CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

206910Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # 206910 SUPPL # HFD # 161

Trade Name Jadenu

Generic Name deferasirox

Applicant Name Novartis Pharmaceuticals, Inc.

Approval Date, If Known

PART I IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. An exclusivity determination will be made for all original applications, and all efficacy supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following questions about the submission.

a) Is it a 505(b)(1), 505(b)(2) or efficacy supplement?

YES ☒ NO ☐

If yes, what type? Specify 505(b)(1), 505(b)(2), SE1, SE2, SE3,SE4, SE5, SE6, SE7, SE8

505(b)(1)

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")

YES ☐ NO ☒

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

The recommendation for the approval of Jadenu is based on the safety and efficacy of the marketed Exjade (deferasirox) product and the available Jadenu supportive safety information from the pharmacokinetic (PK) and bioavailability studies F2101, F2102, and F2103.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

d) Did the applicant request exclusivity?

YES ☐ NO ☒

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?

e) Has pediatric exclusivity been granted for this Active Moiety?

YES ☐ NO ☒

If the answer to the above question in YES, is this approval a result of the studies submitted in response to the Pediatric Written Request?

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS AT THE END OF THIS DOCUMENT.

2. Is this drug product or indication a DESI upgrade?

YES ☐ NO ☐

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8 (even if a study was required for the upgrade).

PART II FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES
(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety.

YES ☐ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.)

YES ☐ NO ☐

If "yes," identify the approved drug product(s) containing the active moiety, and, if known, the NDA #(s).

NDA#

NDA#

NDA#

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8. (Caution: The questions in part II of the summary should only be answered "NO" for original approvals of new molecular entities.)
IF "YES," GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDAs AND SUPPLEMENTS

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations? (The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a). If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation.

YES ☐ NO ☐

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 8.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement?

YES ☐ NO ☐

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 8:

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application?

YES ☐ NO ☐

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO.

YES ☐ NO ☐

If yes, explain:

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product?

YES ☐ NO ☐

If yes, explain:

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigations, identify each such investigation and the NDA in which each was relied upon:

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES ☐ NO ☐

Investigation #2 YES ☐ NO ☐

If you have answered "yes" for one or more investigation, identify the NDA in which a similar investigation was relied on:

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 !
!
IND # YES ☐ ! NO ☐
! Explain:

Investigation #2 !
!
IND # YES ☐ ! NO ☐
! Explain:

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

Investigation #1	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

Investigation #2	!
	!
YES ☐	! NO ☐
Explain:	! Explain:

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES ☐ NO ☐

If yes, explain:

==========

Name of person completing form: Kris Kolibab, PhD
Title: Regulatory Project Manager, Division of Hematology Products
Date: 3/16/2015

Name of Office/Division Director signing form: Ann T. Farrell, MD
Title: Director, Division of Hematology Products

Form OGD-011347; Revised 05/10/2004; formatted 2/15/05; removed hidden data 8/22/12

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

/s/

KRISTOPHER KOLIBAB
03/24/2015

ANN T FARRELL
03/30/2015

PEDIATRIC PAGE
(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: NDA 206910 Supplement Number: _____ NDA Supplement Type (e.g. SE5): _____

Division Name:Division of Hematology PDUFA Goal Date: 5/30/2015 Stamp Date: 5/30/2014

Proprietary Name: Jadenu

Established/Generic Name: deferasirox

Dosage Form: Film coated tablets

Applicant/Sponsor: Novartis Pharmaceuticals Corporation

Indication(s) *previously approved* (please complete this question for supplements and Type 6 NDAs only):
(1) _____
(2) _____
(3) _____
(4) _____

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 2
(Attach a completed Pediatric Page for each indication in current application.)

Indication: Treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older.

Q1: Is this application in response to a PREA PMR? Yes ☐ Continue
No ☒ Please proceed to Question 2.

If Yes, NDA/BLA#: _____ Supplement #:_____ PMR #:_____

Does the division agree that this is a complete response to the PMR?

☐ Yes. Please proceed to Section D.

☐ No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

Q2: Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW ☐ active ingredient(s) (includes new combination); ☒ indication(s); ☒ dosage form; ☒ dosing regimen; or ☐ route of administration?*

(b) ☐ No. PREA does not apply. **Skip to signature block.**

**** Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.***

Q3: Does this indication have orphan designation?

☒ Yes. PREA does not apply. **Skip to signature block.**

☐ No. Please proceed to the next question.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

- ☐ Yes: (Complete Section A.)
- ☐ No: Please check all that apply:
  - ☐ Partial Waiver for selected pediatric subpopulations (Complete Sections B)
  - ☐ Deferred for some or all pediatric subpopulations (Complete Sections C)
  - ☐ Completed for some or all pediatric subpopulations (Complete Sections D)
  - ☐ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
  - ☐ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

  (Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

- ☐ Necessary studies would be impossible or highly impracticable because:
  - ☐ Disease/condition does not exist in children
  - ☐ Too few children with disease/condition to study
  - ☐ Other (e.g., patients geographically dispersed): _____
- ☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- ☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

				Reason (see below for further detail):			
		minimum	maximum	Not feasible[#]	Not meaningful therapeutic benefit[*]	Ineffective or unsafe[†]	Formulation failed[Δ]
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief**

justification):

Not feasible:

☐ Necessary studies would be impossible or highly impracticable because:

☐ Disease/condition does not exist in children

☐ Too few children with disease/condition to study

☐ Other (e.g., patients geographically dispersed): _____

***** Not meaningful therapeutic benefit:

☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

Δ Formulation failed:

☐ Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)*

☐ Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for selected pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				**Reason for Deferral**			**Applicant Certification** †
Population		minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐	☐	☐
	Date studies are due (mm/dd/yy): _____						

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

* Other Reason: _____

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?.	
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes ☐	No ☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:			
Population		minimum	maximum
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as

pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:					
Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

_____

Regulatory Project Manager

(Revised: 6/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Q1: Does this indication have orphan designation?

- ☐ Yes. PREA does not apply. **Skip to signature block.**
- ☐ No. Please proceed to the next question.

Q2: Is there a full waiver for all pediatric age groups for this indication (check one)?

- ☐ Yes: (Complete Section A.)
- ☐ No: Please check all that apply:
  - ☐ Partial Waiver for selected pediatric subpopulations (Complete Sections B)
  - ☐ Deferred for some or all pediatric subpopulations (Complete Sections C)
  - ☐ Completed for some or all pediatric subpopulations (Complete Sections D)
  - ☐ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
  - ☐ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

  (Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

- ☐ Necessary studies would be impossible or highly impracticable because:
  - ☐ Disease/condition does not exist in children
  - ☐ Too few children with disease/condition to study
  - ☐ Other (e.g., patients geographically dispersed): _____
- ☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- ☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

				Reason (see below for further detail):			
		minimum	maximum	Not feasible#	Not meaningful therapeutic benefit*	Ineffective or unsafe†	Formulation failedΔ
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief justification**):

\# Not feasible:

☐ Necessary studies would be impossible or highly impracticable because:

- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease/condition to study
- ☐ Other (e.g., patients geographically dispersed): _____

* Not meaningful therapeutic benefit:

☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- ☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

Δ Formulation failed:

☐ Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)*

☐ Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Section C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so,

proceed to Section F).. Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for some or all pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				**Reason for Deferral**			**Applicant Certification** †
Population		minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐	☐	☐
	Date studies are due (mm/dd/yy): _____						

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

* Other Reason: _____

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes ☐	No ☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:			
Population		minimum	maximum
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 6/2008)

PEDIATRIC PAGE
(Complete for all filed original applications and efficacy supplements)

NDA/BLA#: NDA 206910 Supplement Number: _____ NDA Supplement Type (e.g. SE5): _____

Division Name:Division of Hematology PDUFA Goal Date: 5/30/2015 Stamp Date: 5/30/2014

Proprietary Name: Jadenu

Established/Generic Name: deferasirox

Dosage Form: Film coated tablets

Applicant/Sponsor: Novartis Pharmaceuticals Corporation

Indication(s) *previously approved* (please complete this question for supplements and Type 6 NDAs only):
(1) _____
(2) _____
(3) _____
(4) _____

Pediatric use for each pediatric subpopulation must be addressed for each indication covered by current application under review. A Pediatric Page must be completed for each indication.

Number of indications for this pending application(s): 2
(Attach a completed Pediatric Page for each indication in current application.)

Indication: Treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron (Fe) concentration (LIC) of at least 5 mg Fe per gram of dry weight and a serum ferritin greater than 300 mcg/L.

Q1: Is this application in response to a PREA PMR? Yes ☐ Continue
No ☒ Please proceed to Question 2.

If Yes, NDA/BLA#: _____ Supplement #:_____ PMR #:_____

Does the division agree that this is a complete response to the PMR?

☐ Yes. Please proceed to Section D.

☐ No. Please proceed to Question 2 and complete the Pediatric Page, as applicable.

Q2: Does this application provide for (If yes, please check all categories that apply and proceed to the next question):

(a) NEW ☐ active ingredient(s) (includes new combination); ☒ indication(s); ☒ dosage form; ☒ dosing regimen; or ☐ route of administration?*

(b) ☐ No. PREA does not apply. **Skip to signature block.**

**** Note for CDER: SE5, SE6, and SE7 submissions may also trigger PREA.***

Q3: Does this indication have orphan designation?

☒ Yes. PREA does not apply. **Skip to signature block.**

☐ No. Please proceed to the next question.

Q4: Is there a full waiver for all pediatric age groups for this indication (check one)?

- ☐ Yes: (Complete Section A.)
- ☐ No: Please check all that apply:
  - ☐ Partial Waiver for selected pediatric subpopulations (Complete Sections B)
  - ☐ Deferred for some or all pediatric subpopulations (Complete Sections C)
  - ☐ Completed for some or all pediatric subpopulations (Complete Sections D)
  - ☐ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
  - ☐ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

  (Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

- ☐ Necessary studies would be impossible or highly impracticable because:
  - ☐ Disease/condition does not exist in children
  - ☐ Too few children with disease/condition to study
  - ☐ Other (e.g., patients geographically dispersed): _____
- ☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- ☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

				Reason (see below for further detail):			
		minimum	maximum	Not feasible[#]	Not meaningful therapeutic benefit[*]	Ineffective or unsafe[†]	Formulation failed[Δ]
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief**

justification):

Not feasible:

☐ Necessary studies would be impossible or highly impracticable because:

☐ Disease/condition does not exist in children

☐ Too few children with disease/condition to study

☐ Other (e.g., patients geographically dispersed): _____

***** Not meaningful therapeutic benefit:

☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

Δ Formulation failed:

☐ Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)*

☐ Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Sections C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so, proceed to Section F). Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for selected pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				**Reason for Deferral**			**Applicant Certification** †
Population		minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐	☐	☐
	Date studies are due (mm/dd/yy): _____						

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

* Other Reason: _____

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?.	
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes ☐	No ☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:			
Population		minimum	maximum
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as

pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:					
Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please complete the attachment for each one of those indications. Otherwise, this Pediatric Page is complete and should be signed and entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

_____

Regulatory Project Manager

(Revised: 6/2008)

NOTE: If you have no other indications for this application, you may delete the attachments from this document.

