

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**210709Orig1s000**

**ADMINISTRATIVE and CORRESPONDENCE  
DOCUMENTS**

DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration		Form Approved: OMB No. 0910-0513 Expiration Date: 09/30/2019 See OMB Statement on last page.	
<b>PATENT INFORMATION SUBMITTED WITH THE FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT</b> <i>For Each Patent That Claims a Drug Substance (Active Ingredient), Drug Product (Formulation and Composition) and/or Method of Use</i>		NDA Number 021985	
		Name of NDA Applicant Noden Pharma DAC	
Refer to instruction sheet (Form FDA 3542a Supplement) for more information.			
The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.			
Trade Name (or proposed Trade Name) Tektuma		Active Ingredient(s) aliskiren	
Dosage Form(s) Oral		Strength(s) 150 mg, 300 mg	
Route(s) of Administration Tablet		Type of Use <input checked="" type="checkbox"/> Prescription <input type="checkbox"/> Over-the-Counter	
This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after the date of approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted on Form FDA 3542 pursuant to 21 CFR 314.53(c)(2)(i) with all of the required information based on the approved NDA or supplement. FDA will not list or publish patent information in the Orange Book if it is not submitted in the declaration form submitted upon or after approval.			
<b>FDA will not list patent information if the patent declaration does not contain the information required by 21 CFR § 314.53(c)(2) or the patent declaration indicates the patent is not eligible for listing.</b>			
<b>For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete the section above and sections 5 and 6.</b>			
<b>1. GENERAL</b> (Please note: If 1.a is NOT entered, then section 5 later in form must be marked as "Yes" in its check box.)			
a. United States Patent Number US 8617595		b. Issue Date of Patent 12/31/2013	c. Expiration Date of Patent 07/02/2026
d. Name of Patent Owner Noden Pharma DAC			
Address (of Patent Owner) D'Olier Chambers, 16A D'Olier Street		City Dublin	
State/Province/Region Dublin	Country Ireland	ZIP or Postal Code 2	
FAX Number (if available)	Telephone Number (857) 707 2416	E-Mail Address (if available) efarah@nodenpharma.com	
Click for additional set of 1.d. entries (includes all address and related contact items above). May be repeated.			Add Section 1.d.
e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (j)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant does not reside or have a place of business within the United States)  Name: Janelle Delk, QuintilesIMS		Address (of agent or representative named in 1.e.) 275 NW Beau Dr.  City/State Blue Springs, Missouri  ZIP Code 64014  Telephone Number 913 626 4766	
		FAX Number (if available) 913 800 4144	E-Mail Address (if available) janelle.delk@quintilesims.com
Click for additional set of 1.e. entries (includes all address and related contact items above). May be repeated.			Add Section 1.e.

f. Name of NDA Applicant Noden Pharma DAC			
Address (of NDA Applicant) D'Olier Chambers, 16A D'Olier Street		City Dublin	
State/Province/Region Dublin		Country Ireland	ZIP or Postal Code 2
FAX Number (if available) N/A	Telephone Number +35386 1409300	E-Mail Address (if available) rdoneian@nodenpharma.com	
g. Has the patent referenced above been submitted previously for the NDA or supplement? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No			
h. If the answer to question 1.g. is "Yes," identify all change(s) from the previously submitted Form 3542a and specify whether each change is related to the patent or related to an FDA action or procedure. Change in patent owner.			
<p><i>For the patent referenced above, provide the following information on whether the patent claims the drug substance, drug product, and/or method of use that is the subject of the pending NDA, amendment, or supplement.</i></p> <ul style="list-style-type: none"> <li><i>If the patent is eligible for listing as claiming the drug substance and section 2 is completed, it is not necessary to complete section 3 even if the patent also is eligible for listing as claiming the drug product.</i></li> <li><i>If the patent is eligible for listing as claiming the drug product and section 3 is completed, it is not necessary to complete section 2 even if the patent also is eligible for listing as claiming the drug substance.</i></li> </ul>			
<b>2. DRUG SUBSTANCE (ACTIVE INGREDIENT)</b>			
2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? If yes, skip to Question 2.5. <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			
2.2 Does the patent claim only a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). <input type="checkbox"/> Yes <input type="checkbox"/> No			
2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.			
2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			
2.6 Does the patent claim only an intermediate? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? <input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> Yes <input type="checkbox"/> No			
<b>3. DRUG PRODUCT (COMPOSITION/FORMULATION)</b>			
3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No			
3.2 Does the patent claim only an intermediate? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			
3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? <input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> Yes <input type="checkbox"/> No			

<b>4. METHOD OF USE</b>	
<p><i>NDA applicants must submit the information in section 4 for each method of using the proposed drug product for which approval is being sought and that is claimed by the patent. An NDA applicant may list together multiple patent claims for each pending method of use; however, each pending method of use claimed by the patent must be separately identified within this section. Continuation pages may be used to separately list method of use information within this section. For each pending method of use claimed by the patent, provide the following information:</i></p>	
<p>4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?</p>	<p><input checked="" type="checkbox"/> Yes (only one pending method of use)      <input type="checkbox"/> No  <input type="checkbox"/> Yes (more than one pending method of use)</p>
<p>4.2 Patent Claim Number(s) (as listed in the patent) (Please separate numbers with commas.) 19</p>	<p>Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?</p> <p><input checked="" type="checkbox"/> Yes      <input type="checkbox"/> No</p>
<p>4.2a If the answer to 4.2 is "Yes," for each pending method of use, separately identify the specific section(s) and subsection(s) of the proposed labeling for the drug product that describe the method of use claimed by the patent. If there is more than one pending method of use, please use the "Add Section 4.2" button for additional entries as needed.</p>	<p>Use (In your answer below, please list each section on a separate line. Within each line, separate each subsection with a comma.) The treatment of hypertension</p>
<p>If more than one pending method of use, click to add a new set of Section 4.2 entries. May be repeated. <span style="border: 1px solid black; padding: 2px;">Add Section 4.2</span></p>	
<b>5. NO RELEVANT PATENTS</b>	
<p>For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.</p> <p style="text-align: right;"><input type="checkbox"/> Yes</p>	

6. DECLARATION CERTIFICATION			
<p><b>6.1 The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</b></p> <p><b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b></p>			
<p>6.2 Authorized Signature of NDA Applicant or Patent Owner (Attorney, Agent, Representative or other Authorized Official) (Provide information below)</p> <p><i>Elie Farah</i> <span style="border: 1px solid black; padding: 2px;">Sign</span></p>		<p>Date Signed</p> <p>March 20, 2017</p>	
<p>6.3 Countersignature of Authorized U.S. Agent</p> <p><span style="border: 1px solid black; padding: 2px;">Countersign</span></p>		<p>Date Signed</p>	
<p><b>NOTE: Only an NDA applicant may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b></p>			
<p>Check applicable box and provide information below.</p>			
<input checked="" type="checkbox"/> NDA Applicant		<input type="checkbox"/> NDA Applicant's Attorney, Agent (Representative) or Other Authorized Official	
<input type="checkbox"/> Patent Owner		<input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official	
<p>Name</p> <p>Elie Farah</p>			
<p>Address</p> <p>D'Olier Chambers, 16A D'Olier Street</p>		<p>City</p> <p>Dublin</p>	
<p>State/Province/Region</p> <p>Dublin</p>		<p>Country</p> <p>Ireland</p>	<p>ZIP or Postal Code</p> <p>2</p>
<p>FAX Number (if available)</p>		<p>Telephone Number</p> <p>(857) 707-2416</p>	<p>E-Mail Address (if available)</p> <p>efarah@nodenpharma.com</p>
<p>This section applies only to requirements of the Paperwork Reduction Act of 1995.</p> <p><b>*DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.*</b></p> <p>The burden time for this collection of information is estimated to average 15 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:</p> <p style="text-align: center;">           Department of Health and Human Services            Food and Drug Administration            Office of Operations            Paperwork Reduction Act (PRA) Staff            PRASStaff@fda.hhs.gov         </p> <p style="text-align: center;"><i>"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."</i></p>			

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Food and Drug Administration

**PATENT INFORMATION SUBMITTED WITH THE  
FILING OF AN NDA, AMENDMENT, OR SUPPLEMENT**  
*For Each Patent That Claims a Drug Substance  
(Active Ingredient), Drug Product (Formulation and  
Composition) and/or Method of Use*

Form Approved: OMB No. 0910-0513  
Expiration Date: 09/30/2019  
See OMB Statement on last page.

NDA Number  
021985

Name of NDA Applicant  
Noden Pharma DAC

Refer to instruction sheet (Form FDA 3542a Supplement) for more information.

The following is provided in accordance with Section 505(b) and (c) of the Federal Food, Drug, and Cosmetic Act.

Trade Name (or proposed Trade Name) Tekturna	Active Ingredient(s) alisikiren
Dosage Form(s) Tablet	Strength(s) 150 mg, 300 mg
Route(s) of Administration Oral	Type of Use <input checked="" type="checkbox"/> Prescription <input type="checkbox"/> Over-the-Counter

This patent declaration form is required to be submitted to the Food and Drug Administration (FDA) with an NDA, amendment, or supplement as required by 21 CFR 314.53 at the address provided in 21 CFR 314.53(d)(4). Within thirty (30) days after the date of approval of an NDA or supplement, or within thirty (30) days of issuance of a new patent, a new patent declaration must be submitted on Form FDA 3542 pursuant to 21 CFR 314.53(c)(2)(ii) with all of the required information based on the approved NDA or supplement. FDA will not list or publish patent information in the Orange Book if it is not submitted in the declaration form submitted upon or after approval.

FDA will not list patent information if the patent declaration does not contain the information required by 21 CFR § 314.53(c)(2) or the patent declaration indicates the patent is not eligible for listing.

For each patent submitted for the pending NDA, amendment, or supplement referenced above, you must submit the information described below. If you are not submitting any patents for this pending NDA, amendment, or supplement, complete the section above and sections 5 and 6.

**1. GENERAL** (Please note: If 1.a is NOT entered, then section 5 later in form must be marked as "Yes" in its check box.)

a. United States Patent Number US 5559111	b. Issue Date of Patent 09/24/1996	c. Expiration Date of Patent 07/21/2018
d. Name of Patent Owner Noden Pharma DAC		
Address (of Patent Owner) D'Olier Chambers, 16A D'Olier Street		City Dublin
State/Province/Region Dublin	Country Ireland	ZIP or Postal Code 2
FAX Number (if available)	Telephone Number (857) 707 2416	E-Mail Address (if available) efarah@nodenpharma.com

Click for additional set of 1.d. entries (includes all address and related contact items above). May be repeated.

Add Section 1.d.

e. Name of agent or representative who resides or maintains a place of business within the United States authorized to receive notice of patent certification under section 505(b)(3) and (i)(2)(B) of the Federal Food, Drug, and Cosmetic Act and 21 CFR 314.52 and 314.95 (if patent owner or NDA applicant does not reside or have a place of business within the United States)  Name: Janelle Delk, QuintilesIMS	Address (of agent or representative named in 1.e.) 275 NW Beau Dr.	
	City/State Blue Springs, Missouri	
	ZIP Code 64014	FAX Number (if available) 913 800 4144
	Telephone Number 913 626 4766	E-Mail Address (if available) janelle.delk@quintilesims.com

Click for additional set of 1.e. entries (includes all address and related contact items above). May be repeated.

Add Section 1.e.

f. Name of NDA Applicant Noden Pharma DAC			
Address (of NDA Applicant) 16A D'Olier Street		City Dublin	
State/Province/Region D'Olier Chambers		Country Ireland	ZIP or Postal Code 2
FAX Number (if available) N/A	Telephone Number +35386 1409300	E-Mail Address (if available) rdonelan@nodenpharma.com	
g. Has the patent referenced above been submitted previously for the NDA or supplement? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No			
h. If the answer to question 1.g. is "Yes," identify all change(s) from the previously submitted Form 3542a and specify whether each change is related to the patent or related to an FDA action or procedure. Change of patent owner.			
<p><i>For the patent referenced above, provide the following information on whether the patent claims the drug substance, drug product, and/or method of use that is the subject of the pending NDA, amendment, or supplement.</i></p> <ul style="list-style-type: none"> <li><i>• If the patent is eligible for listing as claiming the drug substance and section 2 is completed, it is not necessary to complete section 3 even if the patent also is eligible for listing as claiming the drug product.</i></li> <li><i>• If the patent is eligible for listing as claiming the drug product and section 3 is completed, it is not necessary to complete section 2 even if the patent also is eligible for listing as claiming the drug substance.</i></li> </ul>			
<b>2. DRUG SUBSTANCE (ACTIVE INGREDIENT)</b>			
2.1 Does the patent claim the drug substance that is the active ingredient in the drug product described in the pending NDA, amendment, or supplement? If yes, skip to Question 2.5. <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No			
2.2 Does the patent claim only a drug substance that is a different polymorph of the active ingredient described in the pending NDA, amendment, or supplement? <input type="checkbox"/> Yes <input type="checkbox"/> No			
2.3 If the answer to question 2.2 is "Yes," do you certify that, as of the date of this declaration, you have test data demonstrating that a drug product containing the polymorph will perform the same as the drug product described in the NDA? The type of test data required is described at 21 CFR 314.53(b). <input type="checkbox"/> Yes <input type="checkbox"/> No			
2.4 Specify the polymorphic form(s) claimed by the patent for which you have the test results described in 2.3.			
2.5 Does the patent claim only a metabolite of the active ingredient pending in the NDA or supplement? (Complete the information in section 4 below if the patent claims a pending method of using the pending drug product to administer the metabolite.) <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			
2.6 Does the patent claim only an intermediate? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			
2.7 If the patent referenced in 2.1 is a product-by-process patent, is the product claimed in the patent novel? <input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> Yes <input type="checkbox"/> No			
<b>3. DRUG PRODUCT (COMPOSITION/FORMULATION)</b>			
3.1 Does the patent claim the drug product, as defined in 21 CFR 314.3, in the pending NDA, amendment, or supplement? <input checked="" type="checkbox"/> Yes <input type="checkbox"/> No			
3.2 Does the patent claim only an intermediate? <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No			
3.3 If the patent referenced in 3.1 is a product-by-process patent, is the product claimed in the patent novel? <input checked="" type="checkbox"/> Not Applicable <input type="checkbox"/> Yes <input type="checkbox"/> No			

**4. METHOD OF USE**

*NDA applicants must submit the information in section 4 for each method of using the proposed drug product for which approval is being sought and that is claimed by the patent. An NDA applicant may list together multiple patent claims for each pending method of use; however, each pending method of use claimed by the patent must be separately identified within this section. Continuation pages may be used to separately list method of use information within this section. For each pending method of use claimed by the patent, provide the following information:*

4.1 Does the patent claim one or more methods of use for which approval is being sought in the pending NDA, amendment, or supplement?  Yes (only one pending method of use)  No   
  Yes (more than one pending method of use)

4.2 Patent Claim Number(s) (as listed in the patent) (Please separate numbers with commas.)

9

Does (Do) the patent claim(s) referenced in 4.2 claim a pending method of use for which approval is being sought in the pending NDA, amendment, or supplement?

