CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022063Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # 022063 BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: *(an action package is not required for SE8 or SE9 supplements)*
Proprietary Name: Mydayis Established/Proper Name: mixed salts of a single-entity amphetamine product Dosage Form: Capsules		Applicant: Shire, LLC. Agent for Applicant (if applicable): Peggy Sung; psung@shire.com
RPM: Latrice Wilson, PharmD; latrice.wilson@fda.hhs.gov; 240-402-5317		Division: Psychiatry 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 June 20, 2017	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None Approvable 5/18/2007
❖ 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.

Review priority: ☒ Standard ☐ Priority
Chemical classification (new NDAs only): Attention Deficit Hyperactivity Disorder
(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

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

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

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 (Tab A)

❖ 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 (Tab B)	
❖ Copies of all action letters *(including approval letter with final labeling)*	Action(s) and date(s): Approval 6/20/2017 Approvable 05/18/2007
Labeling (Tab C)	
❖ 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
❖ 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)*	04/14/2017 04/13/2017
❖ Labeling reviews *(indicate dates of reviews)*	RPM: ☒ None DMEPA: ☐ None 5/18/2017; 6/19/2017; 6/20/2017 DMPP/PLT (DRISK): ☐ None 5/30/2017 OPDP: ☐ None 05/26/2017; 5/30/2017 SEALD: ☒ None CSS: ☒ None Product Quality ☒ None Other: ☒ None
Administrative / Regulatory Documents (Tab D)	
❖ 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	N/A ☒ Not a (b)(2)
❖ NDAs/NDA supplements only: Exclusivity Summary *(signed by Division Director)*	☒ Completed (Do not include)
❖ 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 5/17/2017 If PeRC review not necessary, explain: _____	
❖ Breakthrough Therapy Designation	☒ N/A
• Breakthrough Therapy Designation Letter(s) (granted, denied, an/or rescinded)	
• CDER Medical Policy Council Breakthrough Therapy Designation Determination Review Template(s) *(include only the completed template(s) and not the meeting minutes)*	
• CDER Medical Policy Council Brief – Evaluating a Breakthrough Therapy Designation for Rescission Template(s) *(include only the completed template(s) and not the meeting minutes)* *(completed CDER MPC templates can be found in DARRTS as clinical reviews or on the MPC SharePoint Site)*	
❖ Outgoing communications: letters, emails, and faxes considered important to include in the action package by the reviewing office/division (e.g., clinical SPA letters, RTF letter, Formal Dispute Resolution Request decisional letters, etc.) *(do not include OPDP letters regarding pre-launch promotional materials as these are non-disclosable; do not include Master File letters; do not include previous action letters, as these are located elsewhere in package)*	Ack Letter: 1/17/2017 Information Requests: 1/17/2017; 3/13/2017; 5/25/2017; PMR: 5/15/2017 Approval Receipt: 6/20/2017
❖ 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)	
❖ 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)*	☒ No mtg
• 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 focused milestone meetings) *(indicate dates of mtgs)*	N/A
❖ Advisory Committee Meeting(s)	☒ No AC meeting
• Date(s) of Meeting(s)	
Decisional and Summary Memos (Tab E)	
❖ Office Director Decisional Memo *(indicate date for each review)*	☒ None
Division Director Summary Review *(indicate date for each review)*	☐ None 6/19/2017
Cross-Discipline Team Leader Review *(indicate date for each review)*	☐ None 6/19/2017
PMR/PMC Development Templates *(indicate total number)*	☐ None 4
Clinical (Tab F)	

❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
• Clinical review(s) *(indicate date for each review)*	6/20/2017
• 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)*	Clinical review dated 6/20/17
❖ Clinical reviews from immunology and other clinical areas/divisions/Centers *(indicate date of each review)*[5]	☒ None
❖ Controlled Substance Staff review(s) and Scheduling Recommendation *(indicate date of each review)*	☐ N/A 6/14/2017
❖ 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)*	☒ Clinical Inspection Summary 05/11/2017
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 See product quality review
Biostatistics (Tab G) ☐ 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 5/18/2017
Clinical Pharmacology (Tab H) ☐ None	
❖ Clinical Pharmacology Division Director Review(s) *(indicate date for each review)*	☒ No separate review
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	No separate review
Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None 6/12/2017
❖ OSI Clinical Pharmacology Inspection Review Summary *(include copies of OSI letters)*	☒ None requested