Attachment A

(This attachment is to be completed for those applications with multiple indications only.)

Indication #2: _____

Q1: Does this indication have orphan designation?

- ☐ Yes. PREA does not apply. **Skip to signature block.**
- ☐ No. Please proceed to the next question.

Q2: Is there a full waiver for all pediatric age groups for this indication (check one)?

- ☐ Yes: (Complete Section A.)
- ☐ No: Please check all that apply:
  - ☐ Partial Waiver for selected pediatric subpopulations (Complete Sections B)
  - ☐ Deferred for some or all pediatric subpopulations (Complete Sections C)
  - ☐ Completed for some or all pediatric subpopulations (Complete Sections D)
  - ☐ Appropriately Labeled for some or all pediatric subpopulations (Complete Sections E)
  - ☐ Extrapolation in One or More Pediatric Age Groups (Complete Section F)

  (Please note that Section F may be used alone or in addition to Sections C, D, and/or E.)

Section A: Fully Waived Studies (for all pediatric age groups)

Reason(s) for full waiver: (**check, and attach a brief justification for the reason(s) selected**)

- ☐ Necessary studies would be impossible or highly impracticable because:
  - ☐ Disease/condition does not exist in children
  - ☐ Too few children with disease/condition to study
  - ☐ Other (e.g., patients geographically dispersed): _____
- ☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients AND is not likely to be used in a substantial number of pediatric patients.
- ☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are fully waived on this ground, this information must be included in the labeling.*)

☐ Justification attached.

If studies are fully waived, then pediatric information is complete for this indication. If there is another indication, please complete another Pediatric Page for each indication. Otherwise, this Pediatric Page is complete and should be signed.

Section B: Partially Waived Studies (for selected pediatric subpopulations)

Check subpopulation(s) and reason for which studies are being partially waived (fill in applicable criteria below):

Note: If Neonate includes premature infants, list minimum and maximum age in "gestational age" (in weeks).

				Reason (see below for further detail):			
		minimum	maximum	Not feasible#	Not meaningful therapeutic benefit*	Ineffective or unsafe†	Formulation failedΔ
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Reason(s) for partial waiver (**check reason** corresponding to the category checked above, and **attach a brief justification**):

\# Not feasible:

☐ Necessary studies would be impossible or highly impracticable because:

- ☐ Disease/condition does not exist in children
- ☐ Too few children with disease/condition to study
- ☐ Other (e.g., patients geographically dispersed): _____

* Not meaningful therapeutic benefit:

☐ Product does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients in this/these pediatric subpopulation(s) AND is not likely to be used in a substantial number of pediatric patients in this/these pediatric subpopulation(s).

† Ineffective or unsafe:

- ☐ Evidence strongly suggests that product would be unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)
- ☐ Evidence strongly suggests that product would be ineffective and unsafe in all pediatric subpopulations (*Note: if studies are partially waived on this ground, this information must be included in the labeling.*)

Δ Formulation failed:

☐ Applicant can demonstrate that reasonable attempts to produce a pediatric formulation necessary for this/these pediatric subpopulation(s) have failed. (*Note: A partial waiver on this ground may only cover the pediatric subpopulation(s) requiring that formulation. An applicant seeking a partial waiver on this ground must submit documentation detailing why a pediatric formulation cannot be developed. This submission will be posted on FDA's website if waiver is granted.)*

☐ Justification attached.

For those pediatric subpopulations for which studies have not been waived, there must be (1) corresponding study plans that have been deferred (if so, proceed to Section C and complete the PeRC Pediatric Plan Template); (2) submitted studies that have been completed (if so, proceed to Section D and complete the PeRC Pediatric Assessment form); (3) additional studies in other age groups that are not needed because the drug is appropriately labeled in one or more pediatric subpopulations (if so, proceed to Section E); and/or (4) additional studies in other age groups that are not needed because efficacy is being extrapolated (if so,

proceed to Section F).. Note that more than one of these options may apply for this indication to cover all of the pediatric subpopulations.

Section C: Deferred Studies (for some or all pediatric subpopulations).

Check pediatric subpopulation(s) for which pediatric studies are being deferred (and fill in applicable reason below):

Deferrals (for each or all age groups):				**Reason for Deferral**			**Applicant Certification** †
Population		minimum	maximum	Ready for Approval in Adults	Need Additional Adult Safety or Efficacy Data	Other Appropriate Reason (specify below)*	Received
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐	☐	☐
☐	All Pediatric Populations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐	☐	☐
	Date studies are due (mm/dd/yy): _____						

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

* Other Reason: _____

† Note: Studies may only be deferred if an applicant submits a certification of grounds for deferring the studies, a description of the planned or ongoing studies, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time, and a timeline for the completion of the studies. If studies are deferred, on an annual basis applicant must submit information detailing the progress made in conducting the studies or, if no progress has been made, evidence and documentation that such studies will be conducted with due diligence and at the earliest possible time. This requirement should be communicated to the applicant in an appropriate manner (e.g., in an approval letter that specifies a required study as a post-marketing commitment.)

If all of the pediatric subpopulations have been covered through partial waivers and deferrals, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section D: Completed Studies (for some or all pediatric subpopulations).

Pediatric subpopulation(s) in which studies have been completed (check below):					
Population		minimum	maximum	PeRC Pediatric Assessment form attached?	
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	Yes ☐	No ☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	Yes ☐	No ☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If there are no further pediatric subpopulations to cover based on partial waivers, deferrals and/or completed studies, Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section E: Drug Appropriately Labeled (for some or all pediatric subpopulations):

Additional pediatric studies are not necessary in the following pediatric subpopulation(s) because product is appropriately labeled for the indication being reviewed:			
Population		minimum	maximum
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	Other	__ yr. __ mo.	__ yr. __ mo.
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

If all pediatric subpopulations have been covered based on partial waivers, deferrals, completed studies, and/or existing appropriate labeling, this Pediatric Page is complete and should be signed. If not, complete the rest of the Pediatric Page as applicable.

Section F: Extrapolation from Other Adult and/or Pediatric Studies (for deferred and/or completed studies)

Note: Pediatric efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations if (and only if) (1) the course of the disease/condition AND (2) the effects of the product are sufficiently similar between the reference population and the pediatric subpopulation for which information will be extrapolated. Extrapolation of efficacy from studies in adults and/or other children usually requires supplementation with other information obtained from the target pediatric subpopulation, such as pharmacokinetic and safety studies. Under the statute, safety cannot be extrapolated.

Pediatric studies are not necessary in the following pediatric subpopulation(s) because efficacy can be extrapolated from adequate and well-controlled studies in adults and/or other pediatric subpopulations:

Population		minimum	maximum	Extrapolated from:	
				Adult Studies?	Other Pediatric Studies?
☐	Neonate	__ wk. __ mo.	__ wk. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	Other	__ yr. __ mo.	__ yr. __ mo.	☐	☐
☐	All Pediatric Subpopulations	0 yr. 0 mo.	16 yr. 11 mo.	☐	☐

Are the indicated age ranges (above) based on weight (kg)? ☐ No; ☐ Yes.

Are the indicated age ranges (above) based on Tanner Stage? ☐ No; ☐ Yes.

Note: If extrapolating data from either adult or pediatric studies, a description of the scientific data supporting the extrapolation must be included in any pertinent reviews for the application.

If there are additional indications, please copy the fields above and complete pediatric information as directed. If there are no other indications, this Pediatric Page is complete and should be entered into DFS or DARRTS as appropriate after clearance by PeRC.

This page was completed by:

{See appended electronic signature page}

Regulatory Project Manager

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT THE PEDIATRIC AND MATERNAL HEALTH STAFF at 301-796-0700

(Revised: 6/2008)

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/s/

KRISTOPHER KOLIBAB
03/23/2015

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 206910 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: *(an action package is not required for SE8 or SE9 supplements)*
Proprietary Name: Jadenu Established/Proper Name: deferasirox Dosage Form: film-coated tablets		Applicant: Novartis Pharmaceuticals Corporation Agent for Applicant (if applicable):
RPM: Kris Kolibab, PhD		Division: Division of Hematology Products

NDA Application Type: ☒ 505(b)(1) ☐ 505(b)(2)
Efficacy Supplement: ☐ 505(b)(1) ☐ 505(b)(2)

BLA Application Type: ☐ 351(k) ☐ 351(a)
Efficacy Supplement: ☐ 351(k) ☐ 351(a)

For ALL 505(b)(2) applications, two months prior to EVERY action:

- **Review the information in the 505(b)(2) Assessment and submit the draft[2] to CDER OND IO for clearance.**
- **Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)**

☐ No changes
☐ New patent/exclusivity *(notify CDER OND IO)*
Date of check:

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.

❖ Actions	
• Proposed action • User Fee Goal Date is 3/30/2015	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☒ 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 http://www fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm069965.pdf). If not submitted, explain _____	☐ Received
❖ Application Characteristics[3]	

[1] 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.
[2] 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).
[3] 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. For example, if the application is a pending BLA supplement, then a new *RMS-BLA Product Information Sheet for TBP* must be completed.

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): Iron Chelators
(confirm chemical classification at time of approval)

☐ Fast Track
☐ Rolling Review
☐ Orphan drug designation
☐ Breakthrough Therapy designation
☐ Rx-to-OTC full switch
☐ Rx-to-OTC partial switch
☐ Direct-to-OTC

NDAs: Subpart H
☒ Accelerated approval (21 CFR 314.510)
☐ Restricted distribution (21 CFR 314.520)
Subpart I
☐ Approval based on animal studies

BLAs: Subpart E
☐ Accelerated approval (21 CFR 601.41)
☐ Restricted distribution (21 CFR 601.42)
Subpart H
☐ 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

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

Comments:

❖ BLAs only: Is the product subject to official FDA lot release per 21 CFR 610.2 *(approvals only)*	☐ Yes ☐ No
❖ Public communications *(approvals only)*	
• Office of Executive Programs (OEP) liaison has been notified of action	☐ Yes ☒ No
• Indicate what types (if any) of information were issued	☒ None ☐ FDA Press Release ☐ FDA Talk Paper ☐ CDER Q&As ☐ Other
❖ 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	☒ No ☐ 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.	☒ Verified ☐ Not applicable because drug is an old antibiotic.