Yes  No

4.2a If the answer to 4.2 is "Yes," for each pending method of use, separately identify the specific section(s) and subsection(s) of the proposed labeling for the drug product that describe the method of use claimed by the patent. If there is more than one pending method of use, please use the "Add Section 4.2" button for additional entries as needed.

Use (in your answer below, please list each section on a separate line. Within each line, separate each subsection with a comma.)

The treatment of hypertension

*If more than one pending method of use, click to add a new set of Section 4.2 entries. May be repeated.*

Add Section 4.2

**5. NO RELEVANT PATENTS**

For this pending NDA, amendment, or supplement, there are no relevant patents that claim the drug substance (active ingredient), drug product (formulation or composition) or method(s) of use, for which the applicant is seeking approval and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the owner of the patent engaged in the manufacture, use, or sale of the drug product.

Yes

6. DECLARATION CERTIFICATION		
<p><b>6.1</b> <i>The undersigned declares that this is an accurate and complete submission of patent information for the NDA, amendment, or supplement pending under section 505 of the Federal Food, Drug, and Cosmetic Act. This time-sensitive patent information is submitted pursuant to 21 CFR 314.53. I attest that I am familiar with 21 CFR 314.53 and this submission complies with the requirements of the regulation. I verify under penalty of perjury that the foregoing is true and correct.</i></p> <p><b>Warning: A willfully and knowingly false statement is a criminal offense under 18 U.S.C. 1001.</b></p>		
<p><b>6.2</b> Authorized Signature of NDA Applicant or Patent Owner (<i>Attorney, Agent, Representative or other Authorized Official</i>) (Provide Information below)</p> <p><b>Elie Farah</b> Digitally signed by Elie Farah Date: 2017.03.20 11:52:14 -04'00'</p> <p style="text-align: right;"><input type="button" value="Sign"/></p>		<p>Date Signed</p> <p>03/20/2017</p>
<p><b>6.3</b> Countersignature of Authorized U.S. Agent</p> <p style="text-align: right;"><input type="button" value="Countersign"/></p>		<p>Date Signed</p>
<p><b>NOTE: Only an NDA applicant may submit this declaration directly to the FDA. A patent owner who is not the NDA applicant is authorized to sign the declaration but may not submit it directly to FDA. 21 CFR 314.53(c)(4) and (d)(4).</b></p>		
<p><b>Check applicable box and provide information below.</b></p>		
<p><input checked="" type="checkbox"/> NDA Applicant</p>		<p><input type="checkbox"/> NDA Applicant's Attorney, Agent (Representative) or Other Authorized Official</p>
<p><input type="checkbox"/> Patent Owner</p>		<p><input type="checkbox"/> Patent Owner's Attorney, Agent (Representative) or Other Authorized Official</p>
<p>Name Elie Farah</p>		
<p>Address Noden Pharma DAC, D'Olier Chambers, D'Olier Street</p>		<p>City Dublin</p>
<p>State/Province/Region Dublin</p>	<p>Country Ireland</p>	<p>ZIP or Postal Code 2</p>
<p>FAX Number (<i>if available</i>)</p>	<p>Telephone Number (857) 707-2416</p>	<p>E-Mail Address (<i>if available</i>) efarah@nodenpharma.com</p>
<p style="text-align: center;">This section applies only to requirements of the Paperwork Reduction Act of 1995.</p> <p style="text-align: center;"><b>*DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.*</b></p> <p>The burden time for this collection of information is estimated to average 15 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:</p> <p style="text-align: center;">Department of Health and Human Services Food and Drug Administration Office of Operations Paperwork Reduction Act (PRA) Staff PRAStaff@fda.hhs.gov</p> <p style="text-align: center;"><i>"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."</i></p>		



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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.**  
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/s/  
-----

MATTHEW A BACHO  
10/03/2017

PETER P STEIN  
10/03/2017



**NDA No. 21-985**  
**sNDA-Pediatric data**

**Tekturna® (aliskiren)**  
**Tablets**

**NODEN CERTIFICATION  
IN COMPLIANCE WITH THE  
GENERIC DRUG ENFORCEMENT ACT OF 1992**

Noden Pharma DAC certifies that it did not and will not use in any capacity the services of any person debarred under section 306(a) or 306(b) of the Federal Food, Drug, and Cosmetic Act in connection with this application.

Sincerely,

A handwritten signature in black ink, appearing to read "Ronan Donelan".

**Ronan Donelan Ph.D.**  
**Head of Regulatory Affairs and Pharmacovigilance**  
**Noden Pharma DAC**  
**D'Olier Chambers, 16A D'Olier Street**  
**Dublin 2, Ireland**  
**Tel: + 353 1 6778350**  
**Mobile: [REDACTED] (b) (6)**  
**[rdonelan@nodenpharma.com](mailto:rdonelan@nodenpharma.com)**

**c.c. Mike McCann, NODEN PHARMA USA INC, 75 Arlington Street, Suite 500, Boston, MA, 2116**  
**c.c. Janelle L. Delk, QUINTILESIMS, 275 NW Beau Dr. Blue Springs, Missouri, 64014**



**NDA No. 21-985**  
**Tekturna® (aliskiren)**  
**Tablets**

**Field Copy Certification Statement 21 CFR 314.50(k)(3)**

Noden Pharma DAC hereby certifies that the field copy of this submission is a true copy of the Chemistry, Manufacturing and Controls technical section; application form; and summary (as applicable) contained in the electronic archival copy of the same application. The field submission copy is being provided to the appropriate Pre-Approval Inspection coordinator, concurrent with the NDA, through notification of electronic access by copy of the NDA cover letter and Field Copy Certification Statement.

Sincerely,

A handwritten signature in black ink, appearing to read "Ronan Donelan", is written over a horizontal line.

Ronan Donelan Ph.D.  
Head of Regulatory Affairs and Pharmacovigilance  
Noden Pharma DAC  
D'Olier Chambers, 16A D'Olier Street  
Dublin 2, Ireland  
Tel: + 353 1 6778350  
Mobile: (b) (6)  
[rdonelan@nodenpharma.com](mailto:rdonelan@nodenpharma.com)

c.c. Mike McCann, NODEN PHARMA USA INC, 75 Arlington Street, Suite 500, Boston, MA, 2116  
c.c. Janelle L. Delk, QUINTILESIMS, 275 NW Beau Dr. Blue Springs, Missouri, 64014

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

/s/  
-----

ASHLEY N WALLACE  
11/22/2017

# ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION <sup>1</sup>		
NDA # 210709 BLA # N/A	NDA Supplement # N/A BLA Supplement # N/A	If NDA, Efficacy Supplement Type: N/A <i>(an action package is not required for SE8 or SE9 supplements)</i>
Proprietary Name: Tekturna® Established/Proper Name: aliskiren hemifumarate Dosage Form: Oral Pellets in Capsules		Applicant: Noden Pharma DAC Agent for Applicant (if applicable): Janelle Delk
RPM: Maryam Changi		Division: DCaRP
NDA Application Type: <input checked="" type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2) Efficacy Supplement: <input type="checkbox"/> 505(b)(1) <input type="checkbox"/> 505(b)(2)  BLA Application Type: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a) Efficacy Supplement: <input type="checkbox"/> 351(k) <input type="checkbox"/> 351(a)		<p><b><u>For ALL 505(b)(2) applications, two months prior to EVERY action:</u></b></p> <ul style="list-style-type: none"> <li><b>Review the information in the 505(b)(2) Assessment and submit the draft<sup>2</sup> to CDER OND IO for clearance.</b></li> <li><b>Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)</b></li> </ul> <p><input type="checkbox"/> No changes  <input type="checkbox"/> New patent/exclusivity <i>(notify CDER OND IO)</i>            Date of check:</p> <p><i>Note: If pediatric exclusivity has been granted or the pediatric information in the labeling of the listed drug changed, determine whether pediatric information needs to be added to or deleted from the labeling of this drug.</i></p>
❖ Actions		
<ul style="list-style-type: none"> <li>Proposed action</li> <li>User Fee Goal Date is <u>November 15, 2017</u></li> </ul>		<input checked="" type="checkbox"/> AP <input type="checkbox"/> TA <input type="checkbox"/> CR
<ul style="list-style-type: none"> <li>Previous actions <i>(specify type and date for each action taken)</i></li> </ul>		<input checked="" type="checkbox"/> None
❖ If accelerated approval or approval based on efficacy studies in animals, were promotional materials received? Note: Promotional materials to be used within 120 days after approval must have been submitted (for exceptions, see <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf</a> ). If not submitted, explain _____		<input type="checkbox"/> Received
❖ Application Characteristics <sup>3</sup>		

<sup>1</sup> The **Application Information** Section is (only) a checklist. The **Contents of Action Package** Section (beginning on page 2) lists the documents to be included in the Action Package.

<sup>2</sup> For resubmissions, 505(b)(2) applications must be cleared before the action, but it is not necessary to resubmit the draft 505(b)(2) Assessment to CDER OND IO unless the Assessment has been substantively revised (e.g., new listed drug, patent certification revised).

<sup>3</sup> Answer all questions in all sections in relation to the pending application, i.e., if the pending application is an NDA or BLA supplement, then the questions should be answered in relation to that supplement, not in relation to the original NDA or BLA.

Review priority:  Standard  Priority  
 Chemical classification (new NDAs only):  
 (*confirm chemical classification at time of approval*)

- |   |   |
|---|---|
| <input type="checkbox"/> Fast Track                       | <input type="checkbox"/> Rx-to-OTC full switch    |
| <input type="checkbox"/> Rolling Review                   | <input type="checkbox"/> Rx-to-OTC partial switch |
| <input type="checkbox"/> Orphan drug designation          | <input type="checkbox"/> Direct-to-OTC            |
| <input type="checkbox"/> Breakthrough Therapy designation |   |

(NOTE: Set the submission property in DARRTS and notify the CDER Breakthrough Therapy Program Manager;  
 Refer to the "RPM BT Checklist for Considerations after Designation Granted" for other required actions: [CST SharePoint](#))

NDAs: Subpart H

- Accelerated approval (21 CFR 314.510)  
 Restricted distribution (21 CFR 314.520)

Subpart I

- Approval based on animal studies

- Submitted in response to a PMR  
 Submitted in response to a PMC  
 Submitted in response to a Pediatric Written Request

BLAs: Subpart E

- Accelerated approval (21 CFR 601.41)  
 Restricted distribution (21 CFR 601.42)

Subpart H

- Approval based on animal studies

- REMS:  MedGuide  
 Communication Plan  
 ETASU  
 MedGuide w/o REMS  
 REMS not required

Comments: This application came as an efficacy supplement under NDA 21985, on April 6, 2017. Since the applicant introduced the new dosage form (after confirming with CMC and user fee staff), it was decided that the new NDA is a more appropriate approach. The sponsor paid the appropriate user fee for new NDA on 5/15/2017.