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

Nonclinical (Tab I) ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☒ No separate review
• Supervisory Review(s) *(indicate date for each review)*	☒ No separate review
• Pharm/tox review(s), including referenced IND reviews *(indicate date for each review)*	☐ None 5/25/2017
❖ 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 (Tab J) ☐ None	
❖ Product Quality Discipline Reviews[6]	
• Tertiary review (*indicate date for each review*)	☒ None
• Secondary review (e.g., Branch Chief) *(indicate date for each review)*	☐ None 06/05/2017
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) *(indicate date for each review)*	☐ None 06/05/2017
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team *(indicate date of each review)*	☐ None 06/05/2017
❖ 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)*	
☐ Review & FONSI *(indicate date of review)*	
☒ Review & Environmental Impact Statement *(indicate date of each review)*	5/17/2017
❖ Facilities Review/Inspection	
☒ Facilities inspections (indicate date of recommendation; within one week of taking an approval action, confirm that there is an acceptable recommendation before issuing approval letter) *(only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)*	☒ Acceptable; 6/1/2017 ☐ Withhold recommendation ☐ Not applicable

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

Day of Approval Activities	
❖ For all 505(b)(2) applications: • 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): Flush List • 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
❖ Take Action Package (if in paper) down to Document Room for scanning within **two business days**	

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

/s/

LATRICE WILSON
06/23/2017

Wilson, Latrice

'om: Sung, Peggy <psung@shire.com>
Sent: Tuesday, June 20, 2017 4:19 PM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Approval

Categories: 1Sponsor

Hi Latrice,

Thanks for sending the approval letter. I'd like to confirm receipt of the email.

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Tuesday, June 20, 2017 4:00 PM
To: Sung, Peggy
Subject: NDA 022063 Mydayis Approval

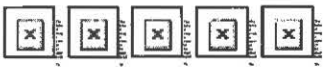
Hi Peggy,

The Division has granted approval for NDA 022063, Mydayis (mixed salts of a single-entity amphetamine product) extended release tablets. Please see attached for a courtesy copy of the approval letter. Official correspondence will be received via email.

Please confirm receipt of this email as soon as possible.
Sincerely,

Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov



Wilson, Latrice

'om: Sung, Peggy <psung@shire.com>
ɔent: Tuesday, June 20, 2017 4:37 PM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Approval

Categories: 1Sponsor

Hi Latrice,

Upon review, Shire has noticed a misspelling in Section 2.4 Dosing Information (does → dose). The misspelling will be corrected in the final labels and SPL, which will be submitted to ESG and uploaded to DailyMed within 14 days of approval.

Pediatric Use (13 to 17 years)
The recommended starting does is 12.5 mg once daily in the morning upon awakening. Dosage may be adjusted in increments of 12.5 mg no sooner than weekly, up to a recommended maximum dose of 25 mg once daily. The dose should be individualized according to the needs and response of the patient. Doses higher than 25 mg have not been evaluated in clinical trials in pediatric patients.

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Tuesday, June 20, 2017 4:00 PM
To: Sung, Peggy
ɹbject: NDA 022063 Mydayis Approval

Hi Peggy,

The Division has granted approval for NDA 022063, Mydayis (mixed salts of a single-entity amphetamine product) extended release tablets. Please see attached for a courtesy copy of the approval letter. Official correspondence will be received via email.

Please confirm receipt of this email as soon as possible.
Sincerely,

Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov

Wilson, Latrice

om: Sung, Peggy <psung@shire.com>
ent: Thursday, June 15, 2017 3:26 PM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Categories: 1Sponsor

Hi Latrice,

Shire agrees to the proposed timelines for the PMRs as well.

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Thursday, June 15, 2017 3:20 PM
To: Sung, Peggy
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Peggy,

Thanks for confirming our response.