CONTENTS OF ACTION PACKAGE

Officer/Employee List

❖ List of officers/employees who participated in the decision to approve this application and consented to be identified on this list *(approvals only)*	☒ Included
Documentation of consent/non-consent by officers/employees	☒ Included

Action Letters	
❖ Copies of all action letters *(including approval letter with final labeling)*	Accelerated Approval 3/30/2015
Labeling	
❖ Package Insert *(write submission/communication date at upper right of first page of PI)*	
• Most recent draft labeling *(if it is division-proposed labeling, it should be in track-changes format)*	☐ Included
• Original applicant-proposed labeling	☒ Included 5/30/2014
❖ Medication Guide/Patient Package Insert/Instructions for Use/Device Labeling *(write submission/communication date at upper right of first page of each piece)*	☐ Medication Guide ☐ Patient Package Insert ☐ Instructions for Use ☐ Device Labeling ☒ None
• Most-recent draft labeling *(if it is division-proposed labeling, it should be in track-changes format)*	☐ Included
• Original applicant-proposed labeling	☐ Included
❖ Labels (**full color** carton and immediate-container labels) *(write submission/communication date on upper right of first page of each submission)*	
• Most-recent draft labeling	☒ Included
❖ Proprietary Name • Acceptability/non-acceptability letter(s) *(indicate date(s))* • Review(s) *(indicate date(s)*	Acceptability Letter 12/3/2014 Non-Acceptability Letter 8/26/2014 Reviews 12/3/2014 and 8/22/2014
❖ Labeling reviews *(indicate dates of reviews)*	RPM: ☐ 7/22/2014 DMEPA: ☐ 9/24/2014 DMPP/PLT (DRISK): ☒ None OPDP: ☐ 2/25/2015 SEALD: ☒ None CSS: ☒ None Other: ☒ None
Administrative / Regulatory Documents	
❖ RPM Filing Review[4]/Memo of Filing Meeting *(indicate date of each review)* ❖ All NDA 505(b)(2) Actions: Date each action cleared by 505(b)(2) Clearance Committee	RPM Filing Review 7/22/2014 ☒ Not a (b)(2)
❖ NDAs only: Exclusivity Summary *(signed by Division Director)*	☒ Included 3/30/2015
❖ Application Integrity Policy (AIP) Status and Related Documents http://www fda.gov/ICECI/EnforcementActions/ApplicationIntegrityPolicy/default.htm	
• Applicant is on the AIP	☐ Yes ☒ No

[4] Filing reviews for scientific disciplines are NOT required to be included in the action package.

• This application is on the AIP ○ If yes, Center Director's Exception for Review memo *(indicate date)* ○ If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC N/A If PeRC review not necessary, explain: Orphan Designation	Pediatric Page 3/23/2015
❖ 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, etc.) *(do not include previous action letters, as these are located elsewhere in package)*	March 26, 23, 22, 16, 11, 3 (2), February 13, January 23, 9 (2) 2015; July 25, 10, 1, June 23 and 5, 2014
❖ 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)	10/3/2014 TCON
❖ Minutes of Meetings	
• If not the first review cycle, any end-of-review meeting *(indicate date of mtg)*	☒ N/A or no mtg
• Pre-NDA/BLA meeting *(indicate date of mtg)*	3/20/2014
• EOP2 meeting *(indicate date of mtg)*	☒ No mtg
• Mid-cycle Communication *(indicate date of mtg)*	☒ N/A
• Late-cycle Meeting *(indicate date of mtg)*	☒ N/A
• Other milestone meetings (e.g., EOP2a, CMC pilots) *(indicate dates of mtgs)*	
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
Decisional and Summary Memos	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	3/30/2015
Cross-Discipline Team Leader Review *(indicate date for each review)*	3/31/2015
PMR/PMC Development Templates *(indicate total number)*	PMRs - 9
Clinical	
❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	3/17/2015 cosigned primary
• Clinical review(s) *(indicate date for each review)*	3/17/2015 primary review
• Social scientist review(s) (if OTC drug) *(indicate date for each review)*	☒ None
❖ Financial Disclosure reviews(s) or location/date if addressed in another review OR If no financial disclosure information was required, check here ☐ and include a review/memo explaining why not *(indicate date of review/memo)*	See Page 13 of clinical primary review dated 3/17/2015
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☒ N/A

❖ Risk Management • REMS Documents and REMS Supporting Document *(indicate date(s) of submission(s))* • REMS Memo(s) and letter(s) *(indicate date(s))* • Risk management review(s) and recommendations (including those by OSE and CSS) *(indicate date of each review and indicate location/date if incorporated into another review)*	☒ None
❖ OSI Clinical Inspection Review Summary(ies) *(include copies of OSI letters to investigators)*	☒ None requested
Clinical Microbiology ☒ None	
❖ Clinical Microbiology Team Leader Review(s) *(indicate date for each review)*	☐ No separate review
Clinical Microbiology Review(s) *(indicate date for each review)*	☐ None
Biostatistics ☒ None	
❖ Statistical Division Director Review(s) *(indicate date for each review)*	☐ No separate review
Statistical Team Leader Review(s) *(indicate date for each review)*	☐ No separate review
Statistical Review(s) *(indicate date for each review)*	☐ None
Clinical Pharmacology ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	2/3/2015 cosigned primary
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	2/3/2015 cosigned primary
Clinical Pharmacology review(s) *(indicate date for each review)*	2/3/2015 primary review
❖ OSI Clinical Pharmacology Inspection Review Summary *(include copies of OSI letters)*	10/22/2014
Nonclinical ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	1/21/2015 cosigned supervisory
• Supervisory Review(s) *(indicate date for each review)*	1/21/2015
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	11/20/2014 primary review
❖ Review(s) by other disciplines/divisions/Centers requested by P/T reviewer *(indicate date for each review)*	☒ None
❖ Statistical review(s) of carcinogenicity studies *(indicate date for each review)*	☒ No carc
❖ ECAC/CAC report/memo of meeting	☒ None Included in P/T review, page
❖ OSI Nonclinical Inspection Review Summary *(include copies of OSI letters)*	☒ None requested

Product Quality ☐ None	
❖ Product Quality Discipline Reviews	
• ONDQA/OBP Division Director Review(s) *(indicate date for each review)*	12/3/2014 cosigned primary
• Branch Chief/Team Leader Review(s) *(indicate date for each review)*	12/3/2014 cosigned primary
• Product quality review(s) including ONDQA biopharmaceutics reviews *(indicate date for each review)*	3/18/2015 ONDQA 3/13/2015 Biopharm Addendum 2/23/2015 Primary Biopharm 12/3/2014 Primary ONDQA 11/20/2014 ONDQA
❖ Microbiology Reviews ☒ NDAs: Microbiology reviews (sterility & pyrogenicity) (OPS/NDMS) *(indicate date of each review)* ☐ BLAs: Sterility assurance, microbiology, facilities reviews (OMPQ/MAPCB/BMT) *(indicate date of each review)*	8/1/2014
❖ Reviews by other disciplines/divisions/Centers requested by CMC/quality reviewer *(indicate date of each review)*	☒ None
❖ Environmental Assessment (check one) (original and supplemental applications)	
☒ Categorical Exclusion *(indicate review date)(all original applications and all efficacy supplements that could increase the patient population)*	Page 68 Primary ONDQA dated 12/3/2014
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Facilities Review/Inspection	
☒ NDAs: Facilities inspections (include EER printout or EER Summary Report only; do NOT include EER Detailed Report; date completed must be within **2 years** of action date) *(only original NDAs and supplements that include a new facility or a change that affects the manufacturing sites[5])*	Date completed: 10/14/2014 ☒ Acceptable ☐ Withhold recommendation ☐ Not applicable
☐ BLAs: TB-EER (date of most recent TB-EER must be within **30 days** of action date) *(original and supplemental BLAs)*	Date completed: ☐ Acceptable ☐ Withhold recommendation
❖ NDAs: Methods Validation *(check box only, do not include documents)*	☐ Completed ☐ Requested ☐ Not yet requested ☒ Not needed (per review)

[5] i.e., a new facility or a change in the facility, or a change in the manufacturing process in a way that impacts the Quality Management Systems of the facility.

Day of Approval Activities	
❖ For all 505(b)(2) applications: • Check Orange Book for newly listed patents and/or exclusivity (including pediatric exclusivity)	☐ No changes ☐ New patent/exclusivity *(Notify CDER OND IO)*
• Finalize 505(b)(2) assessment	☐ Done
❖ For Breakthrough Therapy(BT) Designated drugs: • Notify the CDER BT Program Manager	☐ Done *(Send email to CDER OND IO)*
❖ For products that need to be added to the flush list (generally opioids): • Notify the Division of Online Communications, Office of Communications	☐ Done
❖ Send a courtesy copy of approval letter and all attachments to applicant by fax or secure email	☒ Done
❖ If an FDA communication will issue, notify Press Office of approval action after confirming that applicant received courtesy copy of approval letter	☐ Done
❖ Ensure that proprietary name, if any, and established name are listed in the *Application Product Names* section of DARRTS, and that the proprietary name is identified as the "preferred" name	☒ Done
❖ Ensure Pediatric Record is accurate	☒ Done
❖ Send approval email within one business day to CDER-APPROVALS	☒ Done

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/s/

KRISTOPHER KOLIBAB
03/31/2015

Kolibab, Kristopher

From: Kolibab, Kristopher
Sent: Thursday, March 26, 2015 10:04 AM
To: 'Abraham, Abbey'
Subject: NDA 206910/PMR 8 Proposed Dates/Acceptable

Importance: High

Hello Abbey,

The proposed dates for PMR #8 are acceptable. Please submit an amendment officially to NDA 206910 **ASAP** stating that Novartis agrees to all the PMRs.

PMR XXXX-8
Conduct a trial to assess ocular toxicity in patients receiving deferasirox. Examinations should include distance visual acuity, applanation tonometry, lens photography, and wide angle fundus photography of retina and optic nerve and should be done at baseline (prior to deferasirox initiation) and at six month intervals. At least 60 patients should complete 2 years of follow-up.

Final Protocol submission: 10/2015
Final Report Submission: 12/2019

Regards,

Kris Kolibab, Ph.D.
Regulatory Health Project Manager
Division of Hematology Products
OND/CDER/FDA

Phone: 240-402-0277

From: Abraham, Abbey [mailto:abbey.abraham@novartis.com]
Sent: Wednesday, March 25, 2015 4:06 PM
To: Kolibab, Kristopher
Subject: NDA 206910/ Response to PMRs

Hi Kris

Novartis has reviewed the response on PMC 750-10 for NDA 21882 and based on the comments, we propose the following revision for PMR #8 for NDA 206910.