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 ( <i>approvals only</i> )	<input type="checkbox"/> Yes <input type="checkbox"/> No
❖ Public communications ( <i>approvals only</i> )	
• Office of Executive Programs (OEP) liaison has been notified of action	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
• Indicate what types (if any) of information were issued	<input type="checkbox"/> None <input type="checkbox"/> FDA Press Release <input type="checkbox"/> FDA Talk Paper <input type="checkbox"/> CDER Q&As <input checked="" type="checkbox"/> Other Facebook/twitter
❖ Exclusivity	
• Is approval of this application blocked by any type of exclusivity (orphan, 5-year NCE, 3-year, pediatric exclusivity)? • If so, specify the type	<input checked="" type="checkbox"/> No <input type="checkbox"/> Yes
❖ Patent Information (NDAs only)	
• Patent Information: Verify that form FDA-3542a was submitted for patents that claim the drug for which approval is sought.	<input checked="" type="checkbox"/> Verified <input type="checkbox"/> Not applicable because drug is an old antibiotic.
<b>CONTENTS OF ACTION PACKAGE</b>	
<b>Officer/Employee List</b>	
❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list ( <i>approvals only</i> )	<input checked="" type="checkbox"/> Included
Documentation of consent/non-consent by officers/employees	<input checked="" type="checkbox"/> Included

Action Letters	
❖ Copies of all action letters ( <i>including approval letter with final labeling</i> )	Action(s) and date: Approval/ 11/14/17
Labeling	
❖ Package Insert ( <i>write submission/communication date at upper right of first page of PI</i> )	
<ul style="list-style-type: none"> <li>Most recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)</li> </ul>	<input type="checkbox"/> Included
<ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>	<input checked="" type="checkbox"/> Included
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling ( <i>write submission/communication date at upper right of first page of each piece</i> )	<input type="checkbox"/> Medication Guide <input checked="" type="checkbox"/> Patient Package Insert <input checked="" type="checkbox"/> Instructions for Use <input type="checkbox"/> Device Labeling <input type="checkbox"/> None
<ul style="list-style-type: none"> <li>Most-recent draft labeling (<i>if it is division-proposed labeling, it should be in track-changes format</i>)</li> </ul>	<input type="checkbox"/> Included
<ul style="list-style-type: none"> <li>Original applicant-proposed labeling</li> </ul>	<input type="checkbox"/> Included
❖ Labels ( <b>full color</b> carton and immediate-container labels) ( <i>write submission/communication date on upper right of first page of each submission</i> )	
<ul style="list-style-type: none"> <li>Most-recent draft labeling</li> </ul>	<input type="checkbox"/> Included
❖ Proprietary Name	
<ul style="list-style-type: none"> <li>Acceptability/non-acceptability letter(s) (<i>indicate date(s)</i>)</li> <li>Review(s) (<i>indicate date(s)</i>)</li> </ul>	Acceptable 10/20/2017
❖ Labeling reviews ( <i>indicate dates of reviews</i> )	RPM: <input type="checkbox"/> None 07/13/2017; 11/14/17 DMEPA: <input type="checkbox"/> None 10/10/2017; 10/20/2017 DMPP/PLT (DRISK): <input type="checkbox"/> None 10/18/2017 OPDP: <input type="checkbox"/> None 10/17/2017;10/18/2017 SEALD: <input checked="" type="checkbox"/> None CSS: <input checked="" type="checkbox"/> None Product Quality <input checked="" type="checkbox"/> None Other: <input checked="" type="checkbox"/> None
Administrative / Regulatory Documents	
❖ RPM Filing Review <sup>4</sup> /Memo of Filing Meeting ( <i>indicate date of each review</i> )	7/14/2017
❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	<input checked="" type="checkbox"/> Not a (b)(2)
❖ NDAs/NDA supplements only: Exclusivity Summary ( <i>signed by Division Director</i> )	<input checked="" type="checkbox"/> Completed ( <b>Do not include</b> )
❖ Application Integrity Policy (AIP) Status and Related Documents <a href="http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm">http://www.fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm</a>	
<ul style="list-style-type: none"> <li>Applicant is on the AIP</li> </ul>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

<sup>4</sup> Filing reviews for scientific disciplines are NOT required to be included in the action package.

<ul style="list-style-type: none"> <li>• This application is on the AIP <ul style="list-style-type: none"> <li>○ If yes, Center Director’s Exception for Review memo (<i>indicate date</i>)</li> <li>○ If yes, OC clearance for approval (<i>indicate date of clearance communication</i>)</li> </ul> </li> </ul>	<input type="checkbox"/> Yes <input type="checkbox"/> No  <input type="checkbox"/> Not an AP action
<ul style="list-style-type: none"> <li>❖ Pediatrics (<i>approvals only</i>) <ul style="list-style-type: none"> <li>• Date reviewed by PeRC <u>09/20/2017</u> If PeRC review not necessary, explain: _____</li> </ul> </li> </ul>	<p>The sponsor submitted this application is 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). We met with Pediatrics exclusivity Board on 9/12/2017, in which the pediatric exclusivity was granted (the Division was notified on 10/3/2017) an email was sent to the applicant on 10/5/2017.</p>
<ul style="list-style-type: none"> <li>❖ Breakthrough Therapy Designation</li> </ul>	<input checked="" type="checkbox"/> N/A
<ul style="list-style-type: none"> <li>• Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)</li> </ul>	N/A
<ul style="list-style-type: none"> <li>• CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) (<i>include only the completed template(s) and not the meeting minutes</i>)</li> </ul>	N/A
<ul style="list-style-type: none"> <li>• CDER Medical Policy Council Brief – Evaluating a Breakthrough Therapy Designation for Rescission Template(s) (<i>include only the completed template(s) and not the meeting minutes</i>)</li> </ul> <p>(<i>completed CDER MPC templates can be found in DARRTS as clinical reviews or on the <a href="#">MPC SharePoint Site</a></i>)</p>	N/A
<ul style="list-style-type: none"> <li>❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, Formal Dispute Resolution Request decisional letters, etc.) (<i>do not include OPDP letters regarding pre-launch promotional materials as these are non-disclosable; do not include Master File letters; do not include previous action letters, as these are located elsewhere in package</i>)</li> </ul>	Included
<ul style="list-style-type: none"> <li>❖ Internal documents: memoranda, telecons, emails, and other documents considered important to include in the action package by the reviewing office/division (e.g., Regulatory Briefing minutes, Medical Policy Council meeting minutes)</li> </ul>	Included
<ul style="list-style-type: none"> <li>❖ Minutes of Meetings</li> </ul>	
<ul style="list-style-type: none"> <li>• If not the first review cycle, any end-of-review meeting (<i>indicate date of mtg</i>)</li> </ul>	<input type="checkbox"/> N/A or no mtg
<ul style="list-style-type: none"> <li>• Pre-NDA/BLA meeting (<i>indicate date of mtg</i>)</li> </ul>	<input type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>• EOP2 meeting (<i>indicate date of mtg</i>)</li> </ul>	<input type="checkbox"/> No mtg
<ul style="list-style-type: none"> <li>• Mid-cycle Communication (<i>indicate date of mtg</i>)</li> </ul>	<input type="checkbox"/> N/A
<ul style="list-style-type: none"> <li>• Late-cycle Meeting (<i>indicate date of mtg</i>)</li> </ul>	<input type="checkbox"/> N/A
<ul style="list-style-type: none"> <li>• Other milestone meetings (e.g., EOP2a, CMC focused milestone meetings) (<i>indicate dates of mtgs</i>)</li> </ul>	Type A Meeting with CMC on 9/7/2016; unofficial T-Con on March 24, 2016 (no Minutes)

❖ Advisory Committee Meeting(s)	<input checked="" type="checkbox"/> No AC meeting
• Date(s) of Meeting(s)	
<b>Decisional and Summary Memos</b>	
❖ Office Director Decisional Memo ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
Division Director Summary Review ( <i>indicate date for each review</i> )	<input type="checkbox"/> None In concurrence with Dr. Thompson's review Dated: 11/14/2017
Cross-Discipline Team Leader Review ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 11/14/2017
PMR/PMC Development Templates ( <i>indicate total number</i> )	<input checked="" type="checkbox"/> None
<b>Clinical</b>	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> No separate review 10/12/2017
• Clinical review(s) ( <i>indicate date for each review</i> )	10/12/2017
• Social scientist review(s) (if OTC drug) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here <input type="checkbox"/> and include a review/memo explaining why not ( <i>indicate date of review/memo</i> )	Clinical Review dated: 10/12/2017
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers ( <i>indicate date of each review</i> ) <sup>5</sup>	<input type="checkbox"/> None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation ( <i>indicate date of each review</i> )	<input checked="" type="checkbox"/> N/A
❖ Risk Management <ul style="list-style-type: none"> <li>REMS Documents and REMS Supporting Document (<i>indicate date(s) of submission(s)</i>)</li> <li>REMS Memo(s) and letter(s) (<i>indicate date(s)</i>)</li> <li>Risk management review(s) and recommendations (including those by OSE and CSS) (<i>indicate date of each review and indicate location/date if incorporated into another review</i>)</li> </ul>	<input checked="" type="checkbox"/> None
❖ OSI Clinical Inspection Review Summary(ies) ( <i>include copies of OSI letters to investigators</i> )	<input checked="" type="checkbox"/> None requested
<b>Clinical Microbiology</b> <input checked="" type="checkbox"/> None	
❖ Clinical Microbiology Team Leader Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> No separate review
Clinical Microbiology Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None
<b>Biostatistics</b> <input type="checkbox"/> None	
❖ Statistical Division Director Review(s) ( <i>indicate date for each review</i> )	<input checked="" type="checkbox"/> No separate review 9/22/2017
Statistical Team Leader Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> No separate review
Statistical Review(s) ( <i>indicate date for each review</i> )	<input type="checkbox"/> None 09/22/2017

<sup>5</sup> For Part 3 combination products, all reviews from the reviewing Center(s) should be entered into the official archive (for further instructions, see "Section 508 Compliant Documents: Process for Regulatory Project Managers" located in the CST electronic repository).

<b>Clinical Pharmacology</b> <input type="checkbox"/> None	
❖ Clinical Pharmacology Division Director Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> No separate review
Clinical Pharmacology Team Leader Review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> No separate review 10/12/2017
Clinical Pharmacology review(s) <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> None in joint with Clinical Review dated: 10/12/2017
❖ OSI Clinical Pharmacology Inspection Review Summary <i>(include copies of OSI letters)</i>	<input checked="" type="checkbox"/> None requested
<b>Nonclinical</b> <input type="checkbox"/> None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> No separate review
• Supervisory Review(s) <i>(indicate date for each review)</i>	<input type="checkbox"/> No separate review 9/14/2017
• Pharm/tox review(s), including referenced IND reviews <i>(indicate date for each review)</i>	<input type="checkbox"/> None 9/14/2017
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer <i>(indicate date for each review)</i>	<input type="checkbox"/> None
❖ Statistical review(s) of carcinogenicity studies <i>(indicate date for each review)</i>	<input checked="" type="checkbox"/> No carc
❖ ECAC/CAC report/memo of meeting	<input type="checkbox"/> None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary <i>(include copies of OSI letters)</i>	<input checked="" type="checkbox"/> None requested
<b>Product Quality</b> <input type="checkbox"/> None	
❖ Product Quality Discipline Reviews <sup>6</sup>	
• Tertiary review <i>(indicate date for each review)</i>	<input type="checkbox"/> None
• Secondary review (e.g., Branch Chief) <i>(indicate date for each review)</i>	<input type="checkbox"/> None
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) <i>(indicate date for each review)</i>	<input type="checkbox"/> None 10/11/2017
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team <i>(indicate date of each review)</i>	<input checked="" type="checkbox"/> None
❖ Environmental Assessment (check one) (original and supplemental applications)	
<input checked="" type="checkbox"/> Categorical Exclusion <i>(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)</i>	Per CMC review dated 10/11/2017
<input type="checkbox"/> Review & FONSI <i>(indicate date of review)</i>	
<input type="checkbox"/> Review & Environmental Impact Statement <i>(indicate date of each review)</i>	
❖ Facilities Review/Inspection	
<input type="checkbox"/> Facilities inspections (indicate date of recommendation; within one week of taking an approval action, confirm that there is an acceptable recommendation <b>before issuing approval letter</b> ) <i>(only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)</i>	Last confirmed by CMC on 10/31/2017 <input checked="" type="checkbox"/> Acceptable <input type="checkbox"/> Withhold recommendation <input type="checkbox"/> Not applicable

<sup>6</sup> Do not include Master File (MF) reviews or communications to MF holders. However, these documents should be made available upon signatory request.

Day of Approval Activities	
❖ For all 505(b)(2) applications: <ul style="list-style-type: none"> <li>• Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)</li> </ul>	<input type="checkbox"/> No changes <input type="checkbox"/> New patent/exclusivity <i>(Notify CDER OND IO)</i> <b>N/A</b>
<ul style="list-style-type: none"> <li>• Finalize 505(b)(2) assessment</li> </ul>	<input type="checkbox"/> Done <b>N/A</b>
❖ For Breakthrough Therapy (BT) Designated drugs: <ul style="list-style-type: none"> <li>• Notify the CDER BT Program Manager</li> </ul>	<input type="checkbox"/> Done <i>(Send email to CDER OND IO)</i>
❖ For products that need to be added to the flush list (generally opioids): <a href="#">Flush List</a> <ul style="list-style-type: none"> <li>• Notify the Division of Online Communications, Office of Communications</li> </ul>	<input type="checkbox"/> Done <b>N/A</b>
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	<input checked="" type="checkbox"/> Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	<input checked="" type="checkbox"/> Done
❖ Ensure that proprietary name, if any, and established name are listed in the <i>Application Product Names</i> section of DARRTS, and that the proprietary name is identified as the “preferred” name	<input checked="" type="checkbox"/> Done
❖ Ensure Pediatric Record is accurate	<input checked="" type="checkbox"/> Done
❖ Send approval email within one business day to CDER-APPROVALS	
❖ Take Action Package (if in paper) down to Document Room for scanning within <b>two business days</b>	

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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.**  
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/s/  
-----

MARYAM K CHANGI  
11/14/2017

## Kord Bacheh Changi, Maryam

---

**From:** Delk, Janelle L. <Janelle.Delk@iqvia.com>  
**Sent:** Tuesday, November 14, 2017 4:02 PM  
**To:** Kord Bacheh Changi, Maryam; 'Ronan Donelan'  
**Subject:** RE: Noden NDA 210709

Good news Maryam!