In addition to the PMR, does Shire agree to the proposed timelines as well? I know that your internal timelines may be ioner, keeping exclusivity in mind, but I wanted to confirm.

Sincerely,

Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov

FDA U.S. FOOD & DRUG ADMINISTRATION

From: Sung, Peggy [mailto:psung@shire.com]
Sent: Thursday, June 15, 2017 3:10 PM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Latrice,

I wanted to send another quick email to confirm that Shire agrees to conducting the studies for the post market requirements in your June 13th email since Shire did not have a teleconference with the Division today.

Also, if there is any possibility of accelerating the comments for the container labels, that would really be great.

Kind regards,
Peggy

From: Sung, Peggy
Sent: Thursday, June 15, 2017 2:46 PM
To: 'Wilson, Latrice'
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Latrice,

Thanks very much for the update. Shire will await FDA's comments to the label and med guide this evening.

With regards to the Division's responses to Shire's questions, Shire confirms that enrolling de novo patients into the safety study are in addition to recruiting from the two safety and efficacy trials.

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Thursday, June 15, 2017 1:57 PM
To: Sung, Peggy
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Peggy,

We have concluded the meeting. The aim is to send the label/med guide to you this evening. Any anticipated changes to the carton/container labels are forthcoming. Hopefully, I will have an update to you by Monday for those.

In lieu of a teleconference, the Division has drafted the following responses to your questions:

1) Based on prior FDA feedback regarding the consideration of a PWR, Shire submitted a PPSR which now includes a PK study, a safety/efficacy study and an open-label safety study. These studies outlined in the PPSR are generally consistent with the PMR requirements. Further to these 3 studies, FDA has included one additional study in ADHD patients 6-12 years old in the PMR communication.
    a) While we recognize that a formal decision cannot be issued during the teleconference without review from the Pediatric Review Committee (PeRC), Shire would like to propose that these 4 PMR studies be issued as the PWR for SHP465 as well as fulfill our PREA requirements. Does FDA agree? Yes.
    b) Would FDA issue a PWR for the 4 PMR studies without the need for a revised PPSR resubmission? Yes.

2) As per the response to FDA's information request issued in May 2017 pertaining to the PPSR, Shire committed to submitting a 6-month study report as part of an open-label 12 month safety study to provide the requested information in 4-5 year old subjects with ADHD. Shire proposed to submit a 6-month study report by the filing date to satisfy the requirements of the PWR.
    a) A 12-month study report will be submitted by the PMR deadline. Will FDA accept a 6-month study report to fulfill the PWR requirement? Yes. We would accept an interim 6-month study report. We understand that the open-label safety study will be continuing past the timeframe for the PWR.
    b) Does FDA concur with direct enrollment into the open-label safety study? Please clarify if enrolling de novo patients into the safety study is in addition to recruiting from the two safety and efficacy trials. If so, direct enrollment is acceptable.

3) In light of the requirement to submit final study reports 15 months prior to expiration of the exclusivity and the projected study timelines, Shire is proposing to submit draft PMR/PWR protocols to FDA as soon as possible following the action date. Would FDA be able to commit to a 2-week review timeline of the draft protocols? The Division cannot commit to a 2-week review timeline. We will review the protocols as quickly as possible, but the timeframe will largely depend on our resources at the time of submission.

Sincerely,

Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov

From: Sung, Peggy [mailto:psung@shire.com]
Sent: Thursday, June 15, 2017 10:40 AM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Thanks, Latrice. Are you able to share when your labeling meeting is so that Shire's team can internally prepare for standby to promptly address all of FDA's comments? Would there also be any possibility to reserve time with the Division for a teleconference on Friday to review the labeling in order that issues can be quickly addressed?

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Thursday, June 15, 2017 10:00 AM
To: Sung, Peggy
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Peggy,

I received your voicemail. I am currently preparing for the labeling meeting that we have later today. I believe we will respond via email to your questions. I will update you later today.