PMR XXXX-8
Conduct a trial to assess ocular toxicity in patients receiving deferasirox. Examinations should include distance visual acuity, applanation tonometry, lens photography, and wide angle fundus photography of retina and optic nerve and should be done at baseline (prior to deferasirox initiation) and at six month intervals. At least 60 patients should complete 2 years of follow-up.

Final Protocol submission: ~~07/2015~~ 10/2015
Final Report Submission: ~~05/2018~~ 12/2019

Novartis would like to confirm we have the option to either propose a (b) (4) or revise one that is ongoing to fulfill the PMR. In either case, we estimate that it will take approx. 6 months for protocol development. To help ensure follow-up of 60 patients for 2 years and avoid the data collection deficiencies noted for 2204, we need to ensure appropriate site selection, confirm patient enrollment targets and review assessment procedures with investigators before the protocol can be developed/final.

Thank you

Abbey Abraham, PharmD
Oncology Drug Regulatory Affairs
Novartis Pharmaceuticals Corporation

Phone +1 862-778-8998
Fax +1 973-781-5217
abbey.abraham@novartis.com
www.novartis.com

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/s/

KRISTOPHER KOLIBAB
03/26/2015

Kolibab, Kristopher

From: Kolibab, Kristopher
Sent: Monday, March 23, 2015 10:55 AM
To: abbey.abraham@novartis.com
Subject: NDA 206910/PI Acceptable/Official Submission

Importance: High

Hello Abbey,

The Agency accepts the PI version received on March 18th, 2015 via e-mail. Please officially submit a **clean version** (PDF and word formats) of the PI to NDA 206910 **as soon as possible** and also email to me.

Please confirm receipt of this message by e-mail.

Thanks,

Kris Kolibab, Ph.D.
Regulatory Health Project Manager
Division of Hematology Products
OND/CDER/FDA

Phone: 240-402-0277

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/s/

KRISTOPHER KOLIBAB
03/23/2015

Kolibab, Kristopher

From: Kolibab, Kristopher
Sent: Sunday, March 22, 2015 8:53 PM
To: abbey.abraham@novartis.com
Subject: NDA 206910/PMRs/Due March 24

Importance: High

Hello Abbey,

Please refer to the NDA 206910 received May 30, 2014, which provides for the proposed indications "treatment of chronic iron overload due to blood transfusions in patients 2 years of age and older and treatment of chronic iron overload in patients 10 years of age and older with non-transfusion-dependent thalassemia (NTDT) syndromes and with a liver iron (Fe) concentration (LIC) of at least 5 mg Fe per gram of dry weight and a serum ferritin greater than 300 mcg/L."

Below are the revised proposed PMRs for NDA 206910 Jadenu. We propose these revisions either to clarify text or dates. We ask that Novartis provide a commitment officially NLT March 24, 2015. Again, note that final set numbers will be provided later.

Please advise by email and also submit an amendment ASAP stating that Novartis agrees with the following PMRs officially to NDA 206910.

PMR XXXX-1 Establish a registry for children aged 2 to < 6 years to enroll approximately 200 patients receiving deferasirox and follow them for 5 years. Collect data at least monthly for renal function and blood pressure and yearly for growth and development, and analyze the data for adverse renal reactions and delayed growth and development. Submit your monitoring scheme for our review and comment.

Final Report Submission: 02/2016

PMR XXXX-2 Conduct a trial to assess the long-term efficacy and safety of deferasirox in patients with NTDT and high LIC. The trial should assess response rates in the subset of patients with baseline LIC values >15 mg Fe/g dw (proportion of patients achieving an LIC <5 mg Fe/g dw and time to achieving an LIC <5 mg Fe/g dw). Follow-up of all subjects for up to 5 years is necessary.

Trial Completion: 05/2019
Final Report Submission: 11/2019

PMR XXXX-3 Conduct a trial to assess the long-term efficacy (and safety) of deferasirox treatment to a target LIC of 3 mg Fe/g dw followed by one or more treatment holidays until the LIC is ≥5 mg Fe/g dw in patients with NTDT. Follow-up of all subjects for up to 5 years is necessary.

Trial Completion: 05/2019
Final Report Submission: 11/2019

PMR XXXX-4 Conduct a prospective, randomized trial in at least 210 patients with low to intermediate risk myelodysplastic syndromes (MDS) receiving deferasirox for transfusional iron overload (approximately 140 patients) or placebo (approximately 70 patients) to determine the efficacy and safety of deferasirox in this population. The trial will continue for 3 years from the date the last patient is enrolled.

Trial Completion: 03/2018
Final Report Submission: 09/2018

PMR XXXX-5 Conduct a study, using your established registry, to evaluate the risk of growth inhibition in children (aged 10 to <18 years old at enrollment) with NTDT and treated with deferasirox for documented iron overload. Follow at least 40 children for up to 5 years to assess and analyze the long-term safety of treatment with deferasirox, including an assessment of growth, compared to children on a regular transfusion program receiving deferasirox (based on historical data). Provide annual interim reports on enrollment and outcomes.

Interim Report Submission: 12/2015
Interim Report Submission: 12/2016
Interim Report Submission: 12/2017
Interim Report Submission: 12/2018
Interim Report Submission: 12/2019
Interim Report Submission: 12/2020
Study Completion: 06/2021
Final Report Submission: 12/2021

PMR XXXX-6 Conduct an enhanced pharmacovigilance study, including proactive surveillance and follow-up of spontaneous reports, to characterize the frequency and severity of adverse Events of Special Interest (ESIs), defined as all deaths and severe or serious events of kidney or liver toxicity, in adults receiving deferasirox for documented iron overload related to multiple transfusions for myelodysplastic syndrome with anemia requiring transfusions. This study does not replace monitoring and reporting as required by regulations.

Interim Report Submission: 01/2015
Interim Report Submission: 07/2015
Interim Report Submission: 01/2016
Interim Report Submission: 01/2017
Interim Report Submission: 01/2018
Study Completion: 01/2019
Final Report Submission: 07/2019

PMR XXXX-7 Complete a study of long-term follow-up (3 years) in 150 patients with myelodysplastic syndromes (MDS) receiving deferasirox to evaluate safety (including cardiac, hepatic, endocrine and renal) and hematologic and clinical benefit of deferasirox in these patients.

Final Report Submission: 12/ 2019

PMR XXXX-8 Conduct a trial to assess ocular toxicity in patients receiving deferasirox. Examinations should include distance visual acuity, applanation tonometry, lens photography, and wide angle fundus photography of retina and optic nerve and should be done at baseline (prior to deferasirox initiation) and at six month intervals. At least 60 patients should complete 2 years of follow-up.

Final Protocol submission: 07/2015
Final Report Submission: 05/2018

(Note: We propose these dates to allow you the time interval to perform this trial for Jadenu should the report submitted for Exjade not fulfill that requirement.)

PMR XXXX-9 Conduct a trial to assess the long-term safety of deferasirox in patients with NTDT by conducting a trial of deferasirox for the treatment of iron overload (LIC ≥5 mg Fe/g dw) in non-transfusion dependent thalassemia (NTDT) in patients aged 10 years and greater with up to 5 years total follow-up.

Trial Completion: 05/2019
Final Report Submission: 11/2019

Please confirm receipt of this message via email.

Regards,

Kris Kolibab, Ph.D.
Regulatory Health Project Manager
Division of Hematology Products
OND/CDER/FDA

Phone: 240-402-0277

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/s/

KRISTOPHER KOLIBAB
03/22/2015

Kolibab, Kristopher

From: Kolibab, Kristopher
Sent: Monday, March 16, 2015 5:50 PM
To: abbey.abraham@novartis.com
Subject: NDA 206910 Label and Information Request
Attachments: NDA 206910 Label 3-16-15.doc

Hello Abbey,

Please find attached the FDA revised version of the PI for your review and information request.

Please review the changes/comments and do the following to the same draft:

- Accept any changes that you agree with including all format/minor editorial changes
- Edit over the ones that you do not agree with **(do not reject any changes that the FDA proposed)**

After you have made the changes, please e-mail a revised PI (in tracked changes word document) to me by **12 PM (EST) Wednesday, March 18, 2015** and officially submit to NDA 206910.

Information Request:
The Highlights section of the PI must be ½ page or less unless a waiver is granted. Please submit a waiver request regarding the length of the Highlights.

Please confirm receipt of this message by e-mail.

Thank you,

Kris Kolibab, Ph.D.
Regulatory Health Project Manager
Division of Hematology Products
OND/CDER/FDA

Phone: 240-402-0277

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

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/s/

KRISTOPHER KOLIBAB
03/16/2015

Kolibab, Kristopher

From: Kolibab, Kristopher
Sent: Wednesday, March 11, 2015 2:59 PM
To: abbey.abraham@novartis.com
Subject: NDA 206910/Label/Due March 13
Attachments: NDA 206910 Label March 11.doc

Importance: High

Hello Abbey,

Please find attached the FDA revised version of the PI for your review.

Please review the changes/comments and do the following to the same draft:

- Accept any changes that you agree with including all format/minor editorial changes
- Edit over the ones that you do not agree with **(do not reject any changes that the FDA proposed)**

After you have made the changes, please e-mail a revised PI (in tracked changes word document) to me by **12 PM (EST) Friday, March 13, 2015** and officially submit to NDA 206910.

Please confirm receipt of this message by e-mail.

Thank you,

Kris Kolibab, Ph.D.
Regulatory Health Project Manager
Division of Hematology Products
OND/CDER/FDA

Phone: 240-402-0277

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

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/s/

KRISTOPHER KOLIBAB
03/11/2015

Kolibab, Kristopher

From: Kolibab, Kristopher
Sent: Tuesday, March 03, 2015 12:07 PM
To: 'abbey.abraham@novartis.com'
Subject: NDA 206910/Labeling PI/Due March 9
Attachments: NDA 206910 Label.doc

Importance: High

Hello Abbey,

Please find attached the FDA revised version of the PI for your review.

Please review the changes/comments and do the following to the same draft:

- Accept any changes that you agree with including all format/minor editorial changes
- Edit over the ones that you do not agree with **(do not reject any changes that the FDA proposed)**

After you have made the changes, please email a revised PI (in tracked changes word document) to me by **10 AM (EST) Monday, March 9, 2015**.

Please confirm receipt of this message by e-mail.