Noden accepts the FDA dose proposal. They accept the change they have proposed in the PI.  
Michael has already confirmed that there will be no change to the IFU.

Thank you for all your help, we are very grateful for your advice and support throughout this review process for the new NDA!

Kind regards,

*Janelle Delk*

IQVIA

Mobile: (b) (6)

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**From:** Kord Bacheh Changi, Maryam [mailto:Maryam.KordBachehChangi@fda.hhs.gov]  
**Sent:** Tuesday, November 14, 2017 2:37 PM  
**To:** 'Ronan Donelan' <rdonelan@nodenpharma.com>; Delk, Janelle L. <Janelle.Delk@quintiles.com>  
**Subject:** RE: Noden NDA 210709  
**Importance:** High

Any news???

---

**From:** Kord Bacheh Changi, Maryam  
**Sent:** Tuesday, November 14, 2017 2:52 PM  
**To:** Ronan Donelan <[rdonelan@nodenpharma.com](mailto:rdonelan@nodenpharma.com)>; Monteleone, Michael V. <[Michael.Monteleone@fda.hhs.gov](mailto:Michael.Monteleone@fda.hhs.gov)>  
**Cc:** [janelle.delk@iqvia.com](mailto:janelle.delk@iqvia.com)  
**Subject:** RE: Noden NDA 210709  
**Importance:** High

Thanks, Mike for taking care of this in my absent.

Ronan- just following up to see if you have your team agreement.

Best,  
Maryam

---

**From:** Ronan Donelan [mailto:[rdonelan@nodenpharma.com](mailto:rdonelan@nodenpharma.com)]  
**Sent:** Tuesday, November 14, 2017 1:28 PM  
**To:** Monteleone, Michael V. <[Michael.Monteleone@fda.hhs.gov](mailto:Michael.Monteleone@fda.hhs.gov)>  
**Cc:** [janelle.delk@iqvia.com](mailto:janelle.delk@iqvia.com); Kord Bacheh Changi, Maryam <[Maryam.KordBachehChangi@fda.hhs.gov](mailto:Maryam.KordBachehChangi@fda.hhs.gov)>  
**Subject:** Re: Noden NDA 210709

Thanks Michael. This is appreciated.  
We will get back to you asap.  
Regards

Ronán

Sent from my iPhone

On 14 Nov 2017, at 18:17, Monteleone, Michael V. <[Michael.Monteleone@fda.hhs.gov](mailto:Michael.Monteleone@fda.hhs.gov)> wrote:

Hi Ronan –

We think the IFU can stay as it is ‘...1 to 8 capsules...’ it is possible a patient will be on just one capsule in practice, e.g. through down titration, or initiating therapy on less than the recommended starting dose at the prescriber’s discretion.

Sincerely,  
Mike

---

Michael Monteleone, MS, RAC  
Associate Director for Labeling  
Division of Cardiovascular and Renal Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
[michael.monteleone@fda.hhs.gov](mailto:michael.monteleone@fda.hhs.gov)  
p:(301) 796-1952  
f:(301) 796-9838

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**From:** Ronan Donelan [<mailto:rdonelan@nodenpharma.com>]  
**Sent:** Tuesday, November 14, 2017 12:48 PM  
**To:** Monteleone, Michael V. <[Michael.Monteleone@fda.hhs.gov](mailto:Michael.Monteleone@fda.hhs.gov)>  
**Cc:** [janelle.delk@iqvia.com](mailto:janelle.delk@iqvia.com); Kord Bacheh Changi, Maryam <[Maryam.KordBachehChangi@fda.hhs.gov](mailto:Maryam.KordBachehChangi@fda.hhs.gov)>  
**Subject:** Re: Noden NDA 210709

Thanks Michael  
Ronán

Sent from my iPhone

On 14 Nov 2017, at 17:06, Monteleone, Michael V. <[Michael.Monteleone@fda.hhs.gov](mailto:Michael.Monteleone@fda.hhs.gov)> wrote:

Hi Ronan –

We are discussing here, I hope to respond in the next hour or so.

Sincerely,  
Mike

---

Michael Monteleone, MS, RAC  
Associate Director for Labeling  
Division of Cardiovascular and Renal Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
[michael.monteleone@fda.hhs.gov](mailto:michael.monteleone@fda.hhs.gov)  
p:(301) 796-1952  
f:(301) 796-9838  
<><>

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**From:** Ronan Donelan [<mailto:rdonelan@nodenpharma.com>]  
**Sent:** Tuesday, November 14, 2017 10:43 AM  
**To:** Monteleone, Michael V. <[Michael.Monteleone@fda.hhs.gov](mailto:Michael.Monteleone@fda.hhs.gov)>;  
'[janelle.delk@iqvia.com](mailto:janelle.delk@iqvia.com)' <[janelle.delk@iqvia.com](mailto:janelle.delk@iqvia.com)>  
**Cc:** Kord Bacheh Changi, Maryam <[Maryam.KordBachehChangi@fda.hhs.gov](mailto:Maryam.KordBachehChangi@fda.hhs.gov)>  
**Subject:** RE: Noden NDA 210709

Dear Michael,  
Thank you for your email. We will review and get back to you shortly.

The IFU advises "The prescribed dose may be the contents of 1 to 8 capsules of Tekturna Oral Pellets." Should this be changed to (b) (4) ?

Thanks for your guidance and we will also be in contact.

Kind regards,  
Ronan

Ronan Donelan Ph.D.  
Head of Regulatory Affairs and Pharmacovigilance  
Noden Pharma DAC  
D'Olier Chambers, 16A D'Olier Street  
Dublin 2, Ireland

Tel: + 353 1 6778350  
Mobile: (b) (6)  
[rdonelan@nodenpharma.com](mailto:rdonelan@nodenpharma.com)

<image001.jpg>

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**From:** Monteleone, Michael V. [<mailto:Michael.Monteleone@fda.hhs.gov>]  
**Sent:** Tuesday 14 November 2017 15:26  
**To:** '[janelle.delk@iqvia.com](mailto:janelle.delk@iqvia.com)' <[janelle.delk@iqvia.com](mailto:janelle.delk@iqvia.com)>  
**Cc:** Ronan Donelan <[rdonelan@nodenpharma.com](mailto:rdonelan@nodenpharma.com)>; Kord Bacheh Changi, Maryam <[Maryam.KordBachehChangi@fda.hhs.gov](mailto:Maryam.KordBachehChangi@fda.hhs.gov)>  
**Subject:** Noden NDA 210709

Hi Janelle –

Maryam had to step out of the office for a few hours this morning and asked me to contact you. We have identified a last minute edit to the prescribing information that we would like to get your agreement on with respect to the starting dose for pediatric patients 20 kg to 50 kg. Please see attached revised PI with our rationale for the change. We'd like to have your response as soon as possible, this afternoon if you can, as we hope to be able to take action later today. If you are amenable, you can convey your agreement over email.

Please feel free to call or email with any questions,  
Sincerely,  
Mike

---

Michael Monteleone, MS, RAC  
Associate Director for Labeling  
Division of Cardiovascular and Renal Products  
Center for Drug Evaluation and Research  
Food and Drug Administration  
[michael.monteleone@fda.hhs.gov](mailto:michael.monteleone@fda.hhs.gov)  
p:(301) 796-1952  
f:(301) 796-9838  
<><>

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/s/  
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MARYAM K CHANGI  
11/14/2017

## **Kord Bacheh Changi, Maryam**

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**From:** Kord Bacheh Changi, Maryam  
**Sent:** Monday, October 30, 2017 11:28 AM  
**To:** Delk, Janelle L.  
**Subject:** Carton and Container Information Request

**Importance:** High

Dear Janelle,

We have the following Carton and Container Information Requests. 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  (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).

Please submit your response as an amendment to you NDA and via email to me by **close of business day on Thursday, November 2, 2017.**

Please confirm the receipt.

Kind Regards,

**Maryam Changi, PharmD,**

Regulatory Project Manager

Office of Drug evaluation 1

Division of Cardiovascular and Renal Products

Phone:(240) 402-2725

Email: [Maryam.Kordbachehchangi@fda.hhs.gov](mailto:Maryam.Kordbachehchangi@fda.hhs.gov)

Address for desk and courtesy copies:

Food and Drug Administration

10903 New Hampshire Avenue

White Oak, Building 22, Room 4175

Silver Spring, MD 20993

Address for official submissions to your administrative file:

Division of Cardiovascular and Renal Products

FDA, CDER, HFD-110

5901-B Ammendale Rd.

Beltsville, MD 20705-1266

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MARYAM K CHANGI  
10/30/2017

## Kord Bacheh Changi, Maryam

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**From:** Kord Bacheh Changi, Maryam  
**Sent:** Monday, October 30, 2017 11:14 AM  
**To:** Delk, Janelle L.  
**Subject:** proposed labeling NDA 210709  
**Attachments:** Final PI with Comments.docx; Final aliskiren IFU.docx; Final aliskiren ppi.docx  
**Importance:** High

Dear Janelle,

Please find attached, our proposed draft the revised labeling (PI/PPI/IFU) recommendations for NDA 210709, with the Agency's comments included. Please review with your team and let us know if you can agree to these changes

Please submit your response via email to me by close of business day on Wednesday, November 1, 2017.

Please confirm the receipt.

Kind Regards,

**Maryam Changi, PharmD,**

Regulatory Project Manager

Office of Drug evaluation 1

Division of Cardiovascular and Renal Products

Phone:(240) 402-2725

Email: [Maryam.Kordbachehchangi@fda.hhs.gov](mailto:Maryam.Kordbachehchangi@fda.hhs.gov)

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## **Kord Bacheh Changi, Maryam**

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**From:** Kord Bacheh Changi, Maryam  
**Sent:** Thursday, October 05, 2017 2:00 PM  
**To:** Delk, Janelle L.  
**Subject:** Pediatric Exclusivity Granted NDA 210709

**Importance:** High

Dear Janelle,

Pediatric Exclusivity has been granted for studies conducted on aliskiren, effective October 3, 2017, under section 505A of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 355a). This information will be reflected on CDER's pediatric web site and in the monthly update of the Orange Book.

In accordance with section 505A(e)(1) of the FD&C Act, approved drugs for which a pediatric exclusivity determination was made on or after September 27, 2007, shall have a copy of the Written Request and any amendments posted on CDER's pediatric web site within 30 days of FDA's exclusivity determination. Further, in accordance with section 505A(k)(1) of the FD&C Act, not later than 210 days after a submission of a pediatric study report seeking exclusivity the Secretary shall make available to the public the medical, statistical, and clinical pharmacology reviews of the pediatric studies contained in that report.

In addition, we remind you that section 505A(l) of the FD&C Act requires FDA to refer to its Office of Pediatric Therapeutics any report of an adverse event associated with the drug granted exclusivity that is received by FDA during the 18 months after a labeling change reflecting results of the pediatric studies you submitted to qualify for exclusivity is approved. The Director of the Office of Pediatric Therapeutics will provide for a review of the adverse event reports by the Pediatric Advisory Committee (PAC) and will obtain recommendations from that Committee on the actions, if any, FDA should take in response.

Please confirm the receipt.

Kind Regards,

**Maryam Changi, PharmD,**

Regulatory Project Manager

Office of Drug evaluation 1

Division of Cardiovascular and Renal Products

Phone:(240) 402-2725

Email: [Maryam.Kordbachehchangi@fda.hhs.gov](mailto:Maryam.Kordbachehchangi@fda.hhs.gov)

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MARYAM K CHANGI  
10/05/2017

## MEMORANDUM

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

**DATE:** October 3, 2017

**FROM:** Pediatric Exclusivity Board

**SUBJECT:** Granting of Pediatric Exclusivity for Tekturna (aliskiren) 37.5 mg Oral Pellet in Capsule

**TO:** NDA 210709/000

The Pediatric Exclusivity Board (Board) met to discuss the exclusivity determination for aliskiren. The Division of Cardiovascular and Renal Products (Division) noted that the studies were successful, and that pediatric dosing, safety, and efficacy information for treatment of hypertension in patients 6 years of age and older will be included in labeling.

