" and other words to identify the subject of the warning. (Even if there is more than one warning, the term, "**WARNING**" and not "**WARNINGS**" should be used.) For example: "**WARNING: SERIOUS INFECTIONS and ACUTE HEPATIC FAILURE**". If there is more than one warning in the BW title, the word "and" in lower case can separate the warnings.

Comment:

CONTRAINDICATIONS Section in the FPI

N/A 37. If no Contraindications are known, this section must state "None."

Comment:

ADVERSE REACTIONS Section in the FPI

YES 38. When clinical trials adverse reactions data are included (typically in the "Clinical Trials Experience" subsection), the following verbatim statement (or appropriate modification) should precede the presentation of adverse reactions from clinical trials:

"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 39. When postmarketing adverse reaction data are included (typically in the "Postmarketing Experience" subsection), 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

YES 40. Must reference any FDA-approved patient labeling in Section 17 (PATIENT COUNSELING INFORMATION). The reference statement should appear at the beginning of Section 17 and include the type(s) of FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide). Recommended language for the reference statement should include one of the following five verbatim statements that is most applicable:

- Advise the patient to read the FDA-approved patient labeling (Patient Information).
- Advise the patient to read the FDA-approved patient labeling (Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide).
- Advise the patient to read the FDA-approved patient labeling (Medication Guide and Instructions for Use).

Comment:

YES 41. FDA-approved patient labeling (e.g., Patient Information, Instructions for Use, or Medication Guide) 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:

Selected Requirements of Prescribing Information

Appendix: Highlights and Table of Contents Format

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

PROPRIETARY NAME (non-proprietary name) dosage form, route of administration, controlled substance symbol
Initial U.S. Approval: YYYY

WARNING: TITLE OF WARNING
See full prescribing information for complete boxed warning.

- **Text (4)**
- **Text (5.x)**

----------RECENT MAJOR CHANGES----------
Section Title, Subsection Title (x.x) M/201Y
Section Title, Subsection Title (x.x) M/201Y

----------INDICATIONS AND USAGE----------
PROPRIETARY NAME is a (insert FDA established pharmacologic class text phrase) indicated for … (1)

Limitations of Use: Text (1)

----------DOSAGE AND ADMINISTRATION----------
- Text (2.x)
- Text (2.x)

----------DOSAGE FORMS AND STRENGTHS----------
Dosage form(s): strength(s) (3)

----------CONTRAINDICATIONS----------
- Text (4)
- Text (4)

----------WARNINGS AND PRECAUTIONS----------
- Text (5.x)
- Text (5.x)

----------ADVERSE REACTIONS----------
Most common adverse reactions (incidence > x%) are text (6.x)

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

----------DRUG INTERACTIONS----------
- Text (7.x)
- Text (7.x)

----------USE IN SPECIFIC POPULATIONS----------
- Text (8.x)
- Text (8.x)

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

Revised: M/201Y

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/

MARYAM K CHANGI
07/13/2017

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)]

<table>
<tr><th colspan="3">Application Information</th></tr>
<tr><td>NDA # 210709</td><td>NDA Supplement #: N/A</td><td>Efficacy Supplement Category:
☐ New Indication (SE1)
☐ New Dosing Regimen (SE2)
☐ New Route Of Administration (SE3)
☐ Comparative Efficacy Claim (SE4)
☐ New Patient Population (SE5)
☐ Rx To OTC Switch (SE6)
☐ Accelerated Approval Confirmatory Study (SE7)
☐ Labeling Change With Clinical Data (SE8)
☐ Manufacturing Change With Clinical Data (SE9)
☐ Animal Rule Confirmatory Study (SE10)</td></tr>
<tr><td colspan="3">Proprietary Name: Tekturna®
Established/Proper Name: aliskiren
Dosage Form: Oral Pellet in Capsule
Strengths: 37.5 mg</td></tr>
<tr><td colspan="3">Applicant: NODEN Pharma DAC
Agent for Applicant (if applicable): Janelle Delk</td></tr>
<tr><td colspan="3">Date of Application: April 6, 2017 (sNDA) ; June 5, 2017 (NDA)
Date of Receipt: April 6, 2017 (sNDA) ; June 5, 2017 (NDA)
Date clock started after Unacceptable for Filing (UN): May 15, 2017</td></tr>
<tr><td colspan="2">PDUFA/BsUFA Goal Date: November 15, 2017</td><td>Action Goal Date (if different): November14, 2017</td></tr>
<tr><td colspan="2">Filing Date: July 14, 2017</td><td>Date of Filing Meeting: June 19, 2017</td></tr>
<tr><td colspan="3">Chemical Classification (original NDAs only) :
☐ Type 1- New Molecular Entity (NME); NME and New Combination
☐ Type 2- New Active Ingredient; New Active Ingredient and New Dosage Form; New Active Ingredient and New Combination
☒ Type 3- New Dosage Form; New Dosage Form and New Combination
☐ Type 4- New Combination
☐ Type 5- New Formulation or New Manufacturer
☐ Type 7- Drug Already Marketed without Approved NDA
☐ Type 8- Partial Rx to OTC Switch
☐ Type 9-New Indication or Claim (will <u>not</u> be marketed as a separate NDA after approval)
☐ Type 10-New Indication or Claim (will be marketed as a separate NDA after approval)</td></tr>
<tr><td colspan="3">Proposed indication(s)/Proposed change(s): The Treatment of Hypertension in Pediatrics</td></tr>
<tr><td colspan="2" rowspan="2"></td><td>☒ 505(b)(1)
☐ 505(b)(2)</td></tr>
<tr><td>☐ 505(b)(1)
☐ 505(b)(2)</td></tr>
</table>