Thank you,

Kris Kolibab, Ph.D.
Regulatory Health Project Manager
Division of Hematology Products
OND/CDER/FDA

Phone: 240-402-0277

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

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/s/

KRISTOPHER KOLIBAB
03/03/2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206910

GENERAL ADVICE

Novartis Pharmaceuticals Corporation
Attention: Abbey Abraham, Pharm D.
Senior Associate Director, Drug Regulatory Affairs
Oncology Global Development
One Health Plaza, Bldg. 337/B10-6
East Hanover, NJ 07936-1080

Dear Dr. Abraham:

Please refer to your New Drug Application (NDA) submitted May 30, 2014 (received May 30, 2014) under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Jadenu™ (deferasirox) film-coated Tablets, 90 mg, 180 mg and 360 mg.

We also refer to your February 9, 2015, submission, containing your acknowledgement of the post-marketing requirements (PMRs) for Jadenu in our January 26, 2015 letter and your request for confirmation that final study reports already submitted to the Exjade NDA for any of these PMR/PMCs would also apply for the respective Jadenu PMRs.

We have reviewed the referenced material and have the following comments:

1. Novartis requests confirmation that final study reports already submitted to the Exjade NDA for any of these PMR/PMCs would also apply for the respective Jadenu PMR.

   FDA Response: Yes, send all final reports to both NDAs once Jadenu is approved. In addition, please resubmit the final study reports already submitted to the Exjade NDA to the Jadenu NDA once Jadenu has been approved. These will also apply to the respective Jadenu PMRs.

2. Please also confirm if future interim and final reports should be submitted to both NDAs, should the Jadenu NDA be approved.

   FDA Response: Yes, submit future reports to both NDAs.

3. Jadenu PMR 8-Novartis references PMC 750-9 for Exjade and an email from FDA project manager Mara Miller on September 30, 2013, where FDA reiterated that if the study report for PMR 1994-4 also fulfills the intent for PMC 750-9, both could be fulfilled when the study report for PMR 1994-4 is submitted and reviewed. Novartis acknowledges the above mentioned PMR for the Jadenu NDA and requests confirmation that the assessment for PMC 750-9 would also apply for this PMR.

FDA Response: Yes. As was agreed previously, if the study report for PMR 1994-4 fulfills the intent for PMC 750-9, both could be fulfilled

4. Jadenu PMR 9: Novartis references PMC 750-10 for Exjade for which a final study report (Study 2204) was submitted on September 28, 2012. Comments and additional data analysis was requested from FDA on July 31, 2013 for which Novartis submitted a response on September 4, 2014 to NDA 21,882. Novartis acknowledges the above mentioned PMR for the Jadenu NDA and requests confirmation that the assessment for PMC 750-10 would also apply for this PMR.

   FDA Response: Yes. As was agreed previously, if the study report for PMR 1994-4 fulfills the intent for PMC 750-9, both could be fulfilled

If you have any questions, call Diane Leaman, Safety Regulatory Project Manager, at (301) 796-1424.

Sincerely,

{See appended electronic signature page}

Robert C. Kane, MD
Deputy Director for Safety
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/s/

ROBERT C KANE
03/03/2015

Tzeng, Linhua

From: Tzeng, Linhua
Sent: Friday, February 13, 2015 12:10 PM
To: Abraham, Abbey
Cc: Tzeng, Linhua
Subject: RE: NDA-206910 Information Request

Good afternoon Dr. Abraham,

Thank you for your email.

In the cover letter with this submission, Novartis requests confirmation of the following:

"Novartis requests confirmation that final study reports already submitted to the Exjade NDA for any of these PMR/PMCs would also apply for the respective Jadenu PMR."

FDA reply: Yes, this is correct.

"Please also confirm if future interim and final reports should be submitted to both NDAs, should the Jadenu NDA be
approved. "

FDA reply: Yes, this is correct.

Thank you,
Lin

Linhua Tzeng, BSN, MS (HSM)
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Hematology Products (DHP)
FDA/CDER/OHOP
Phone: (240) 402-4619

From: Abraham, Abbey [mailto:abbey.abraham@novartis.com]
Sent: Tuesday, February 10, 2015 9:36 AM
To: Tzeng, Linhua
Subject: RE: NDA-206910 Information Request

Hi Lin

We have submitted responses to the PMR list. Please let me know if you have any questions on the submission.

Thanks

Abbey Abraham, PharmD
Oncology Drug Regulatory Affairs
Novartis Pharmaceuticals Corporation

Phone +1 862-778-8998
Fax +1 973-781-5217
abbey.abraham@novartis.com
www.novartis.com

From: Tzeng, Linhua [mailto:Linhua.Tzeng@fda.hhs.gov]
Sent: Monday, January 26, 2015 11:22 AM
To: Abraham, Abbey
Subject: RE: NDA-206910 Information Request

Great. Thanks.
Lin

From: Abraham, Abbey [mailto:abbey.abraham@novartis.com]
Sent: Monday, January 26, 2015 11:18 AM
To: Tzeng, Linhua
Subject: RE: NDA-206910 Information Request

Thank you, Lin, confirmed that I did receive and will respond by Feb 9th as requested.

Abbey Abraham, PharmD
Oncology Drug Regulatory Affairs
Novartis Pharmaceuticals Corporation

Phone +1 862-778-8998
Fax +1 973-781-5217
abbey.abraham@novartis.com
www.novartis.com

From: Tzeng, Linhua [mailto:Linhua.Tzeng@fda.hhs.gov]
Sent: Monday, January 26, 2015 10:58 AM
To: Abraham, Abbey
Cc: Tzeng, Linhua
Subject: FW: NDA-206910 Information Request

Good morning Dr. Abraham,

Please acknowledge receipt of this email.

Thanks,
Lin

Linhua Tzeng, BSN, MS (HSM)
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Hematology Products (DHP)
FDA/CDER/OHOP
Phone: (240) 402-4619

From: Tzeng, Linhua
Sent: Friday, January 23, 2015 1:25 PM
To: Abraham, Abbey
Cc: Tzeng, Linhua
Subject: NDA-206910 Information Request

Good afternoon Dr. Abraham,

Please see attached a courtesy copy of the information request letter. Let me know if you have any questions.

Thank you,
Lin

Linhua Tzeng, BSN, MS (HSM)
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Hematology Products (DHP)
FDA/CDER/OHOP
Phone: (240) 402-4619

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/s/

LINHUA TZENG
02/13/2015

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206910

INFORMATION REQUEST

Novartis Pharmaceuticals Corporation
Attention: Abbey Abraham, Pharm D.
Senior Associate Director, Drug Regulatory Affairs
Oncology Global Development
One Health Plaza, Bldg. 337/B10-6
East Hanover, NJ 07936-1080

Dear Dr. Abraham:

Please refer to your New Drug Application (NDA) submitted May 30, 2014 (received May 30, 2014) under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Jadenu™ (deferasirox) film-coated Tablets, 90 mg, 180 mg and 360 mg.

As we continue our review of your Application, our policy is to initiate discussions of post-marketing requirements (PMRs) and post-marketing commitments (PMCs), so that concurrence on the design of these studies and trials can be completed in advance of the action date. After reviewing the open PMRs and PMCs for Exjade® (deferasirox) tablets for oral suspension to further refine the efficacy and safety of deferasirox, we have determined that the following studies and clinical trials are required for both Exjade® (deferasirox) and Jadenu™ (deferasirox) film-coated tablets. We reference the original summary descriptions below, as described in the original and supplement approval letters for Exjade® (deferasirox) tablets of 2005 and 2013.

For each PMR listed below, submit confirmation to NDA 206910 by February 9, 2015 acknowledging these requirements for Jadenu™ (deferasirox). Also, submit confirmation to IND 58554 and NDA 21882, with a cross-reference to NDA 206910, by February 9, 2015, that you will amend ongoing protocols for Exjade® (deferasirox) tablets to allow for the use of Jadenu™ and/or Exjade® deferasirox formulations in each of the studies/trials described in these PMRs and PMCs

Final PMR set designation numbers for Jadenu™ (deferasirox) tablets will be assigned in the action letter, as appropriate. The number sequence listed here is temporary.

Accelerated Approval PMRs:

PMR 1 Establish a registry for children aged 2 to < 6 years to enroll approximately 200 patients receiving deferasirox and follow them for 5 years. Data collection will be at least

monthly for renal function and blood pressure and yearly for growth and development. Submit your monitoring scheme for our review and comment.

Final Report Submission: 02/2016

PMR 2 Conduct a trial to assess the long-term efficacy of deferasirox in patients with NTDT and high LIC. The trial should assess response rates in the subset of patients with baseline LIC values >15 mg Fe/g dw (proportion of patients achieving an LIC <5 mg Fe/g dw and time to achieving an LIC <5 mg Fe/g dw). Follow-up of all subjects for up to 5 years is necessary.

Trial Completion: 05/2019
Final Report Submission: 11/2019

PMR 3 Assess the long-term efficacy (and safety) of deferasirox treatment to a target LIC of 3 mg Fe/g dw followed by one or more treatment holidays until the LIC is ≥5 mg Fe/g dw in patients with NTDT. Follow-up of all subjects for up to 5 years is necessary.

Trial Completion: 05/2019
Final Report Submission: 11/2019

PMR 4 Conduct a prospective, randomized trial in at least 210 patients with low to intermediate risk myelodysplastic syndromes (MDS) receiving deferasirox for transfusional iron overload (approximately 140) or placebo (approximately 70) to determine the efficacy and safety of (b) (4) (deferasirox) in this population. The trial will continue for 3 years from the date the last patient is enrolled.

Trial Completion: 03/2018
Final Report Submission: 09/2018

FDAAA

PMR 5 Establish a registry (b) (4) children (aged 10 to <18 years old at enrollment) with NTDT and treated with deferasirox for documented iron overload. (b) (4) follow at least 40 children for up to 5 years to assess and analyze the long-term safety of treatment with (b) (4) (deferasirox), including an assessment of growth, compared to children on a regular transfusion program receiving (b) (4) (deferasirox) (based on historical data). Provide annual interim reports on enrollment and outcomes.

You will conduct this study according to the following schedule:

Interim Report Submission: 12/2015
Interim Report Submission: 12/2016
Interim Report Submission: 12/2017
Interim Report Submission: 12/2018

Interim Report Submission: 12/2019
Interim Report Submission: 12/2020
Study Completion: 06/2021
Final Report Submission: 12/2021

PMR 6 Conduct an enhanced pharmacovigilance study (including proactive surveillance and follow-up of spontaneous reports) to characterize the frequency and severity of adverse Events of Special Interest (ESIs), defined as all deaths and severe or serious events of kidney or liver toxicity, in adults receiving deferasirox for documented iron overload related to multiple transfusions for myelodysplastic syndrome with anemia requiring transfusions. (b) (4) This study does not replace monitoring and reporting as required by regulations.