The Board noted potential inconsistencies between the studies that were conducted under the Written Request (WR) and the language included in the WR (page 2 of WR Amendment 3, dated August 9, 2016):

- *Age group in which studies will be performed:*

The five pediatric age groups to which we refer in this document are:

- Neonates (age less than 1 month)
- Infants and toddlers (age 1 month to <24 months)
- Preschool children (age 2 to <6 years)
- School age children (age 6 to Tanner stage 2)
- Adolescents (Tanner stage 3 to 16 years)

The Division clarified that this WR was written in an older format in which all age groups were named, even if they were not necessarily being requested for study. Moreover, the WR clearly states that requirements will appear in highlighted text (page 1 WR Amendment 3, dated August 9, 2016): “This Written Request contains a mixture of requirements (failure to fulfill these would result in denial of exclusivity) *and* advice. We have highlighted formal requirements to make this distinction clear.” None of the age groups listed in the WR was highlighted, indicating that no particular age group was required for study. At the time of approval for use for the treatment of hypertension in adults, Noden Pharma DAC (Sponsor) was given a Pediatric Research Equity Act (PREA) postmarketing study requirement to conduct deferred studies in patients ages 6 to 16 years; a partial waiver was granted “due to too few patients < 6 years to study”. Additionally, juvenile nonclinical toxicology data subsequently indicated a potential for a substantial increase in exposure to aliskiren in pediatric patients that made it inadvisable, for

safety reasons, to study the drug in patients under 6 years of age. Specifically, juvenile toxicity studies indicated increased systemic exposure to aliskiren 85- to 385-fold in 14-day and 8-day old rats, respectively, compared with adult rats. Of note, *mdr1* gene expression in juvenile rats was also significantly lower when compared to adult rats. The increased aliskiren exposure in juvenile rats appeared to be mainly attributed to lack of maturation of P-gp. The overexposure in juvenile rats was associated with high mortality. Therefore, the labeling will include a contraindication for patients < 2 years of age, who may be at greatest risk for such an increase in exposure, and will indicate that aliskiren should not be used in patients 2 to < 6 years of age.

The Board noted that it would have been clearer to state explicitly the ages of patients to be studied in the WR, but although the drafting of the WR was not optimal, the Sponsor fairly responded to the WR because it adequately studied and labeled the moiety for patients > 6 years of age, and, given the safety issues, studies in patients < 6 years of age would not have been safe to conduct.

The Board also noted another inconsistency between the studies that were conducted under the WR and the language included in the WR. The statistical analysis section stated that (WR Amendment 3 dated August 9, 2016):

“Statistical considerations

The trial must be designed to detect a treatment effect of conventional ( $p < 0.05$ ) statistical significance. You must obtain agreement on the final statistical analysis plan, including handling of missing data, prior to 25% enrollment.

Your study must be powered to be able to detect a "clinically meaningful" treatment benefit on the primary end point. For the purpose of satisfying the Written Request, a clinically meaningful treatment benefit is considered to be a 3-mmHg effect (placebo-subtracted change from baseline) on either systolic or diastolic pressure.”

The Sponsor did not conduct a study that was adequately powered (90%) to detect a 3-mmHg difference. The Sponsor’s study was designed with 90% power to detect a difference of 5.5 mmHg in msSBP. According to the Sponsor, the conduct of a study with 90% power to detect a 3 mmHg difference was not operationally feasible. According to the Sponsor’s power calculation, based on a 5.5 mmHg treatment difference with 90% power with a standard deviation of 10 mm Hg, 275 patients needed to be randomized. A 3 mmHg treatment difference would have increased the sample size to 907 randomized patients, which the sponsor asserted would have been very difficult to recruit in a reasonable timeframe. The Sponsor asserted that the study as designed would “allow completion of a comparatively large trial with a high probability of obtaining interpretable and clinically meaningful data in a reasonable timeframe.”

The Sponsor noted in their annotated WR that (Appendix 1; Annotated WR from Novartis, page 19):

“In sum, strictly speaking, the study sample size did not meet the terms of the Written Request in that the study was not adequately powered to exclude a 3 mmHg effect size. Nevertheless, given the size of the trial needed to power the study to exclude a 3 mmHg effect size and the fact that the study results can be viewed as interpretable (in so much as

they provide the data need to derive dosing recommendations), we believe the study that was conducted fairly responds to the WR.”

The Sponsor further clarified (Appendix 1; Annotated WR from Novartis, page 15) that:

“As noted in an FDA co-authored paper (Benjamin DK, Smith B, Jadhav P et al 2008), a major advantage of studies of type C trial design is that they are considered interpretable regardless of outcome. The powering of Study SPP100A2365 was appropriate and also consistent with other hypertension studies that have served as the basis of pediatric exclusivity awards from the Agency.”

In discussions before the Board, the Division clarified that language in the statistical considerations section was included to ensure that if the study failed (i.e., the study failed to detect a treatment effect) it could nonetheless be interpretable because they could rule out the possibility that the study failed because it was not adequately powered. Because the study successfully demonstrated a blood pressure effect, this provision of the WR (and the need to ensure that a negative study is interpretable) was not implicated by this development program. Therefore, the Division agreed that the study detected a treatment effect and therefore fairly responded to this aspect of the WR.

The Board again noted that it would have been clearer to amend the statistical analysis plan to reflect the smaller study that the Sponsor planned to conduct (and ultimately conducted) and to state explicitly that the Sponsor assumed the risk for not being granted exclusivity if the study results were uninterpretable because the study failed. However, the Board does not conclude that the failure to obtain an amended WR makes this drug ineligible for pediatric exclusivity since the study did demonstrate a BP response to aliskiren.

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/s/  
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MATTHEW A BACHO  
10/03/2017

PETER P STEIN  
10/03/2017

## Kord Bacheh Changi, Maryam

---

**From:** Kord Bacheh Changi, Maryam  
**Sent:** Friday, September 15, 2017 11:15 PM  
**To:** 'Janelle L. Delk'  
**Subject:** prposed labeling NDA 210709  
**Attachments:** final proposedlabeling 210709 (3).docx

**Importance:** High

Dear Janelle,

Please find attached, our proposed draft the revised labeling recommendations for NDA 210709, with the Agency's comments included. Please review with your team and let us know if you can agree to these changes

Please submit your response via email to me by **close of business day on September 29 , 2017.**

Please confirm the receipt.

Kind Regards,

**Maryam Changi, PharmD,**

Regulatory Project Manager

Office of Drug evaluation 1

Division of Cardiovascular and Renal Products

Phone:(240) 402-2725

Email: [Maryam.Kordbachehchangi@fda.hhs.gov](mailto:Maryam.Kordbachehchangi@fda.hhs.gov)

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MARYAM K CHANGI  
09/16/2017



NDA 210709

**INFORMATION REQUEST**

Noden Pharma DAC  
C/O Quintiles  
Attention: Janice Delk  
Associate Director, Global Regulatory Affairs QuintilesIMS  
NW Beau Drive , Suite 275  
Blue Springs. MO 64014

Dear Ms. Delk:

Please refer to your New Drug Application (NDA) dated April 4, 2017, received, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tekturna (Aliskiren)

We are reviewing the Chemistry Manufacturing and Controls section of your submission and have the following comments and information requests. We request a written response no later than August 31, 2017 in order to continue our evaluation of your NDA.

1. We are concerned about the potential risks associated with direct consumption (i.e. swallowing) of size 0 capsules by young children. Please provide the following information to support our assessment of potential risks presented by swallowing the capsule whole across the age range proposed for this product:
  - a. A risk assessment regarding the potential choking hazard for this dosage form. Include any additional information that supports this risk assessment.
  - b. Information characterizing the solution or suspension made by mixing the pellets in a glass of potable water. Include information on the physico-chemical properties, dose uniformity, and in-use stability of the resulting solution or suspension. Comment on whether or not rinsing of the glass is required to ensure complete administration of the dose across the proposed dose range.
  - c. Information on the amount of water needed for the dissolution of all the pellets required across the proposed dose range. Include information on solubility of the total number of pellets required for each dose in potable water across the proposed dose range. Also include information on the solubility of the total number of whole capsules required for each dose in potable water across the proposed dose range.
  - d. Additional dissolution data to support the formulation bridging between the pellets alone versus the whole capsule filled with pellets. Provide the comparative

- multipoint dissolution profile data (n=12, individual, mean, RSD, and profiles with the time points of 10, 15, 20, 30, 45, and 60 minutes) in multi-media encompassing the physiologic pH range in the gastrointestinal tract (e.g., water, 0.1N HCl, and USP buffer media at pH 4.5 and 6.8) for both pellets and the whole capsule using the same dissolution testing conditions (e.g., USP Apparatus 1 at 100 rpm). Submit the complete dissolution profile data in “.xlsx” or “.xpt” format.
- e. Physical samples of the drug product packaged in the intended commercial packaging. These samples can be of placebo product as long as it is fully representative of the commercial dosage form. If possible, please provide three separate samples.
2. For the Novartis Pharma AG, API (Aliskiren) manufacturing site located in (b) (4), please confirm that the facility is ready for inspection. Identify if API from the facility has been used in regulatory stability batches, and if the facility will be used for commercial API supply. For stability testing by X-ray diffraction pattern, Impurity by ion chromatography, Specific polymorph by X-ray diffraction, Heavy metals by ICP-OES and Microbial Enumeration Test (MET), identify all facilities responsible for this testing. Update all the relevant components in the eCDT format for Module 3 and Form FDA 356h to reflect the current facilities information
  3. Submit stability data to support the proposed maximum hold times for the process intermediates, i.e. (b) (4).
  4. Please update the labeling to include a salt equivalency statement to indicate the amount of active moiety related to the amount of active ingredient (i.e. salt form of the drug substance.) in Section 11. A salt equivalency statement should be included in the carton and container labels, space permitting. Please refer to FDA Guidance for Industry Naming of Drug Products Containing Salt Drug Substances (<https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm379753.pdf>) for more information.
  - 5.

If you have any questions, please contact me, at (240) 402-7765.

Sincerely,

*{See appended electronic signature page}*

CDR Grafton G Adams R.N., M.S.  
Senior Regulatory Business Process Manager  
Office of Program and Regulatory Operations  
Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research



Grafton  
Adams

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NDA 210709

**FILING COMMUNICATION –  
NO FILING REVIEW ISSUES IDENTIFIED**

Noden Pharma DAC  
c/o: Quintiles IMS  
Attention: Janelle Delk  
Associate Director, Global Regulatory Affairs  
NW Beau Drive, Suite 275  
Blue Springs, MO 64014

Dear Ms. Delk:

Please refer to your New Drug Application (NDA) received May 15, 2017, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA), for Tekturna (aliskiren) 37.5 mg Oral Pellet in Capsule.

We also refer to your amendments(s) dated June 5, 20, and 30, 2017 and July 7, and 12, 2017.

We have completed our filing review and have determined that your application is sufficiently complete to permit a substantive review. Therefore, in accordance with 21 CFR 314.101(a), this application is considered filed 60 days after the date we received your application. The review classification for this application is **Priority**. Therefore, the user fee goal date is November 15, 2017.

We are reviewing your application according to the processes described in the Guidance for Review Staff and Industry: Good Review Management Principles and Practices for PDUFA Products. Therefore, we have established internal review timelines as described in the guidance, which includes the timeframes for FDA internal milestone meetings (e.g., filing, planning, mid-cycle, team and wrap-up meetings). Please be aware that the timelines described in the guidance are flexible and subject to change based on workload and other potential review issues (e.g., submission of amendments). We will inform you of any necessary information requests or status updates following the milestone meetings or at other times, as needed, during the process. If major deficiencies are not identified during the review, we plan to communicate proposed labeling and, if necessary, any postmarketing requirement/commitment requests by September 15, 2017.

**PRESCRIBING INFORMATION**

Your proposed prescribing information (PI) must conform to the content and format regulations found at 21 [CFR 201.56\(a\) and \(d\)](#) and [201.57](#). As you develop your proposed PI, we encourage you to review the labeling review resources on the [PLR Requirements for Prescribing Information](#) and [PLLR Requirements for Prescribing Information](#) websites, which include:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- The Final Rule (Pregnancy and Lactation Labeling Rule) on the content and format of information in the PI on pregnancy, lactation, and females and males of reproductive potential
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents
- The Selected Requirements for Prescribing Information (SRPI) – a checklist of important format items from labeling regulations and guidances and
- FDA’s established pharmacologic class (EPC) text phrases for inclusion in the Highlights Indications and Usage heading.

During our preliminary review of your submitted labeling, we have identified the following labeling issues and have the following labeling comments or questions:

1. 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.*
2. 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.*
3. 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.*
4. 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.*
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.*

We request that you resubmit labeling (in Microsoft Word format) that addresses these issues by July 30, 2017. The resubmitted labeling will be used for further labeling discussions. Use the SRPI checklist to correct any formatting errors to ensure conformance with the format items in regulations and guidances. The checklist is available at the following link:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/UCM373025.pdf>

At the end of labeling discussions, use the SRPI checklist to ensure that the PI conforms with format items in regulations and guidances.

Please respond only to the above requests for information. While we anticipate that any response submitted in a timely manner will be reviewed during this review cycle, such review decisions will be made on a case-by-case basis at the time of receipt of the submission.

### **PROMOTIONAL MATERIAL**

You may request advisory comments on proposed introductory advertising and promotional labeling. Please submit, in triplicate, a detailed cover letter requesting advisory comments (list each proposed promotional piece in the cover letter along with the material type and material identification code, if applicable), the proposed promotional materials in draft or mock-up form with annotated references, and the proposed package insert (PI). Submit consumer-directed, professional-directed, and television advertisement materials separately and send each submission to:

OPDP Regulatory Project Manager  
Food and Drug Administration  
Center for Drug Evaluation and Research  
Office of Prescription Drug Promotion (OPDP)  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Alternatively, you may submit a request for advisory comments electronically in eCTD format. For more information about submitting promotional materials in eCTD format, see the draft Guidance for Industry (available at:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM443702.pdf>).