Type of BLA ***If 351(k), notify the OND Therapeutic Biologics and Biosimilars Team***	☐ 351(a) ☐ 351(k)
Review Classification: ***The application will be a priority review if:*** • ***A complete response to a pediatric Written Request (WR) was included (a partial response to a WR that is sufficient to change the labeling should also be a priority review – check with DPMH)*** • ***The product is a Qualified Infectious Disease Product (QIDP)*** • ***A Tropical Disease Priority Review Voucher was submitted*** • ***A Pediatric Rare Disease Priority Review Voucher was submitted***	☐ Standard ☒ Priority ☒ Pediatric WR ☐ QIDP ☐ Tropical Disease Priority Review Voucher ☐ Pediatric Rare Disease Priority Review Voucher
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 ☐ 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 (FDCA Section 505B) ☐ 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*):	
List referenced IND Number(s): IND 62976	

Goal Dates/Product Names/Classification Properties	**YES**	**NO**	**NA**	**Comment**
PDUFA/BsUFA and Action Goal dates correct in the electronic archive? ***If no, ask the document room staff to correct them immediately. These are the dates used for calculating inspection dates.***	☒	☐		
Are the established/proper and applicant names correct in electronic archive?	☒	☐		

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 electronic archive.				
Is the review priority (S or P) and all appropriate classifications/properties entered into tracking system (e.g., chemical classification, combination product classification, orphan drug)? ***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***	☐	☒		
If yes, explain in comment column.				N/A
If affected by AIP, has OC been notified of the submission? **If yes,** date notified:	☐	☐		N/A
User Fees	**YES**	**NO**	**NA**	**Comment**
Is Form 3397 (User Fee Cover Sheet)/Form 3792 (Biosimilar User Fee Cover Sheet) included with authorized signature?	☒	☐		

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 from receipt. Review stops. Contact the User Fee Staff. If appropriate, send UN letter.***	Payment for this application *(check daily email from UserFeeAR@fda.hhs.gov):* ☒ Paid ☐ Exempt (orphan, government) ☐ 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. Contact the User Fee Staff. If appropriate, send UN letter.	Payment of other user fees: ☒ Not in arrears ☐ In arrears
User Fee Bundling Policy ***Refer to the guidance for industry, Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees at:*** ***http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf***	Has the user fee bundling policy been appropriately applied? ***If no, or you are not sure, consult the User Fee Staff.*** ☐ Yes ☐ No

505(b)(2) **(NDAs/NDA Efficacy Supplements only)**	**YES**	**NO**	**NA**	**Comment**
Is the application a 505(b)(2) NDA? *(Check the 356h form, cover letter, and annotated labeling).* **If yes**, answer the bulleted questions below:	☐	☒		
• 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 bulleted 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 for advice.***	☐	☐		
• Is there unexpired exclusivity on another listed drug product containing the same 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 another listed drug product containing the same active moiety, 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 orphan or 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***	☐	☒		
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***	☐	☒	☐	
NDAs/NDA efficacy supplements only: Has the applicant requested 5-year or 3-year Waxman-Hatch exclusivity?	☐	☒	☐	

If yes, # years requested: ***Note:*** *An applicant can receive exclusivity without requesting it; therefore, requesting exclusivity is not required.*				
NDAs only: Is the proposed product a single enantiomer of a racemic drug previously approved for a different therapeutic use?	☐	☒	☐	
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).***	☐	☐	☒	
BLAs only: Has the applicant requested 12-year exclusivity under section 351(k)(7) of the PHS Act? ***If yes, notify Marlene Schultz-DePalo, CDER Purple Book Manager*** ***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	☒	☐		