You will conduct this study according to the following schedule:

Interim Report Submission: 01/2015
Interim Report Submission: 07/2015
Interim Report Submission: 01/2016
Interim Report Submission: 01/2017
Interim Report Submission: 01/2018
Study Completion: 01/2019
Final Report Submission: 07/2019

(b) (4)

PMR 8 Complete study of long-term follow-up (3 years) in 150 patients with myelodysplastic syndromes (MDS) receiving deferasirox to evaluate safety (including cardiac, hepatic, endocrine and renal) and hematologic and clinical benefit of deferasirox in these patients.

Final Report Submission: by December 31, 2009

PMR 9 Conduct (b) (4) in patients receiving deferasirox. Examinations should include distance visual acuity, applanation tonometry, lens photography, and wide angle fundus photography of retina and optic nerve and should be done at baseline (prior to deferasirox initiation) and at six month intervals. At least 60 patients should complete 2 years of follow-up.

Final Report Submission: March 31, 2010

If you have any questions, please contact me at (301) 796-1424.

Sincerely,

{See appended electronic signature page}

Diane Leaman
Safety Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/s/

DIANE V LEAMAN
01/23/2015

Tzeng, Linhua

From: Tzeng, Linhua
Sent: Friday, January 09, 2015 3:35 PM
To: Abraham, Abbey
Cc: Tzeng, Linhua
Subject: RE: Recommendation for NDA 206910/Deferasirox

Hi Dr. Abraham,

The team is looking for:

1. Summary of the plan for education campaign
2. Proposed Dear Healthcare Provider Letter (if you plan one)
3. Any other educational type of documents that focus on providing clear information regarding the differences between two dosage forms and their dosing Novartis will distribute to HCPs.

Please submitted to the NDA.

Thanks,
Lin

Linhua Tzeng, BSN, MS (HSM)
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Hematology Products (DHP)
FDA/CDER/OHOP
Phone: (240) 402-4619

From: Abraham, Abbey [mailto:abbey.abraham@novartis.com]
Sent: Friday, January 09, 2015 1:01 PM
To: Tzeng, Linhua
Subject: RE: Recommendation for NDA 206910/Deferasirox

Thank you Lin.

Just had a few clarification questions as to what exactly is the team is looking for by Jan 22nd date. Is the team looking for just a formal written agreement on the recommendation or would you like to have an summary of the campaign? Also would you like to have this submitted to the NDA or just an email response?

Abbey Abraham, PharmD
Oncology Drug Regulatory Affairs
Novartis Pharmaceuticals Corporation

Phone +1 862-778-8998
Fax +1 973-781-5217
abbey.abraham@novartis.com
www.novartis.com

From: Tzeng, Linhua [mailto:Linhua.Tzeng@fda.hhs.gov]
Sent: Friday, January 09, 2015 10:25 AM
To: Abraham, Abbey
Cc: Tzeng, Linhua
Subject: Recommendation for NDA 206910/Deferasirox

Good Morning Dr. Abraham,

We are reviewing your NDA 206910 and would like to request a prompt written response to the below recommendation.

- We recommend you consider providing education campaign to Health Care Practitioners (HCPs) that focus on providing clear information regarding the differences between two dosage forms and provide specific information regarding the dosing for each of them. The campaign should also instruct HCPs to give clear administration instructions to their patients (i.e., how to administer a specific dosage form correctly). This may help minimize any potential dosing errors and wrong administration technique errors.

Please respond before **Thursday on January 22, 2015**.

Thank you,

Lin

Linhua Tzeng, BSN, MS (HSM)
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Hematology Products (DHP)
FDA/CDER/OHOP
Phone: (240) 402-4619

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/s/

LINHUA TZENG
01/09/2015

Tzeng, Linhua

From: Tzeng, Linhua
Sent: Friday, January 09, 2015 10:25 AM
To: Abraham, Abbey (abbey.abraham@novartis.com)
Cc: Tzeng, Linhua
Subject: Recommendation for NDA 206910/Deferasirox

Good Morning Dr. Abraham,

We are reviewing your NDA 206910 and would like to request a prompt written response to the below recommendation.

- We recommend you consider providing education campaign to Health Care Practitioners (HCPs) that focus on providing clear information regarding the differences between two dosage forms and provide specific information regarding the dosing for each of them. The campaign should also instruct HCPs to give clear administration instructions to their patients (i.e., how to administer a specific dosage form correctly). This may help minimize any potential dosing errors and wrong administration technique errors.

Please respond before **Thursday on January 22, 2015**.

Thank you,

Lin

Linhua Tzeng, BSN, MS (HSM)
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Hematology Products (DHP)
FDA/CDER/OHOP
Phone: (240) 402-4619

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/s/

LINHUA TZENG
01/09/2015

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 206910

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Novartis Pharmaceutical Corporation
One Health Plaza
Bldg. 339 - 1187
East Hanover, NJ 07936-1080

ATTENTION: Abbey Abraham, PharmD
Senior Associate Director, Drug Regulatory Affairs

Dear Dr. Abraham:

Please refer to your New Drug Application (NDA) dated and received May 30, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Deferasirox Tablets, 90 mg, 180 mg, and 360 mg.

We also refer to your October 22, 2014, correspondence, received October 22, 2014, requesting reconsideration of your proposed proprietary name, Jadenu. This request concerned an August 26, 2014 decision finding the proposed proprietary name, Jadenu, unacceptable based on our conclusion that the name is misleading,

We carefully reviewed the materials submitted in support of your reconsideration request, along with reviews prepared by staffs in the Division of Medication Error Prevention and Analysis and the Office of Prescription Drug Promotion. Although our review of the (b) (4) study identified some methodological weaknesses with respect to the data gathered, our overall interpretation of the data collected from the physician study indicates that the name is not likely to be misleading. Therefore, since there are no outstanding concerns from a safety or misbranding perspective with your proposed proprietary name, Jadenu, we find the name conditionally acceptable.

If any of the proposed product characteristics as stated in your October 22, 2014, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Sarah Harris, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (240) 402-4774. For any other information regarding this application, contact Linhua Tzeng, Regulatory Project Manager in the Office of New Drugs, at (240) 402-4619.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

KELLIE A TAYLOR
12/03/2014

MEMORANDUM of TELECONFERENCE

MEETING DATE: October 3, 2014
TIME: 2:30 PM – 3:00 PM EST
LOCATION: White Oak Bldg 22, Rm 4440
APPLICATION: NDA 206910
DRUG NAME: Deferasirox
TYPE OF MEETING: Proprietary Name Teleconference

MEETING CHAIRS: Kellie Taylor

FDA ATTENDEES:
Kellie Taylor, Pharm.D., MPH, Deputy Director, OMEPRM
Lubna Merchant, Associate Director, DMEPA
Yelena Maslov, Pharm.D., Team Leader, DMEPA
Rhiannon Leutner, Pharm.D., MPH, MBA, Team Leader, DMEPA
Neil Vora, Pharm.D., MBA, Safety Evaluator, DMEPA
Meeta Patel, Pharm.D., Regulatory Review Officer, OPDP
Amie O'Donoghue, Ph.D., Social Science Analyst, OPDP
Bryant M. Godfrey, J.D., M.H.A., Senior Lead Regulatory Counsel, OPDP
Sarah Harris, Pharm.D., Project Manager, OSE

SPONSOR ATTENDEES:
Krista McKerracher, Global Program Head
Abbey Abraham, Senior Associate Director Regulatory Affairs
Shanthi Ganeshan, North America Head, Regulatory Affairs
Sandip Roy, Senior Director, Regulatory Affairs
Dorothy LinvillNeal, Executive Director, Regulatory Strategy& Trademarks
Judith Shevell, Regulatory Strategy & Trademarks

BACKGROUND:

On June 4, 2014 Novartis submitted a correspondence to NDA 206910 requesting review of the proposed proprietary name, Jadenu. On August 26, 2014 FDA issued a letter informing Novartis that the name is unacceptable for promotional reasons. On September 9, 2014 Novartis requested a teleconference via phone and email to discuss the denial of the proprietary name. On October 3, 2014, FDA and Novartis met via teleconference for this discussion.

MEETING OBJECTIVES:

Novartis requested this TCon with DMEPA to discuss the rejection of the Jadenu proprietary name. They would like to clarify that their intent with the "nu" designation in the name, was to communicate the availability of a new formulation, and assure patients who have been on Exjade therapy for up to 9 years (and their caregivers) that this new formulation has the same efficacy (based on the PK comparability) but is different from Exjade in terms of dose, excipients and

presentation. Novartis would like to ensure this information was taken into account as part of the OPDP review. They would also like to discuss whether there is any path forward with this name (or a clone of this name).

OPDP CONCERNS WITH THE PROPOSED NAME

The use of the suffix "nu" (evoking "new") in the proposed proprietary name, Jadenu, would be overly fanciful because the active ingredient, deferasirox, is a common substance for which the limitations are readily recognized when Jadenu is listed by its established name [21 CFR 201.10(c)(3)]. Furthermore, "Jadenu" implies superiority over another drug (Exjade) which has an identical active ingredient (deferasirox). The use of a large part of the name "Exjade" in combination with a word that evokes "new" (i.e., novel) implies that Jadenu (deferasirox) is a new drug; however, Exjade (deferasirox) has been on the market since 2005. Because the proposed trade name would be overly fanciful and would imply superiority over Exjade, it is misleading.

Please note that the Federal Food Drug and Cosmetic Act (FD&C Act) provides that labeling or advertising can misbrand a product if misleading representations are made (See 21 U.S.C. 321(n)). The FD&C Act also provides that a drug is misbranded if its labeling is false or misleading in any particular (21 USC 352(a)). A proprietary name, which appears in labeling, could result in such misbranding if it is false or misleading , such as by making misrepresentations with respect to safety or efficacy.

REGULATORY OPTIONS

- Submit "Request for Reconsideration of Proprietary Name".
- Submit new proprietary name.

DISCUSSION

- Novartis explained their rationale for requesting the name Jadenu and their desire to keep the name consistent amongst worldwide markets
- FDA further clarified their reasons for denying the name based upon promotional concerns with the suffix "nu".
- Novartis informed FDA that they had additional data (in the form of studies) supporting the use of the name "Jadenu".
- FDA explained that there are two possible paths forward for Novartis:
    - Submit "Request for Reconsideration of Proprietary Name" for the name Jadenu, with the additional data.
    - Submit new proprietary name.
- Novartis expressed interest in pursuing a "Request for Reconsideration of Proprietary Name".

- FDA referred Novartis to both the "PDUFA Pilot Project- Proprietary Name Review- Concept Paper" and the "Guidance for Industry- Contents of a Complete Submission for the Evaluation of Proprietary Names" for additional information on current FDA thinking regarding promotional concerns as well as best practices for submissions.
- FDA strongly encouraged Novartis to submit any data or studies that they may have regarding this name, with the reconsideration request.