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), Medication Guide, and patient PI (as applicable), and you believe the labeling is close to the final version.

For more information regarding OPDP submissions, please see <http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm>. If you have any questions, call OPDP at 301-796-1200.

### **REQUIRED PEDIATRIC ASSESSMENTS**

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We note that you have submitted pediatric studies with this application. Once the review of this application is complete, we will notify you whether you have fulfilled the pediatric study requirement for this application.

Pediatric studies conducted under the terms of section 505B of the Federal Food, Drug, and Cosmetic Act (the Act) may also qualify for pediatric exclusivity under the terms of section 505A of the Act.

If you have any questions, please call Maryam Changi, Regulatory Project Manager, at (240) 402-2725.

Sincerely,

*{See appended electronic signature page}*

Norman Stockbridge, MD, PhD  
Director  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation I  
Center for Drug Evaluation and Research

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NORMAN L STOCKBRIDGE  
07/14/2017



NDA 210709

**INFORMATION REQUEST**

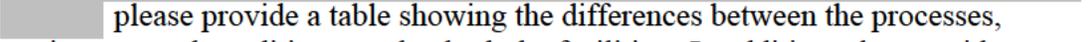
Noden Pharma DAC  
C/O Quintiles  
Attention: Janice Delk  
Associate Director, Global Regulatory Affairs QuintilesIMS  
NW Beau Drive , Suite 275  
Blue Springs. MO 64014

Dear Ms. Delk:

Please refer to your New Drug Application (NDA) dated April 4, 2017, received, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tekturna (Aliskiren)

We are reviewing the Chemistry Manufacturing and Controls section of your submission and have the following comments and information requests. We request a written response no later than June 30, 2017 in order to continue our evaluation of your NDA.

1. Provide an updated 356(h) form that lists the appropriate dosage form – capsule. The current 356(h) still lists “tablet” as the dosage form. This is inconsistent with the information provided in Module 3. Please note that the official dosage form designation is still under review.
2. Please provide a confirmatory listing of all manufacturing, testing, and packaging facilities associated with the NDA. Include the full corporate name of the facility and address where the manufacturing function is performed, with the FEI number, and specific manufacturing responsibilities for each facility. Also provide the name and title of an onsite contact person, including their phone number, fax number, and email address. Provide a brief description of the manufacturing operation conducted at each facility, including the type of testing and DMF number (if applicable).
3. Please provide the appropriate cross-reference to the drug substance information supporting the NDA such as a letter of authorization to a Drug Master File or a previous NDA submission. Alternatively, please update the appropriate sections of the submission to include the drug substance information (e.g. Modules 2 and 3).

4. Please provide the master batch records for commercial manufacturing process in 3.2.P.3.3. Description of Manufacturing Process and Process Controls.
5. Since the facilities proposed for the commercial manufacturing and testing <sup>(b) (4)</sup>   
  
 please provide a table showing the differences between the processes, equipment, and conditions used at both the facilities. In addition, also provide a justification for the data generated from the stability batches supporting the proposed expiration dating period for the commercial drug product, if approved.

If you have any questions, please contact me, at (240) 402-7765.

Sincerely,

*{See appended electronic signature page}*

CDR Grafton G Adams R.N., M.S.  
Senior Regulatory Business Process Manager  
Office of Program and Regulatory Operations  
Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research



Grafton  
Adams

Digitally signed by Grafton Adams  
Date: 6/20/2017 02:20:48PM  
GUID: 5670149e00816c175ddc15ff426aa5ee



## Kord Bacheh Changi, Maryam

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**From:** Kord Bacheh Changi, Maryam  
**Sent:** Tuesday, June 20, 2017 11:12 AM  
**To:** 'Janelle L. Delk'  
**Subject:** Information Request NDA 210709

**Importance:** High

Good Morning Janelle,

Please refer to your New Drug Application (NDA) received May 15, 2017 of the Federal Food, Drug, and Cosmetic Act for aliskiren. We are reviewing your submission and have the following information requests. We request a prompt written response in order to continue our evaluation of your NDA.

- We request that you submit the CSR and the associated appendices and datasets for Study CSPP100A2365 and everything to support this regulatory action from NDA 21985 to new NDA 210709.

Please submit your response as an amendment to your NDA and email to me by **close of business day on July 7, 2017**.

Please confirm the receipt and as always feel free to contact me if you have any questions or concerns.

Kind Regards,

### **Maryam Changi, PharmD,**

Regulatory Project Manager

Office of Drug evaluation 1

Division of Cardiovascular and Renal Products

Phone:(240) 402-2725

Email: [Maryam.Kordbachehchangi@fda.hhs.gov](mailto:Maryam.Kordbachehchangi@fda.hhs.gov)

*Address for desk and courtesy copies:*

Food and Drug Administration

10903 New Hampshire Avenue

White Oak, Building 22, Room 4175

Silver Spring, MD 20993

*Address for official submissions to your administrative file:*

Division of Cardiovascular and Renal Products

FDA, CDER, HFD-110

5901-B Ammendale Rd.

Beltsville, MD 20705-1266

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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.**  
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/s/  
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MARYAM K CHANGI  
06/20/2017



NDA 210709

## INFORMATION REQUEST

Noden Pharma DAC  
C/O Quintiles  
Attention: Janice Delk  
Associate Director, Global Regulatory Affairs Quintiles IMS  
NW Beau Drive, Suite 275  
Blue Springs, MO 64014

Dear Ms. Delk:

Please refer to your New Drug Application (NDA) dated April 4, 2017, received, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tekturna (Aliskiren)

We are reviewing the Chemistry Manufacturing and Controls section of your submission and have the following comments and information requests. We request a written response no later than September 15, 2017 in order to continue our evaluation of your NDA.

We acknowledge your responses to our August 25, 2017 Information Request, received August 31, 2017. We also acknowledge your product design (i.e. capsules as a dispensing aid) as well as your proposed administration instructions with respect to not swallowing intact capsules and identified soft foods as vehicles. However, we are evaluating various administration scenarios as part of our assessment of potential product quality issues that may impact patient safety or efficacy. To that end, please address the following:

1. Provide additional justification, supported by data, as to why water is not a compatible liquid vehicle for administration. Based on the information provided in the submission, we note [REDACTED] (b) (4). Per current EPA guidelines, the expected pH range for most drinking water sources ranges between 6.5 and 8.5. Given the difference in pH for the film-coat and drinking water, the impact of [REDACTED] (b) (4) should be minimal. Directions to consume the mixture immediately should further mitigate any potential impact to film-coat integrity.
2. Comment on the compatibility of the oral pellets with both dairy-based and non-dairy based milk products (e.g. cow milk, goat milk, soy milk, almond milk, etc.). Publically available information on the approximate pH ranges for these products show that these vehicles may be suitable for administration of the drug product. Include in the response data to support either the compatibility or the incompatibility of the drug product with this class of potential administration vehicles.

3. Provide a rationale, supported by data, for the selection of HPMC-based capsule shells in lieu of gelatin-based capsules as the proposed dispensing aid. We could not easily identify this information in the submission. If this information was previously submitted, please provide a location in the response. This information will provide additional insight into the product design chosen for commercialization.

4. Provide additional justification, supported by data, to support the assertion that (b) (4)

We could not find any data in the submission that compared fill variations or dose uniformity for the proposed drug product and drug product filled into other disposable containers. This information also will provide additional insight into the product design chosen for commercialization.

NDA 210709

Page

If you have any questions, please contact me, at (301) 796.8427

Sincerely,

*{See appended electronic signature page}*

Dahlia A. Walters, M.S., PMP  
Regulatory Business Process Manager  
Division of New Drug Products I  
Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research



Grafton  
Adams

Digitally signed by Grafton Adams  
Date: 6/6/2017 02:20:48PM  
GUID: 5870149e00816c175ddc15ff426aa5ee





Dahlia A.  
Walters

Digitally signed by Dahlia A. Walters  
Date: 9/08/2017 09:38:03AM  
GUID: 549378e2002d59c90ffeba218024f890





NDA 210709

**UNACCEPTABLE FOR FILING**

Noden Pharma DAC  
c/o: Quintiles IMS  
Attention: Janelle Delk  
Associate Director, Global Regulatory Affairs  
NW Beau Drive, Suite 275  
Blue Springs, MO 64014

Dear Ms. Delk:

Please refer to your supplemental New Drug Application (sNDA)(21985/S-033) dated and received April 6, 2017, submitted under section 505(b), Drug, and Cosmetic Act for Tekturna® (aliskiren), 150 mg and 300 mg Tablets.

We also refer to the Agency's acknowledgment letter dated April 18, 2017 for this supplement.

Under Section 736(e) of the Prescription Drug User Fee Act of 1992 as amended by the Food and Drug Administration Modernization Act of 1997, an application is considered incomplete and will not be acceptable for filing until all fees owed have been paid.

This supplemental application proposes the following change(s): 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 your submission you also proposed a new indication for the treatment of pediatric hypertension in children 6 to 17 years of age and provided complete CMC information to support the "SPP100 37.5 mg oral pellets in HPMC Capsule" formulation.

Per FDA guidance '*Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees*' (the Bundling Guidance), under section III.B., subsection 2, it specifies that a change to an approved product in terms of strength/concentration/formulation can be submitted as a supplement to the approved application, unless it changes the dosage form or routes of administration. In this case, the proposed **37.5 mg pellets in capsule** formulation has a different dosage form than the currently approved **150mg and 300mg tablets**. Therefore, the new product has to come in and be reviewed as a new NDA.

We have administratively assigned NDA 210709 to this application and all future amendments should be submitted to this application number.

Since this is a new NDA with clinical data, you need to pay a full application fee. We have verified that you paid only half application user fee (User fee I.D. PD 3016758 on April 3, 2017). From a user fee perspective the application was not correctly submitted and its user fee obligations are not met.

An application is considered incomplete and cannot be accepted for filing until all fees owed have been paid. Therefore, this application is not accepted for filing. We will not begin a review of this application's adequacy for filing until FDA has been notified that the appropriate fee has been paid. Payment should be submitted to the following address:

Food and Drug Administration  
P.O. Box 979107  
St. Louis, MO 63197-9000

Checks sent by courier should be addressed to:

U.S. Bank  
Attention: Government Lockbox 979107  
1005 Convention Plaza  
St. Louis, MO 63101

**When submitting payment for an application fee, include the User Fee I.D. Number, the Application number, and a copy of the appropriate user fee coversheet (Form 3397 or 3792) with your application fee payment. When submitting payment for previously unpaid product and establishment fees, please include the Invoice Number(s) for the unpaid fees and the summary portion of the invoice(s) with your payment. The FDA P.O. Box number P.O. Box 979107 should be included on any check you submit.**

The receipt date for this submission (which begins the filing review) will be the date the review division is notified that payment has been received by the bank. Please notify the regulatory project manager indicated below when the appropriate user fees have been sent.

Please cite the supplemental NDA number listed above at the top of the first page of all submissions to this supplemental application. Unless you are using the FDA Electronic Submissions Gateway (ESG), send all submissions by overnight mail or courier to the following address:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Cardiovascular and Renal Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

Secure email is required for all email communications from FDA when confidential information (e.g., trade secrets, manufacturing, or patient information) is included in the message. To receive email communications from FDA that include confidential information (e.g., information requests, labeling revisions, courtesy copies of letters), you must establish secure email. To establish secure email with FDA, send an email request to [SecureEmail@fda.hhs.gov](mailto:SecureEmail@fda.hhs.gov). Please note that secure email may not be used for formal regulatory submissions to applications (except for 7-day safety reports for INDs not in eCTD format).

If you wish to send payment by wire transfer, or if you have any other user fee questions, please call the Prescription Drug User Fee staff at 301-796-7900.

If you have any questions regarding this application, please contact Maryam Changi, Regulatory Project Manager, at (240) 402-2725.

Sincerely,

*{See appended electronic signature page}*

Edward Fromm, RPh, RAC  
Chief, Project Management Staff  
Division of Cardiovascular and Renal  
Products  
Office of Drug Evaluation 1  
Center for Drug Evaluation and Research

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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.**  
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/s/  
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EDWARD J FROMM  
05/30/2017



NDA 210709

**NDA ACKNOWLEDGEMENT  
USER FEES RECEIVED**

Noden Pharma DAC  
c/o: Quintiles IMS  
Attention: Janelle Delk  
Associate Director, Global Regulatory Affairs  
NW Beau Drive, Suite 275  
Blue Springs, MO 64014

Dear Ms. Delk:

Please refer to your new drug application (NDA) originally submitted April 6, 2017 (as NDA 21985/S-033) under section 505(b) of the Federal Food, Drug and Cosmetic Act for Tekturna (aliskiren) Tablets.

Please also refer to our Unacceptable for Filing letter dated May 30, 2017 that describes the reasons for changing NDA 21985/S-033 to NDA 210709.

You were notified in our letter dated May 30, 2017, that your application was not accepted for filing due to non-payment of fees. This is to inform you that the Agency has received the required fees and therefore your application has been accepted as of May 15, 2017.