[1] http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm333969.pdf

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 (3397/3792), 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 314.50(a)(5)].***	☒	☐		
Are all establishments and their registration numbers listed on the form/attached to the form?	☒	☐	☐	An IR sent by CMC requesting applicant to provide a confirmatory list of all manufacturing, testing, and packaging facilities
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)?	☒	☐	☐	
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, return them to CDR for delivery to the appropriate field office.***	☒	☐	☐	
Controlled Substance/Product with Abuse Potential	**YES**	**NO**	**NA**	**Comment**
<u>For NMEs:</u> 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:* <u>For non-NMEs</u>: *Date of consult sent to Controlled Substance Staff* :	☐	☐	☒	
Pediatrics	**YES**	**NO**	**NA**	**Comment**

PREA Does the application trigger PREA? New Dosage Form ***If yes, notify PeRC@fda.hhs.gov to schedule required PeRC meeting[2]*** ***Note**: NDAs/BLAs/efficacy supplements for new active ingredients (including new fixed combinations), 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.*	☒	☐		The submission is pediatric study reports required to fulfill the conditions of a Written Request under the Best Pharmaceuticals for Children's Act (BPCA), and to fulfill the "assessments" required under the Pediatric Research Equity Act (PREA).PeRC has been scheduled for 9/20/2017
If the application triggers PREA, is there an agreed Initial Pediatric Study Plan (iPSP)? ***If no, may be an RTF issue - contact DPMH for advice.***	☐	☒	☐	
If required by the agreed iPSP, are the pediatric studies outlined in the agreed iPSP completed and included in the application? ***If no, may be an RTF issue - contact DPMH for advice.***	☐	☐	☒	
BPCA: Is this submission a complete response to a pediatric Written Request? ***If yes, notify Pediatric Exclusivity Board RPM (pediatric exclusivity determination is required[3]***	☒	☐		Meeting with exclusivity board scheduled for 09/12/2017
Proprietary Name	**YES**	**NO**	**NA**	**Comment**
Is a proposed proprietary name submitted? ***If yes, ensure that the application is also coded with the supporting document category, "Proprietary Name/Request for Review."***	☐	☒	☐	OSE submitted an email to sponsor.
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 (Prescribing Information)(PI) ☒ Patient Package Insert (PPI)			

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

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

	☒ Instructions for Use (IFU) ☐ Medication Guide (MedGuide) ☒ Carton labeling ☒ Immediate container labels ☐ Diluent labeling ☐ Other (specify)			
	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 Physician Labeling Rule (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.***	☒	☐	☐	
For applications submitted on or after June 30, 2015: Is the PI submitted in Pregnancy and Lactation Labeling Rule (PLLR) format? Has a review of the available pregnancy, lactation, and females and males of reproductive potential data (if applicable) been included?	☒ ☐	☐ ☐	☐ ☐	
For applications submitted on or after June 30, 2015: If PI not submitted in PLLR 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 PLLR format before the filing date.***	☒	☐	☐	
Has all labeling [(PI, patient labeling (PPI, MedGuide, IFU), carton and immediate container labeling)] been consulted to OPDP?	☒	☐	☐	
Has PI and patient labeling (PPI, MedGuide, IFU) been consulted to OSE/DRISK? (*send WORD version if available*)	☒	☐	☐	
Has all labeling [PI, patient labeling (PPI, MedGuide, IFU) carton and immediate container labeling, PI, PPI been consulted/sent to OSE/DMEPA and appropriate CMC review office in OPQ (OBP or ONDP)?	☒	☐	☐	

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

OTC Labeling	☒ **Not Applicable**			
Check all types of labeling submitted.	☐ Outer carton label ☐ Immediate container label ☐ Blister card ☐ Blister backing label ☐ Consumer Information Leaflet (CIL) ☐ Physician sample ☐ Consumer sample ☐ Other (specify)			
	YES	**NO**	**NA**	**Comment**
Is electronic content of labeling (COL) submitted? ***If no, request in 74-day letter.***	☒	☐		
Are annotated specifications submitted for all stock keeping units (SKUs)? ***If no, request in 74-day letter.***	☐	☐	☒	
If representative labeling is submitted, are all represented SKUs defined? ***If no, request in 74-day letter.***	☐	☐	☒	
All labeling/packaging sent to OSE/DMEPA?	☒	☐	☐	A link to the labeling was included in the consult.
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:***	☒	☐	☐	PLT/ DMEPA/OPDP consulted
Meeting Minutes/SPAs	**YES**	**NO**	**NA**	**Comment**
End-of Phase 2 meeting(s)? **Date(s):** September 22, 2014	☒	☐		EOP2: Chemistry, Manufacturing and Controls
Pre-NDA/Pre-BLA/Pre-Supplement meeting(s)? **Date(s):**	☒	☐		Clinical Type C meeting was held on 5/17/2007 (NDA 021985) CMC type C meeting was held on 07/27/2007, Type A meeting CMC only, held on 9/7/2016
Any Special Protocol Assessments (SPAs)? **Date(s):** 4/19/2004, 11/30/2006 5/17/2007, 12/19/2007	☒			Agreement letter submitted on 1/25/2008