ACTION ITEMS

- Novartis will plan to submit a "Request for Reconsideration of Proprietary Name" with additional data.

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/s/

SARAH J HARRIS
10/09/2014

LUBNA A MERCHANT
10/09/2014

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 206910

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Novartis Pharmaceutical Corporation
One Health Plaza
East Hanover, NJ 07936-1080

ATTENTION: Abbey Abraham, PharmD
Senior Associate Director of Drug Regulatory Affairs

Dear Dr. Abraham:

Please refer to your New Drug Application (NDA) dated and received May 30, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Deferasirox Tablets, 90 mg, 180 mg, and 360 mg.

We also refer to your June 4, 2014, correspondence, received June 4, 2014, requesting review of your proposed proprietary name, Jadenu.

We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

The use of the suffix "nu" (evoking "new") in the proposed proprietary name, Jadenu, would be overly fanciful because the active ingredient, deferasirox, is a common substance for which the limitations are readily recognized when Jadenu is listed by its established name [21 CFR 201.10(c)(3)]. Furthermore, "Jadenu" implies superiority over another drug (Exjade) which has an identical active ingredient (deferasirox). The use of a large part of the name "Exjade" in combination with a word that evokes "new" (i.e., novel) implies that Jadenu (deferasirox) is a new drug; however, Exjade (deferasirox) has been on the market since 2005. Because the proposed trade name would be overly fanciful and would imply superiority over Exjade, it is misleading.

Please note that the Federal Food Drug and Cosmetic Act (FD&C Act) provides that labeling or advertising can misbrand a product if misleading representations are made (See 21 U.S.C. 321(n)). The FD&C Act also provides that a drug is misbranded if its labeling is false or misleading in any particular (21 USC 352(a)). A proprietary name, which appears in labeling, could result in such misbranding if it is false or misleading , such as by making misrepresentations with respect to safety or efficacy.

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names,* http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf and "PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012".)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Kevin Wright, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-3621. For any other information regarding this application, contact Linhua Tzeng, Regulatory Project Manager in the Office of New Drugs, at (240) 402-4619.

Sincerely,

{See appended electronic signature page}

Kellie A. Taylor, Pharm.D., MPH
Deputy Director
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

KELLIE A TAYLOR
08/26/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206910

FILING COMMUNICATION –
NO FILING REVIEW ISSUES IDENTIFIED

Novartis Pharmaceuticals Corporation
Attention: Abbey Abraham, Pharm D.
Senior Associate Director
Drug Regulatory Affairs
Oncology Global Development
One Health Plaza, Bldg. 337/B10-6
East Hanover, NJ 07936-1080

Dear Dr. Abraham:

Please refer to your New Drug Application (NDA) dated May 30, 2014, received May 30, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, for deferasirox film-coated tablets under a new trade name, Jadenu™.

We also refer to your amendments dated June 4 and July 14, 2014.

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 **Standard**. Therefore, the user fee goal date is March 30, 2015.

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 commitment requests by March 2, 2015.

At this time, we are notifying you that, we have not identified any potential review issues. Please note that our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review.

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. We encourage you to review the labeling review resources on the *PLR Requirements for Prescribing Information* website including:

- The Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products
- Regulations and related guidance documents
- A sample tool illustrating the format for Highlights and Contents, and
- The Selected Requirements for Prescribing Information (SRPI) − a checklist of 42 important format items from labeling regulations and guidances.

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

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:

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

Do not submit launch materials until you have received our proposed revisions to the package insert (PI), 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.

Because none of these criteria apply to your application, you are exempt from this requirement.

If you have any questions, call Linhua Tzeng, Regulatory Project Manager, at (240) 402-4619.

Sincerely,

{See appended electronic signature page}

Edvardas Kaminskas, M.D.
Deputy Director
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/s/

EDVARDAS KAMINSKAS
07/25/2014

Tzeng, Linhua

From: Tzeng, Linhua
Sent: Thursday, July 10, 2014 7:39 PM
To: Abraham, Abbey
Cc: Tzeng, Linhua
Subject: Biopharmaceutics Information Request for NDA 206910/Deferasirox

Good evening Abbey,

We are reviewing your NDA 206910 and would like to request a prompt written response to the below request for additional information from our Biopharmaceutics team.

Information Request:

- Please clarify the discrepancy on the information provided in your Email response dated July 03, 2014, indicating that the bioanalytical site for Study CICL670F2102 was (b) (4) and (b) (4) was the Principal Analytical Investigator; versus the information provided in your NDA submission, pages 2 and 11 of the Bioanalytical Data Report for Study CICL670F2102 (Location 5.3.1.2 Compliance and Drug Concentration Data) indicating that the bioanalytical facility was (b) (4) and (b) (4) was the Bioanalytical Study Director.

Please respond by **noon, Tuesday July 15, 2014**.

Thank you,
Lin

Linhua Tzeng, BSN, MS (HSM)
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Hematology Products (DHP)
FDA/CDER/OHOP
Phone: (240) 402-4619

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LINHUA TZENG
07/10/2014

Tzeng, Linhua

From: Tzeng, Linhua
Sent: Tuesday, July 01, 2014 9:54 AM
To: Abraham, Abbey
Cc: Akinsanya, Lara; Tzeng, Linhua
Subject: Clinical Pharmacology and Pharmacometrics Information Request for NDA 206910/Deferasirox

Good morning Abbey,

We are reviewing your NDA 206910 and would like to request a prompt written response to the below request for additional information from our Clinical Pharmacology and Pharmacometrics team.

Information Request:

- Please submit the following contact information for the clinical and analytical sites used in Study CICL670F2102:

Clinical Facility Name: Address: (Tel) (Fax)	Analytical Facility Name: Address: (Tel) (Fax)
Clinical Investigator: (email)	Principal Analytical Investigator: (email)

- We could not locate the supporting materials for your PK/PD analyses (PK/renal laboratory values, PK/efficacy) as referenced in 'section 3 Statistical methodology' from the study report of CICL670A2409 (PK/PD analysis).

  Please submit full analysis datasets, define files and model codes for these analyses. If already submitted in the original NDA, please point us to the correct location. Please refer to the following link regarding general expectations for submitting pharmacometric data and models. (http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm180482.htm)

Please respond by **COB, Thursday July 3, 2014**.

Thank you,
Lin

Linhua Tzeng, BSN, MS (HSM)
LCDR, U.S. Public Health Service
Regulatory Project Manager
Division of Hematology Products (DHP)
FDA/CDER/OHOP
Phone: (240) 402-4619

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/s/

LINHUA TZENG
07/01/2014

From: Agosto, Teicher
To: "abbey.abraham@novartis.com"
Subject: NDA 206910- Information Request
Date: Monday, June 23, 2014 1:05:00 PM

Dear Ms. Abraham,

We are requesting the following information concerning your New Drug Application – NDA 206910. Can you please provide a table with all manufacturing sites(drug substance and drug product) with site responsibilities and the contact information (name, address, Registration (FEI) number, Establishment DUNS number, telephone number, email and fax) by COB Thursday, June 26, 2014.

In addition to formally submitting this information, please send me a courtesy copy via email.

Please confirm receipt of this email.

Kind Regards,
Teicher Agosto, Pharm D, RPh
Regulatory Health Project Manager
FDA\CDER\OPS
Office of New Drug Quality Assessment
10903 New Hampshire Ave W021,Rm 2615
Silver Spring, MD 20993
Teicher.agosto@fda.hhs.gov
P: (240) 402-3777

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/s/

TEICHER N AGOSTO
06/23/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 206910

NDA ACKNOWLEDGMENT

Novartis Pharmaceuticals Corporation
Attention: Abbey Abraham, Pharm D.
Senior Associate Director
Drug Regulatory Affairs
Oncology Global Development
One Health Plaza, Bldng 337/B10-6
East Hanover, NJ 07936-1080

Dear Dr. Abraham:

We have received your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: Jadenu™ (deferasirox)

Date of Application: May 30, 2014

Date of Receipt: May 30, 2014

Our Reference Number: NDA 206910

Unless we notify you within 60 days of the receipt date that the application is not sufficiently complete to permit a substantive review, we will file the application on July 29, 2014, in accordance with 21 CFR 314.101(a).

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 provided above should be cited 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 Hematology Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

All regulatory documents submitted in paper should be three-hole punched on the left side of the page and bound. The left margin should be at least three-fourths of an inch to assure text is not obscured in the fastened area. Standard paper size (8-1/2 by 11 inches) should be used; however, it may occasionally be necessary to use individual pages larger than standard paper size. Non-standard, large pages should be folded and mounted to allow the page to be opened for review without disassembling the jacket and refolded without damage when the volume is shelved. Shipping unbound documents may result in the loss of portions of the submission or an unnecessary delay in processing which could have an adverse impact on the review of the submission. For additional information, please see http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/DrugMasterFilesDMFs/ucm073080.htm.

Secure email between CDER and applicants is useful for informal communications when confidential information may be included in the message (for example, trade secrets or patient information). If you have not already established secure email with the FDA and would like to set it up, send an email request to SecureEmail@fda.hhs.gov. Please note that secure email may not be used for formal regulatory submissions to applications.

If you have any questions, call me at (240) 402-4619.

Sincerely,

{See appended electronic signature page}

Linhua Tzeng, BSN, MS
Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

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/s/

LINHUA TZENG
06/05/2014

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

IND 058554

MEETING PRELIMINARY COMMENTS

Novartis Pharmaceuticals Corporation
Attention: Abbey Abraham, PharmD.
Senior Associate Director of DRA
One Health Plaza
East Hanover, NJ 07936

Dear Dr. Abraham:

Please refer to your Investigational New Drug Application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for Exjade® (deferasirox) dispersible tablets (125 mg, 250 mg, 500 mg).

We also refer to your January 27, 2014, correspondence, received January 28, 2014, requesting a meeting to discuss the registration package for the new film-coated tablet of deferasirox targeted for April 30, 2014.

Our preliminary responses to your meeting questions are enclosed.

You should provide, to the Regulatory Project Manager, a hardcopy or electronic version of any materials (i.e., slides or handouts) to be presented and/or discussed at the meeting.

If you have any questions, call me at (240) 402-4230.