If you have not already done so, promptly submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at <http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm>. Failure to submit the content of labeling in SPL format may result in a refusal-to-file action under 21 CFR 314.101(d)(3). The content of labeling must conform to the content and format requirements of revised 21 CFR 201.56-57.

You are also responsible for complying with the applicable provisions of sections 402(i) and 402(j) of the Public Health Service Act (PHS Act) [42 USC §§ 282 (i) and (j)], which was amended by Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) (Public Law No, 110-85, 121 Stat. 904).

The NDA number cited above should be included at the top of the first page of all submissions to this application. Send all submissions, electronic or paper, including those sent by overnight mail or courier, to the following address:

Food and Drug Administration  
Center for Drug Evaluation and Research  
Division of Cardiovascular and Renal Products  
5901-B Ammendale Road  
Beltsville, MD 20705-1266

If you have any questions, please contact Maryam Changi, Regulatory Project Manager, at (240)  
402- 2745

Sincerely,

*{See appended electronic signature page}*

Edward Fromm, RPh., RAC  
Chief, Project Management Staff  
Division of Cardiovascular and Renal Products  
Office of Drug Evaluation 1  
Center for Drug Evaluation and Research

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/s/  
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EDWARD J FROMM  
05/30/2017

Form Approved: OMB No. 0910 - 0297 Expiration Date: March 31, 2019. See instructions for OMB Statement, below.

**DEPARTMENT OF HEALTH AND HUMAN  
SERVICES  
FOOD AND DRUG ADMINISTRATION**

**PRESCRIPTION DRUG USER FEE  
COVERSHEET**

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on FDA's website:  
<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119184.htm>

<p>1. APPLICANT'S NAME AND ADDRESS</p> <p>Noden Pharma DAC Ronan Donelan D'Olier Chambers 16A D'Olier Street Dublin 2</p> <p>IE</p>	<p>4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER</p> <p>021-985</p>
<p>2. NAME AND TELEPHONE NUMBER OF REPRESENTATIVE</p> <p>353 86 1409300</p>	<p>5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?</p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p>IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:</p> <p><input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION</p> <p><input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:</p> <p>00202</p>
<p>3. PRODUCT NAME</p> <p>Tekturna ( aliskiren )</p>	<p>6. USER FEE I.D. NUMBER</p> <p>PD3016758</p>
<p>7. ARE YOU REDEEMING A PRIORITY REVIEW VOUCHER FOR THE TREATMENT OF TROPICAL DISEASES? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO</p> <p>PRIORITY REVIEW VOUCHER NUMBER:</p>	
<p>8. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.</p> <p><input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)</p> <p><input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act</p>	

[https://userfees.fda.gov/OA\\_HTML/pdufaCScdCfItemsPopup.jsp?vcname=Ronan%20Donelan&vcmpname=Noden%20Pharma%20DAC&vemail=rdonelan@...](https://userfees.fda.gov/OA_HTML/pdufaCScdCfItemsPopup.jsp?vcname=Ronan%20Donelan&vcmpname=Noden%20Pharma%20DAC&vemail=rdonelan@...) 1/4

[ ] THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY

9. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION? [ ] YES [X] NO

If a waiver has been granted, include a copy of the official FDA notification with your submission.

**Privacy Act Notice:**

This notice is provided pursuant to the Privacy Act of 1974, 5 U.S.C. 552a. The collection of this information is authorized by 21 U.S.C. 371, 379, 379e, 379h, 379h-1, 379j, 379j-12, 379j-21, 387s, and 393(d)(2); 42 U.S.C. 263b(r)(1); 5 U.S.C. 301 and 552; and 42 U.S.C. 3101. FDA will use the information to assess, collect and process user fee payments, and, facilitate debt collection under the Debt Collection Improvement Act. FDA may disclose information to courts and the Department of Justice in the context of litigation and requests for legal advice; to other Federal agencies in response to subpoenas issued by such agencies; to HHS and FDA employees and contractors to perform user fee services; to the National Archives and Records Administration and General Services Administration for records management inspections; to the Department of Homeland Security and other Federal agencies and contractors in order to respond to system breaches; to banks in order to process payment made by credit card; to Dun and Bradstreet to validate submitter contact information, and to other entities as permitted under the Debt Collection Improvement Act. Furnishing the requested information is mandatory. Failure to supply the information could prevent FDA from processing user fee payments. Additional detail regarding FDA's use of information is available online:

<http://www.fda.gov/RegulatoryInformation/FOI/PrivacyAct/default.htm>.

**OMB Statement:**

Public reporting burden for this collection of information is estimated to average 30 minutes per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to:

Department of Health and Human Services Food and Drug Administration Center for Biologics Evaluation and Research Office of Information Management (HFA-710) 8455 Colesville Road, COLE-14-14253 Silver Spring, MD 20993-0002	Department of Health and Human Services Food and Drug Administration Center for Drug Evaluation and Research Office of Information Management (HFA-710) 8455 Colesville Road, COLE-14-14253 Silver Spring, MD 20993-0002	An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.
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PRINTED NAME AND SIGNATURE OF AUTHORIZED REPRESENTATIVE	TITLE	DATE
<i>Ronan Donelan</i>	<i>Dr.</i>	<i>16 March 2017</i>

9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION

\$1,019,050.00

Form FDA 3397 (03/16)

**INSTRUCTIONS FOR COMPLETING PRESCRIPTION DRUG USER FEE COVER SHEET  
FORM FDA 3397**

Form FDA 3397 is to be completed for and submitted with each new drug or biologic product original application or supplemental application submitted to the Agency, unless specifically exempted below. Form FDA 3397 should be placed in the first volume of the application with the application (FORM FDA 356(h)) form. Form FDA 3397 is to be completed on-line at [http://userfees.fda.gov/OA\\_HTML/pdufaCAddlCovrShet.jsp](http://userfees.fda.gov/OA_HTML/pdufaCAddlCovrShet.jsp). If you need assistance in completing the form call 301-796-7200 or email: [userfees@fda.gov](mailto:userfees@fda.gov).

**NOTE:** Form FDA 3397 need not be submitted for:

**CDER**

- 505(j) applications
- Supplements to 505(j) applications
- 351(k) applications

**CBER**

Any supplement that does not require clinical data for approval.  
Applications and supplements for:

- \* Products for further manufacturing use only
- \* Whole blood or blood components for transfusion
- \* Bovine blood product for topical application licensed before September 1, 1992
- \* A crude allergenic extract product
- \* An in vitro diagnostic biological product licensed under Section 351 of the PHS Act
- \* 351(k) applications

ITEM NO.	INSTRUCTIONS
1-2.	<b>Self-explanatory</b>
3.	<b>PRODUCT NAME:</b> Include generic or proper name and trade name, as applicable.
4.	<b>BLA STN / NDA NUMBER - FOR AN ORIGINAL BIOLOGIC LICENSE APPLICATION (BLA)</b> - Indicate the 6-digit BLA number (Submission Tracking Number (STN)) if pre-assigned, otherwise leave blank. For A SUPPLEMENT enter the BLA STN.  <b>FOR DRUG PRODUCTS:</b> Indicate the new drug application (NDA) number. NDA numbers can be obtained by completing the information at <a href="http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm114927.htm">http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm114927.htm</a> .
5.	<b>CLINICAL DATA:</b> The definition of 'clinical data' for the assessment of user fees is found in FDA's Guidance for Industry: Submitting Separate Marketing Applications and Clinical Data for Purposes of Assessing User Fees. FDA's guidance on the definition of clinical data can be found on FDA's web site: <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079320.pdf</a> .
6.	<b>USER FEE I.D. NUMBER:</b> Please include the ID number (generated when completing Form FDA 3397) on the application payment check.
7.	<b>PRIORITY REVIEW VOUCHER:</b> If you are redeeming a priority review voucher awarded to a sponsor of a tropical disease product application (see section 524 of the Federal Food, Drug, and Cosmetic Act (FD&C Act)), please include the priority review voucher number assigned when the voucher was initially granted. See FDA's Guidance for Industry: Tropical Disease Priority Review Vouchers for further information. FDA's guidance can be found on FDA's web site: <a href="http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM080599.pdf">http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM080599.pdf</a> .
8.	<b>EXCLUSIONS:</b> The application is for an orphan drug product. Under section 736(a) (1) (F) of the FD&C Act, a human drug application is not subject to an application fee if the proposed product is for a rare disease or condition designated under section 526 of the FD&C Act (orphan drug designation) AND the application does not include an indication that is not so designated. A supplement is not subject to an application fee if it proposes to include a new indication for a rare disease or condition, and the drug has been designated pursuant to section 526 for a rare disease or condition with regard to the indication proposed in the supplement. A copy of the FDA letter granting orphan designation should be included with the BLA/NDA submission.
9.	<b>WAIVER:</b> Complete this section only if a waiver of user fees, including the small business waiver, has been granted for this application. A copy of the official FDA notification that the waiver has been granted must be provided with the BLA/NDA submission.

Form FDA 3397 (03/16) (BACK)

[Close](#) [Print](#) Cover sheet

Payment Details

Payment Reference No. 99550531

Printed On  
Tuesday, April 04, 2017  
09:56:19 AM

Pay From >	IB REPUBLIC CURRENT ACCOUNT , International , 75063001
Pay To >	FOOD AND DRUG ADMINISTRATION , 75060099
Payment Details >	\$1,019,050.00 on 03/04/2017, International Third Party Payment
Payment Currency:	USD
Payment Type:	Same Day
Payment Amount:	1,019,050.00
Payment Date:	03-04-2017
End to End Reference:	NODEN PHARMA
Payment Message:	NODEN PHARMA BLA NUMBER 021985 AND USER FEE ID NUMBER / PIN PD3016758
Status >	Payment Processed

Payment Details

Payment Reference No. 100893527

Printed On  
Monday, May 15, 2017  
02:29:45 PM

Pay From	International .
Pay To	FOOD AND DRUG ADMINISTRATION , 75060099
Payment Details	\$1,019,050.00 on 15/05/2017, International Third Party Payment
Payment Currency:	USD
Payment Type:	International
Payment Amount:	1,019,050.00
Payment Date:	15/05/2017
End to End Reference:	NODEN PHARMA
Payment Message:	PD3016876 AND NDA021985
Status	Payment Processed

Form Approved: OMB No. 0910 - 0297 Expiration Date: March 31, 2019. See instructions for OMB Statement, below.

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

**PRESCRIPTION DRUG USER FEE  
COVERSHEET**

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on FDA's website:

<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119184.htm>

**1. APPLICANT'S NAME AND ADDRESS**

Noden Pharma DAC  
Ronan Donelan  
D'Olier Chambers  
16A D'Olier Street  
Dublin 2

IE

**4. BLA SUBMISSION TRACKING NUMBER  
(STN) / NDA NUMBER**

021-985

**2. NAME AND TELEPHONE NUMBER OF  
REPRESENTATIVE**

353 86 1409300

**5. DOES THIS APPLICATION REQUIRE  
CLINICAL DATA FOR APPROVAL?**

YES  NO

IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM.

IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:

THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION

THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:

**3. PRODUCT NAME**

Tekturna ( aliskiren )

**6. USER FEE I.D. NUMBER**

PD3016876

**7. ARE YOU REDEEMING A PRIORITY REVIEW VOUCHER FOR THE TREATMENT OF TROPICAL DISEASES?**  YES  NO

PRIORITY REVIEW VOUCHER NUMBER:

**8. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.**

A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)

THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act

THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY

**9. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?**

YES  NO

If a waiver has been granted, include a copy of the official FDA notification with your submission.

**Privacy Act Notice:**

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PRINTED NAME AND SIGNATURE OF AUTHORIZED REPRESENTATIVE	TITLE	DATE

**9. USER FEE PAYMENT AMOUNT FOR THIS APPLICATION**

\$2,038,100.00

Form FDA 3397 (03/16)



## INSTRUCTIONS FOR COMPLETING PRESCRIPTION DRUG USER FEE COVER SHEET FORM FDA 3397

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Any supplement that does not require clinical data for approval.  
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ITEM NO.	INSTRUCTIONS
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Form FDA 3397 (03/16) (BACK)

Close Print Cover sheet

Form Approved: OMB No. 0910 - 0297 Expiration Date: March 31, 2019. See instructions for OMB Statement, below.

**DEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION**

**PRESCRIPTION DRUG USER FEE  
COVERSHEET**

A completed form must be signed and accompany each new drug or biologic product application and each new supplement. See exceptions on the reverse side. If payment is sent by U.S. mail or courier, please include a copy of this completed form with payment. Payment instructions and fee rates can be found on FDA's website:  
<http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm119184.htm>

<p><b>1. APPLICANT'S NAME AND ADDRESS</b></p> <p>Noden Pharma DAC Ronan Donelan D'Olier Chambers 16A D'Olier Street Dublin 2</p> <p>IE</p>	<p><b>4. BLA SUBMISSION TRACKING NUMBER (STN) / NDA NUMBER</b></p> <p>210-709</p>
<p><b>2. NAME AND TELEPHONE NUMBER OF REPRESENTATIVE</b></p> <p>353 86 1409300</p>	<p><b>5. DOES THIS APPLICATION REQUIRE CLINICAL DATA FOR APPROVAL?</b></p> <p><input checked="" type="checkbox"/> YES <input type="checkbox"/> NO</p> <p>IF YOUR RESPONSE IS "NO" AND THIS IS FOR A SUPPLEMENT, STOP HERE AND SIGN THIS FORM. IF RESPONSE IS "YES", CHECK THE APPROPRIATE RESPONSE BELOW:</p> <p><input checked="" type="checkbox"/> THE REQUIRED CLINICAL DATA ARE CONTAINED IN THE APPLICATION</p> <p><input type="checkbox"/> THE REQUIRED CLINICAL DATA ARE SUBMITTED BY REFERENCE TO:</p>
<p><b>3. PRODUCT NAME</b></p> <p>Tekturna ( aliskiren )</p>	<p><b>6. USER FEE I.D. NUMBER</b></p> <p>PD3016925</p>
<p><b>7. ARE YOU REDEEMING A PRIORITY REVIEW VOUCHER FOR THE TREATMENT OF TROPICAL DISEASES? <input type="checkbox"/> YES <input checked="" type="checkbox"/> NO</b></p> <p>PRIORITY REVIEW VOUCHER NUMBER:</p>	
<p><b>8. IS THIS APPLICATION COVERED BY ANY OF THE FOLLOWING USER FEE EXCLUSIONS? IF SO, CHECK THE APPLICABLE EXCLUSION.</b></p> <p><input type="checkbox"/> A LARGE VOLUME PARENTERAL DRUG PRODUCT APPROVED UNDER SECTION 505 OF THE FEDERAL FOOD, DRUG, AND COSMETIC ACT BEFORE 9/1/92 (Self Explanatory)</p> <p><input type="checkbox"/> THE APPLICATION QUALIFIES FOR THE ORPHAN EXCEPTION UNDER SECTION 736(a)(1)(F) of the Federal Food, Drug, and Cosmetic Act</p> <p><input type="checkbox"/> THE APPLICATION IS SUBMITTED BY A STATE OR FEDERAL GOVERNMENT ENTITY FOR A DRUG THAT IS NOT DISTRIBUTED COMMERCIALY</p>	

9. HAS A WAIVER OF AN APPLICATION FEE BEEN GRANTED FOR THIS APPLICATION?  
 YES  NO  
 If a waiver has been granted, include a copy of the official FDA notification with your submission.

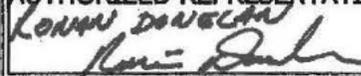
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PRINTED NAME AND SIGNATURE OF AUTHORIZED REPRESENTATIVE RONAN DONELAN 	TITLE HEAD OF REGULATORY AFFAIRS AND PV	DATE 05/25/2017
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Form FDA 3397 (03/16)



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Form FDA 3397 (03/16) (BACK)

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NDA 021985

**MEETING MINUTES**

Novartis Pharmaceuticals Corporation  
Attention: Ann-Marie van der Merwe, Global Program Regulatory Director  
One Health Plaza  
East Hanover, NJ 07869

Dear Ms. van der Merwe:

Please refer to your New Drug Application (NDA) dated August 5, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tekturna® (aliskiren) Tablets.

We also refer to the teleconference between representatives of your firm and the FDA on September 7, 2016. The purpose of the meeting was to discuss and obtain an agreement with the Agency on the proposed technical development plan and regulatory strategy for Tekturna <sup>(b) (4)</sup>, a pediatric formulation of aliskiren.

A copy of the official minutes of the teleconference is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, call Yvonne Knight, Regulatory Business Process Manager, at (301) 796-2133.

Sincerely,

*{See appended electronic signature page}*

Ramesh Raghavachari, Ph.D.  
Chief, Branch I  
Division of Post-Marketing Activities I  
Office of Lifecycle Drug Products  
Office of Pharmaceutical Quality  
Center for Drug Evaluation and Research

Enclosure:  
Meeting Minutes



**FOOD AND DRUG ADMINISTRATION  
CENTER FOR DRUG EVALUATION AND RESEARCH**

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**MEMORANDUM OF MEETING MINUTES**

**Meeting Type:** Type A  
**Meeting Category:** Chemistry

**Meeting Date and Time:** Wednesday September 7, 2016, 9:00 AM- 10 AM (EST)  
**Meeting Location:** Teleconference

**Application Number:** 021985  
**Product Name:** Tekturna® (aliskiren) Tablets

**Indication:** Treatment of hypertension  
**Sponsor/Applicant Name:** Novartis Pharmaceuticals Corp.

**Meeting Chair:** Ramesh Raghavachari, Ph.D.  
**Meeting Recorder:** Yvonne Knight, MS

Office of Lifecycle Drug Products

Ramesh Raghavachari, Ph.D., Branch Chief  
Zedong Dong, Ph.D., Acting Quality Assessment Lead  
Krishna Raman, Ph.D., Quality Reviewer  
Qi Zhang Ph.D., Biopharmaceutics Reviewer  
Elsbeth Chikhale Ph.D., Biopharmaceutics, Team Lead

Office of Process and Facilities

Steven Hertz, Ph.D., Facilities Reviewer

Office of Program and Regulatory Operations

Yvonne Knight MS, Regulatory Business Process Manager

**SPONSOR ATTENDEES**

Paul Aftring, MD	Global Program Head, Established Medicines
Kevin Carl	Global Head, Regulatory Affairs Pharmaceuticals
Fedra Limoncini	Franchise Head, Global Regulatory CMC
Yusuf Aumjaud,	Senior Manager, Global Regulatory CMC
Aldo Hoermann, Ph.D.	Project Lead, Technical Research and Development
Orin Tempkin, Ph.D.	Executive Director, Drug Regulatory Affairs
Anne-Marié van der Merwe	Global Program Regulatory Director, Drug Regulatory Affairs
Elie Farah	Noden CEO
Ronan Donelan	Noden external

Meeting Minutes  
Type A

## 1.0 BACKGROUND

The purpose of this meeting was to obtain the Agency's input and concurrence on a path forward regarding the technical development plan and regulatory strategy for Tekturna <sup>(b) (4)</sup>, a pediatric formulation of aliskiren. NDA 21985 Tekturna® was approved on March 5, 2007, for the treatment of hypertension.

In April 2015, it was determined, based on a preliminary review of the core study data and an agreement with the Division of Cardiovascular and Renal Products, that the data did not support a pediatric indication. Novartis stated that in a teleconference on March 24, 2016, the Division informed them that based on a more detailed review of the core and extension clinical data included in the sNDA, a pediatric indication was supportable, and specified that Novartis needed to submit a CMC module supporting a formulation that allows dosing in children. Novartis then withdrew the sNDA on March 25, 2016, for the purpose of resuming technical development of a pediatric dosage form and developing a CMC dossier. On May 11, 2016, Novartis submitted a request to extend the sNDA submission dates in the Written Request and PMR 91-1 to April 20, 2017 (per Section 505A of the FD&C Act, to qualify for pediatric exclusivity where the sponsor has to file 15 months prior to the patent expiry, which for Tekturna is in July 2018 ; therefore Novartis proposes a filing in April 2017).

Novartis submitted a Type A Meeting request on August 5, 2016. The Type A Teleconference Meeting was granted on August 15, 2016. The meeting package was submitted at the time of the meeting request, August 5, 2016. The Preliminary Responses were sent to the Applicant on September 2, 2016 .

## 2. DISCUSSION

***Question 1:*** *Does the Agency agree with the filing strategy for the manufacturing site and the proposed approach for the commercial supply?*

***FDA Response to Question 1:*** The Agency expects the facilities listed on the 356h FDA FORM are complete in describing the commercial supply chains of active pharmaceutical ingredients and drug products. At the time of application and supplement submission, these facilities should be ready for inspection, and the responsibilities of these facilities should be documented. If your firm intends to submit a supplement for the pediatric indication April 2017, the facilities listed should be current and accurate at that time for the proposed commercial supply chain. These facilities (and additional facilities that had manufactured registration and/or clinical batches) may be scheduled for pre-approval inspections so the Agency can determine readiness for commercial manufacturing, conformance to the application, and data integrity of the submission.

According to Table 2-1, the primary registration batches are manufactured at the Novartis Pharma Stein AG and Novartis Pharma Basel. However, the anticipated registration sites to be filed in the sNDA are Novartis Pharma Produktions GmbH, Wehr, Novartis Pharma Stein AG,

Meeting Minutes  
Type A

and (b) (4), therefore, the establishment information for all three sites should be included in the 356h form. In addition, batch analysis and three months stability data for three batches of drug product produced at the three registration sites should be provided.

Your approach to qualify the validation and commercial launch sites (Novartis Pharma Produktions GmbH, Wehr (b) (4)) appears to be acceptable.

**Meeting Discussion:**

The Agency asked for clarification in regards to sites involved in the pediatric formulation. Novartis explained that Tekturna pediatric is planned to be launched from (b) (4). The Agency reiterated to Novartis that all facilities (manufacturing and testing) submitted in the supplement's 356h form must be ready for inspection. Novartis confirmed they would comply and submit all facilities in Module 3 and the 356h form.

Novartis indicated that stability data obtained from batches manufactured at the facilities indicated in column 1 of the table is in line with ICHQ1A and that 18 months primary registration stability data will be provided. In addition, another 24 months data will be submitted within 30 days of the submission of the pediatric formulation application. Novartis specified (b) (4) will be included in the submission.

The Agency questioned Novartis as to what manufacturing and stability data will be provided for the sites listed in column 2 of the background package. Novartis responded that manufacturing and batch data would be provided for (b) (4). Novartis did state that 3-month stability data will be provided for the processing sequence (b) (4).

The Agency recommended putting the registered batches on stability and submitting the data during the submission of the supplement. Novartis states they will take the recommendation under advisement.

**Question 2:** *Does the Agency agree with the proposed approach for the drug product validation?*

**FDA Response to Question 2:** Any proposed CMC changes (including to the manufacturing equipment and/or process) made during validation should be justified in the supplement for qualifying the commercial production sites of the drug product.

In terms of the process validation life cycle, concurrent release of PPQ batches inherently carries more risk than a standard PPQ evaluation and should only be used in unique circumstances.

Meeting Minutes  
Type A

[REDACTED] (b) (4)

**Meeting Discussion:**

Novartis inquired if the Agency believes that Tektorna pediatric situation qualifies for the application of concurrent release. The Agency responded that the approach is available, but it carries higher risk. Novartis was encouraged to follow the advice of the guidance and that the concurrent release approach may be considered by the Agency if Novartis provides adequate background and justification for using the approach. [REDACTED] (b) (4)

[REDACTED] (b) (4)

**Question 3:** *Does the Agency agree with the proposed description of the dosage form in the labeling and in the quality part of the sNDA?*

**FDA Response to Question 3:** You are recommended to use “Oral Pellets” for the description of the dosage form. Because the capsule is not intended to be swallowed, we recommend that the pellets be packaged in single-unit containers such as a sachet, or similar.

**Meeting Discussion:**

The Agency reiterated the response of switching to an “Oral Pellet” for description due to the possibility of a medication error. The applicant stated they could not make a labeling change of this magnitude within a reasonable time to be able to make the filing date. The Agency then stated that this would be a subject of review and that we could not comment at this time. Novartis was advised to provide justification in the submission.

Novartis then inquired on the rationale behind the change to “Oral Pellets”. The Agency responded that the material [REDACTED] (b) (4) with a defined strength as opposed to a [REDACTED] (b) (4). The Agency stated that the term [REDACTED] (u) (4) may be acceptable but “Capsule” should not be used as the final dosage form. The Agency clarified that this recommendation reflects the current thinking of the Agency’s policy group.

**Question 4:** *Does the Agency agree with the proposed capsule size change between the registration stability batches (size 00) and the commercial product (size 0)?*

Meeting Minutes  
Type A

**FDA Response to Question 4:** Your justification provided in the meeting package appears to be acceptable. As the Agency understands, this will be submitted in the supplement for the qualification of the validation and commercial manufacturing sites. The supplement is expected to provide supporting information (batch analysis, stability data, etc.), the change in capsule size will be evaluated during the review of the supplement.

Please clarify whether there are any other differences (in addition to capsule size) between the pediatric drug product formulation used in the clinical trial(s) and the proposed commercial pediatric formulation.

**Meeting Discussion:**

Novartis concurred with the response and went on to explain that the clinical and proposed commercial pediatric formulations are equivalent and that the composition details and comparative dissolution data will be provided in the pediatric formulation submission. The Agency advised that this information should be provided in the sNDA submission.

**Question 5:** *Does the Agency agree with the proposed plan for submission of stability data during the first 30 days after the submission of the complete original application and consider the additional data for the evaluation of the shelf-life?*

**FDA Response to Question 5:** Your proposed plan appears to be acceptable.

**Meeting Discussion:** *No further discussion*

**Question 6:** *Does the Agency agree with the methodology being evaluated for the testing of the 'Uniformity of Dosage Units'?*

**FDA Response to Question 6:** Weight Variation method appears to be reasonable for the proposed drug product. However, this will be the subject of review.

**Meeting Discussion:** *No further discussion.*

## 5.0 ACTION ITEMS

Action Item/Description	Owner	Due Date
Meeting Minutes	FDA	October 7, 2016

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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.**  
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/s/  
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RAMESH RAGHAVACHARI  
10/07/2016