ATTACHMENT

MEMO OF FILING MEETING

DATE: 06/19/17

BACKGROUND:
We received a new efficacy supplement for Tukturna ® (aliskiren)(sNDA 21985/033) on April 6, 2017. The sponsor submitted this supplement for Tekturna ® tablets to submit pediatric study reports required to fulfill the conditions of a Written Request under the Best Pharmaceuticals for Children's Act (BPCA), and to fulfill the "assessments" required under the Pediatric Research Equity Act (PREA).

In this submission, the sponsor proposed new Pediatrics formulation. After consult with CMC folks, it was determined that this is also a New Dosage Form, which requires new NDA. We later contacted the sponsor to pay the required User-fee to fulfill NDA user fee requirement. The user fee has been paid in full on May 15, 2017, which is the start of the new regulatory clock for this application.

Noden is referring to WR letter that was issued on May 13, 2008, and the following amendments dated March 13, 2009, August 6, 2012, and August 9, 2016. The sponsor provided data to response to a PMC under PREA and a WR. In alignment with the PMC required under PREA and the WR, the sponsor conducted three studies under IND 62976.

This application submitted in response to a Written Request under the Best Pharmaceuticals for Children Act, Noden Pharma is requesting priority review and seeking approval of the following revised indication for Tekturna*: treatment of hypertension, to lower blood pressure in adults and children 6 to 17 years of age.*

REVIEW TEAM:

Discipline/Organization	Names		Present at filing meeting? (Y or N)
Regulatory Project Management	RPM:	Maryam Changi	Y
	CPMS/TL:	Edward Fromm	N
Cross-Discipline Team Leader (CDTL)	Aliza Thompson		Y
Division Director/Deputy	Norma Stockbridge/ Stephen Grant		Y/Y
Office Director/Deputy	N/A		
Clinical	Reviewer:	Christine Garnett	Y
	TL:	Aliza Thompson	Y

Social Scientist Review (*for OTC products*)	Reviewer:		
	TL:		
OTC Labeling Review (*for OTC products*)	Reviewer:		
	TL:		
Clinical Microbiology (*for antimicrobial products*)	Reviewer:		
	TL:		
Clinical Pharmacology	Reviewer:	Martina Sahre	Y
	TL:	Sudharshan Hariharan	Y
• Genomics	Reviewer:		
• Pharmacometrics	Reviewer:		
Biostatistics	Reviewer:	Fanhui Kong	Y
	TL:	Jim Hung	N

Nonclinical (Pharmacology/Toxicology)	Reviewer:	Gowda Jagadeesh	Y
	TL:	Thomas Papoian	Y
Statistics (carcinogenicity)	Reviewer:		
	TL:		
Product Quality (CMC) Review Team:	ATL:	Rao Kambhampati	N
	RBPM:	Grafton Adams	Y
• Drug Substance	Reviewer:	Kambhampati	Y
• Drug Product	Reviewer:	Kambhampati	Y
• Process	Reviewer:	Wong	N
• Microbiology	Reviewer:	N/A	N
• Facility	Reviewer:	Seifert	N
• Biopharmaceutics	Reviewer:	Zhang	Y
• Immunogenicity	Reviewer:		
• Labeling (BLAs only)	Reviewer:		
• Other (e.g., Branch Chiefs, EA Reviewer)	Wendy Wilson-Lee, ATL and CMC Branch Chief (She emailed RPM and updated the CMC issues)		N
OMP/OMPI/DMPP (MedGuide, PPI, IFU)	Reviewer:		