Sincerely,

{See appended electronic signature page}

Tinya Sensie, M.H.A.
Regulatory Health Project Manager
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

ENCLOSURE:
Preliminary Meeting Comments

FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

PRELIMINARY MEETING COMMENTS

Meeting Type: B
Meeting Category: Pre-sNDA

Meeting Date and Time: March 24, 2014; 1:00 pm-2:00 pm
Meeting Location: Bldg 22, Rm 4201

Application Number: IND 058554
Product Name: Exjade
Indication: Iron overload
Sponsor/Applicant Name: Novartis

FDA ATTENDEES

Division of Hematology Products (DHP)

Ann Farrell, M.D., Division Director
Edvardas Kaminskas, M.D., Deputy Division Director
Kathy Robie Suh, M.D. , Clinical Team Leader
Andrew Dmytrijuk, M.D., Clinical Reviewer
Lara Akinsanya, M.S., Senior Regulatory Health Project Manager
Ebla Ali Ibrahim, M.S., Lead Regulatory Health Project Manager
Mara Miller, M.A., Senior Regulatory Health Project Manager
Tinya Sensie, M.H.A., Regulatory Health Project Manager

Division of Hematology Oncology Toxicology (DHOT)

Haleh Saber, Ph.D., Supervisory, Pharmacologist
Ramadevi Gudi, Ph.D, Pharmacologist/Toxicologist

Office of New Drug Quality Assessment (ONDQA)

Janice Brown, M.S., Product Quality Team Leader
Kavita Vyas, Ph.D., Product Quality Reviewer

Office of Clinical Pharmacology (OCP)

Julie Bullock, PharmD, Clinical Pharmacology Team Leader
Joseph Grillo, PharmD, Pharmacologist

Office of Biostatistics, Division of Biometrics V (DBV)

Lei Nie, Ph.D., Statistical Team Leader
Yuan Li Shen, Ph.D., Statistical Team Leader
Chia-Wen Ko, Ph.D., Biostatistics Reviewer

SPONSOR ATTENDEES

Shanthi Ganesh Ph.D., North American Head Drug Regulatory Affairs
Abbey Abraham Pharm.D., Global Regulatory Affairs
JoAnn Horowitz M.D., Global Clinical Program Head
Chiaki Tanaka, Ph.D., Clinical Pharmacology
Euloge Kpamegan, Ph.D., Project Statistician
Sudha Vippagunta, Technical Research & Development
Krista McKerracher, Exjade Global Program Head

Introduction:

This material consists of our preliminary responses to your questions and any additional comments in preparation for the discussion at the meeting scheduled for March 24, 2014, teleconference between Novartis and the Division of Hematology Products. We are sharing this material to promote a collaborative and successful discussion at the meeting. The meeting minutes will reflect agreements, important issues, and any action items discussed during the meeting and may not be identical to these preliminary comments following substantive discussion at the meeting. If you determine that discussion is needed for only some of the original questions, you have the option of reducing the agenda and/or changing the format of the meeting (e.g., from face to face to teleconference). Contact the Regulatory Project Manager (RPM) if there are any major changes to your development plan, the purpose of the meeting, or the questions based on our preliminary responses, as we may not be prepared to discuss or reach agreement on such changes at the meeting.

1.0 BACKGROUND

Novartis submitted a pre-sNDA meeting request on January 27, 2014 to discuss the registration package for the new film-coated tablet of Exjade (deferasirox) targeted for April 30, 2014. The purpose of this Type B meeting is to seek feedback and agreement with FDA on the content and format of the NDA for the deferasirox film-coated tablet formulation. Based on the statement of purpose, objectives, and proposed agenda, FDA considers the meeting a type B meeting. Exjade was approved in the United States on November 2, 2005 for the treatment of iron overload under NDA 21-882. The agency sent a letter on February 14, 2014 granting Novartis' request for a pre-NDA teleconference, on March 24, 2014 from 1-2 pm.

2.0 DISCUSSION

2.1. User Fee

Question 1: ***Does the Agency agree that a User-Fee Waiver is acceptable should both of the above indications have orphan designation at the time of the filing of the new film-coated tablet?***

FDA Response to Question 1:

Each new dosage form will be a separate NDA [i.e., (b) (4) , one for film coated tablets] along with the one for the currently approved product.

According to Section 736(1)(a)(1)(F), "A human drug application for a prescription drug product that has been designated as a drug for a rare disease or condition according to section 526 of the Act, shall not be subject to an application user fee unless the human drug application includes an indication for other than a rare disease or condition…".

So, if both of the indications proposed are orphan designated before Novartis submits the application, then the new application is exempt from the user fee for the new application submission (a waiver request is not required, just note the orphan designation on the user fee coversheet and include a copy of the orphan designation letter(s) for each of the indications).

But, if one (or both) of the indications are not orphan designated, the application fee will need to be paid.

If orphan designation for either indication has been requested and is still pending when the application is submitted, Novartis should pay the application fee for the application, and also submit a request to the PDUFA staff (fax number 301-847-8711) for a refund of the fee in anticipation of Novartis receiving orphan designation. [Note: the request for a refund must be submitted within 180 days of when the fee is due (application fees are due the day the application is submitted)]. If/When orphan designation is granted, the refund request can then be processed and if eligible, the application fee can be refunded but only if the request for the refund was timely.

The fee for the application will be based on whether clinical data are required for approval or whether bioavailability information only is sufficient for approval. This will be determined when the application is received.

More information about the refund request process is available in the Guidance for Industry, User Fee Waivers, Reductions and Refunds for Drug and Biological Products, September 2011)

2.2. Cross-Reference

Question 2: ***Novartis proposes to cross-reference the Exjade NDA (21-882) for the majority of the deferasirox drug substance and non-clinical information as well as clinical efficacy, safety data and clinical pharmacology data. In addition the following information in support of the film coated tablet will be included in the forthcoming NDA,***

- ***Drug substance information as noted in the Type C meeting Minutes of March 2, 2012***
- ***A new PK/PD report for study 2409 (CSR previously submitted to NDA 21882) with respective Case Report Tabulation,***
- ***F2101 (pilot bioavailability study with the film-coated tablets),***
- ***F2102 (pivotal bioequivalence study with the film-coated tablets),***
- ***F2103 (food effect study with the film-coated tablets) and***
- (b) (4)

Does the Agency agree with this approach?

FDA Response to Question 2:

(b) (4)

Overall your proposal to cross-reference NDA 21,882 for nonclinical, clinical and CMC data previously submitted is acceptable. You may include new nonclinical data (e.g. PK studies in the dog) in Modules 2 and 4 of the new NDA submission(s).

In your new NDA submission(s), you should provide cross references to specific locations of relevant sections and documents in the original NDA.

For clinical pharmacology, your proposal is acceptable assuming the following issues are addressed:

1. The Summary of Clinical Pharmacology and the Summary of Biopharmaceutics reports should provide the full breadth of information available to date regarding Exjade with appropriately linked cross-references. New information should be highlighted in a manner that it can be easily identified from that previously submitted to the Agency.

2. Datasets for clinical pharmacology and biopharmaceutics trials should be complete and not be limited to PK/PD. For example, domains related to safety (e.g., ADR's), demographics, non-PK laboratory values, and concomitant drug use should be included. All of these are important in identifying patterns of potential clinical pharmacology related causes of clinical safety outcomes.

3. Provide all concentration-time and derived PK parameter datasets for all studies. In the study reports, present the PK parameter data as geometric mean with coefficient of variation (and mean ± standard deviation) and median with range as appropriate.

4. (b) (4)

2.3. Proposed eCTD table of contents

Question 3: ***Does the Agency agree with the proposed content of the NDA submission as outlined in the draft eCTD table of contents?***

FDA Response to Question 3:

The proposed content of the NDA as outlined is acceptable.

For clinical pharmacology, please see response to question 2.

Options to cross reference information submitted to another application would be to either place a cross reference document under module m1.4.4 (cross reference to other applications), or use cross application links.

1. To use the first option (placing a cross reference document in m1.4.4), a table formatted document can be submitted in section 1.4.4 of the eCTD, detailing previously submitted information (eCTD and/or non- eCTD) that is being referenced by the current application. The information in the document should include (1) the application number, (2) the date of submission (e.g., letter date), (3) the file name, (4) the page number (if necessary), (5) the eCTD sequence number, (6) the eCTD heading location (e.g., m3.2.p.4.1 Control of Excipients – Specifications), (7) the document leaf title and (8) the submission identification (e.g., submission serial number, volume number, electronic folder, file name, etc,.,) of the referenced document along with a hypertext link to the location of the information, when possible.

2. To use the second option (cross application links), both applications would need to be in eCTD format and reside on the same server. The applications need to include the appropriate prefix in the href links (e.g. nda, ind,). Also, when cross application links are used, it's strongly recommended that a cross reference document be placed in m1.4.4, in case any of the links don't work and in the leaf titles of the documents, it is recommended that the leaf title indicate the word “cross reference” and application number (e.g. Cross Ref to nda123456). The cross reference information in the leaf title allows the reviewer to know that the document resides in another application and the application number that is being referenced.

Prior to using cross application linking in an application, it is recommended that sponsor submits an "eCTD cross application links" sample, to ensure successful use of cross application links.

To submit an eCTD cross application links sample, sponsor would need to request two sample application numbers from the ESUB team - esub@fda.hhs.gov. For more information on eCTD sample, please refer to the Sample Process web page which is located at http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm174459.htm

3.0 OTHER IMPORTANT MEETING LANGUAGE

PREA REQUIREMENTS

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.
Because this drug product for this indication has an orphan drug designation, you are exempt from these requirements. If there are any changes to your development plans that would cause your application to trigger PREA, your exempt status would change.

PRESCRIBING INFORMATION

In your application, you must submit proposed prescribing information (PI) that conforms 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 of Prescribing Information* website including the Final Rule (Physician Labeling Rule) on the content and format of the PI for human drug and biological products, regulations, related guidance documents, a sample tool illustrating the format for Highlights and Contents , and the Selected Requirements for Prescribing Information (SRPI) − a checklist of 42 important format items from labeling regulations and guidances. We encourage you to use the SRPI checklist as a quality assurance tool before you submit your proposed PI.

MANUFACTURING FACILITIES

To facilitate our inspectional process, we request that you clearly identify *in a single location*, either on the Form FDA 356h, or an attachment to the form, all manufacturing facilities associated with your application. 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). Each facility should be ready for GMP inspection at the time of submission.

Consider using a table similar to the one below as an attachment to Form FDA 356h. Indicate under Establishment Information on page 1 of Form FDA 356h that the information is provided in the attachment titled, "Product name, NDA/BLA 012345, Establishment Information for Form 356h."

Site Name	Site Address	Federal Establishment Indicator (FEI) or Registration Number (CFN)	Drug Master File Number (if applicable)	Manufacturing Step(s) or Type of Testing [Establishment function]
1.				
2.				

Corresponding names and titles of onsite contact:

Site Name	Site Address	Onsite Contact (Person, Title)	Phone and Fax number	Email address
1.				
2.				

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/s/

TINYA J SENSIE
03/20/2014