Sincerely,

Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov

From: Wilson, Latrice
Sent: Wednesday, June 14, 2017 3:27 PM
To: Sung, Peggy
Subject: Re: NDA 022063 Mydayis Post Market Requirements

Hi Peggy,

Thank you. I will relay these to my team and will send you an update as soon as possible.

Sincerely,

Latrice Wilson, PharmD
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center For Drug Evaluation and Research, FDA
Ph: 240.402.5317
Email: latrice.wilson@fda.hhs.gov

From: Sung, Peggy
Sent: Wednesday, June 14, 2017 3:23 PM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Latrice,

Please find below Shire's questions pertaining to the post market requirements for NDA 022063.

1) Based on prior FDA feedback regarding the consideration of a PWR, Shire submitted a PPSR which now includes a PK study, a safety/efficacy study and an open-label safety study. These studies outlined in the PPSR are generally consistent with the PMR requirements. Further to these 3 studies, FDA has included one additional study in ADHD patients 6-12 years old in the PMR communication.
    a) While we recognize that a formal decision cannot be issued during the teleconference without review from the Pediatric Review Committee (PeRC), Shire would like to propose that these 4 PMR studies be issued as the PWR for SHP465 as well as fulfill our PREA requirements. Does FDA agree?
    b) Would FDA issue a PWR for the 4 PMR studies without the need for a revised PPSR resubmission?

2) As per the response to FDA's information request issued in May 2017 pertaining to the PPSR, Shire committed to submitting a 6-month study report as part of an open-label 12 month safety study to provide the requested information in 4-5 year old subjects with ADHD. Shire proposed to submit a 6-month study report by the filing date to satisfy the requirements of the PWR.
    a) A 12-month study report will be submitted by the PMR deadline. Will FDA accept a 6-month study report to fulfill the PWR requirement?
    b) Does FDA concur with direct enrollment into the open-label safety study?

3) In light of the requirement to submit final study reports 15 months prior to expiration of the exclusivity and the projected study timelines, Shire is proposing to submit draft PMR/PWR protocols to FDA as soon as possible following the action date. Would FDA be able to commit to a 2-week review timeline of the draft protocols?

Shire appreciates any feedback and the potential opportunity for a teleconference to discuss these questions.

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Wednesday, June 14, 2017 12:44 PM
To: Sung, Peggy
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Peggy,

Ok, sounds good.

As of right now, there may be additional comments concerning the carton and container labels. I'm waiting to hear back on that, as well.

Sincerely,

Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov

From: Sung, Peggy [mailto:psung@shire.com]
Sent: Wednesday, June 14, 2017 12:37 PM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Thanks, Latrice. I will send over the questions to you today.

Do you anticipate that there will be any additional comments to the bottle labels?

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Wednesday, June 14, 2017 10:19 AM
To: Sung, Peggy
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Peggy,

If a teleconference were to be granted, we would discuss the timeframe for a response at that time. Can you provide specific questions or topics that prompted a request for a teleconference?

We have a labeling meeting tomorrow. After the meeting, I can provide an update to you.

Sincerely,
Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov

From: Sung, Peggy [mailto:psung@shire.com]
Sent: Wednesday, June 14, 2017 10:11 AM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Latrice,

Thanks for your response. I'll wait to hear from you regarding a teleconference. Can you confirm whether the deadline for Thursday 11am to respond to the PMRs be extended should a teleconference be granted for Thursday afternoon?

Do you also have any updates on the timing of additional FDA feedback on the Mydayis draft label?

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Wednesday, June 14, 2017 9:01 AM
To: Sung, Peggy
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Peggy,

I am awaiting for confirmation. If we agree to the meeting, it will likely be tomorrow afternoon. However, I will let you know as soon as possible.

Sincerely,

Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov

From: Sung, Peggy [mailto:psung@shire.com]
Sent: Tuesday, June 13, 2017 7:58 PM
To: Wilson, Latrice
Subject: RE: NDA 022063 Mydayis Post Market Requirements

Hi Latrice,

Thanks for sending along the post marketing requirements for Shire's NDA 022063. Shire would like to request for a teleconference with the Agency to discuss the proposed post marketing requirements. Can you please confirm if Wednesday, June 14th at 3:00PM EST would work for the Agency?