	TL:		
OMP/OPDP (PI, PPI, MedGuide, IFU, carton and immediate container labeling)	Reviewer:	Zarna Patel (OPDP) Redwood (PTL)	N
	TL:	James Dvorsky (OPDP)	N
OSE/DMEPA (proprietary name, carton/container labeling)	Reviewer:	Rhiannon Leutner Darryl Lyons (PM)	Y
	TL:	Ta-Chen Wu (Alice	N
OSE/DRISK (REMS)	Reviewer:	N/A	
	TL:		
OC/OSI/DSC/PMSB (REMS)	Reviewer:	N/A	
	TL:		
Bioresearch Monitoring (OSI)	Reviewer:		
	TL:		
Controlled Substance Staff (CSS)	Reviewer:		
	TL:		
Other reviewers/disciplines			
• Discipline *For additional lines, highlight this group of cells, copy, then paste: select "insert as new rows"	Reviewer:		
	TL:		
Other attendees	Pharmacovigilance (Thao Tran)		Y
	*For additional lines, right click here and select "insert rows below"		

FILING MEETING DISCUSSION:

GENERAL • 505(b)(2) filing issues:	☒ Not Applicable
○ Is the application for a duplicate of a listed drug and eligible for approval under section 505(j) as an ANDA?	☐ YES ☐ NO
○ Did the applicant provide a scientific "bridge" demonstrating the relationship between the proposed product and the	☐ YES ☐ NO

referenced product(s)/published literature? Describe the scientific bridge (e.g., information to demonstrate sufficient similarity between the proposed product and the listed drug(s) such as BA/BE studies or to justify reliance on information described in published literature):	
• Per reviewers, are all parts in English or English translation? **If no**, explain:	☒ YES ☐ NO
• Electronic Submission comments **List comments**: We asked the applicant to provide: 1 Submit CSR and appendices submitted to the new NDA and everything to support this regulatory action from NDA 21985 to new NDA 210709.	☐ Not Applicable ☒ No comments
CLINICAL **Comments**: an IR sent to the sponsor to provide the CSR. Sponsor responded 7/7/17.	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
• Clinical study site(s) inspections(s) needed? **If no,** explain:	☐ 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:
• If the application is affected by the AIP, has the	☒ Not Applicable

division made a recommendation regarding whether or not an exception to the AIP should be granted to permit review based on medical necessity or public health significance? **Comments**:	☐ YES ☐ NO
CONTROLLED SUBSTANCE STAFF • Abuse Liability/Potential **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CLINICAL MICROBIOLOGY **Comments**:	☒ 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
PRODUCT QUALITY (CMC) **Comments**: CMC IR submitted to the sponsor	☐ Not Applicable ☒ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
<u>New Molecular Entity</u> (NDAs only) • Is the product an NME?	 ☐ YES ☒ NO

Environmental Assessment • Categorical exclusion for environmental assessment (EA) requested? **If no**, was a complete EA submitted? **Comments**:	☒ YES ☐ NO ☐ YES ☐ NO
Facility Inspection • Establishment(s) ready for inspection? **Comments**: 1) We will need to get an international inspection scheduled for the drug substance site in this short window for review. We intend to expedite the request but we are delayed a bit by some technical issues with Integrity Services and Panorama. We are looking for a work around. 2 The drug product facility currently has a potential Official Action Indicated compliance status. We are requesting an expedited review of this case to see if it can be downgraded. The team is waiting on the official response from the site to address the 483 issues identified (data integrity).	☐ Not Applicable ☒ YES ☐ NO
Facility/Microbiology Review (BLAs only) **Comments**:	☒ Not Applicable ☐ FILE ☐ REFUSE TO FILE ☐ Review issues for 74-day letter
CMC Labeling Review (BLAs only) **Comments**:	☐ Review issues for 74-day letter
APPLICATIONS IN THE PROGRAM (PDUFA V) (NME NDAs/Original BLAs) • 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? • If so, were the late submission components all submitted within 30 days?	☒ N/A ☐ YES ☐ NO ☐ YES ☐ NO

• What late submission components, if any, arrived after 30 days?	None
• 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: Norman Stockbridge, MD, PhD, Director

Date of Mid-Cycle Meeting (for NME NDAs/BLAs in "the Program" PDUFA V): N/A

21st Century Review Milestones (see attached) (listing review milestones in this document is optional):

Comments: Not an NME

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

ACTION ITEMS

☐	Ensure that any updates to the review priority (S or P) and classifications/properties are entered into the electronic archive (e.g., chemical classification, combination product classification, orphan drug).
☐	If RTF, notify everyone who already received a consult request, OSE PM, and RBPM
☐	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.
☒	If priority review, notify applicant in writing by day 60 (see CST for choices)
☒	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 applications in the Program)
☐	Other

Annual review of template by OND ADRAs completed: April 2016

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

/s/

MARYAM K CHANGI
07/14/2017