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Tuesday, June 13, 2017 2:32 PM
To: Sung, Peggy
Subject: NDA 022063 Mydayis Post Market Requirements

Hi Peggy,

The Division has determined that Shire will need to complete post marketing requirements, which are outlined below. Please review and indicate if you agree to conduct these studies with the following schedule. Please respond no later than **11:00 am on Thursday, June 15.**

1 A single-dose, open-label, randomized pharmacokinetic study of MYDAYIS (mixed salts of a single-entity amphetamine extended-release) in male and female children (4 to less than 6 years of age) with ADHD.

Final Protocol Submission: 09/01/2017
Study/Trial Completion: 12/31/2018
Final Report Submission: 06/30/2019

2 A 4-week randomized, double-blind, placebo-controlled, fixed -dose study of MYDAYIS (mixed salts of a single-entity amphetamine extended-release) 6.25mg in 4 to 5 year olds diagnosed with ADHD.

Final Protocol Submission: 09/01/2017
Study/Trial Completion: 12/31/2018
Final Report Submission: 06/30/2019

3 Because of adverse reactions identified during your development program, it is not apparent from the studies you have conducted in 6 to 12 year old patients with ADHD that the lowest effective dose of MYDAYIS (mixed salts of a single-entity amphetamine extended-release) has been identified. Conduct a 4-week randomized, double-blind, placebo-controlled, dose optimization study of MYDAYIS (mixed salts of a single-entity amphetamine extended-release) 6.25 and 12.5mg in 6 to 12 year olds diagnosed with ADHD.

Final Protocol Submission: 09/01/2017
Study/Trial Completion: 12/31/2018
Final Report Submission: 06/30/2019

4 A one year Pediatric Open-Label Safety Study for patients age 4 to 12 years (at the time of entry into PMR 3224-1, PMR 3224-2, or PMR 3224-3) with ADHD.

Final Protocol Submission: 09/01/2018
Study/Trial Completion: 12/31/2019
Final Report Submission: 06/30/2020

Sincerely,

Latrice M. Wilson, PharmD
Regulatory Project Manager

Center for Drug Evaluation & Research
Office of Drug Evaluation I
U.S. Food and Drug Administration
Tel: 240-402-5317
latrice.wilson@fda.hhs.gov

U.S. FOOD & DRUG ADMINISTRATION

****
Shire plc, the ultimate parent of the Shire Group of companies, is registered in Jersey No. 99854
Registered Office: 22 Grenville Street, St Helier, Jersey JE4 8PX
****

Please consider the environment before printing this e-mail

****
Shire plc, the ultimate parent of the Shire Group of companies, is registered in Jersey No. 99854
Registered Office: 22 Grenville Street, St Helier, Jersey JE4 8PX
****

Please consider the environment before printing this e-mail

This email and any files transmitted with it are confidential and
may be legally privileged and are intended solely for the use of
the individual or entity to whom they are addressed. If you are
not the intended recipient please note that any disclosure,
distribution, or copying of this email is strictly prohibited and may
be unlawful. If received in error, please delete this email and any
attachments and confirm this to the sender.

****
Shire plc, the ultimate parent of the Shire Group of companies, is registered in Jersey No. 99854
Registered Office: 22 Grenville Street, St Helier, Jersey JE4 8PX
****

Please consider the environment before printing this e-mail

This email and any files transmitted with it are confidential and
may be legally privileged and are intended solely for the use of
the individual or entity to whom they are addressed. If you are
not the intended recipient please note that any disclosure,
distribution, or copying of this email is strictly prohibited and may
be unlawful. If received in error, please delete this email and any
attachments and confirm this to the sender.

****
Shire plc, the ultimate parent of the Shire Group of companies, is registered in Jersey No. 99854

Wilson, Latrice

'om: Adams, Grafton
Sent: Thursday, May 25, 2017 9:20 AM
To: Geissler, Mary
Cc: Sung, Peggy; Wilson, Latrice
Subject: RE: Request for information NDA 022063

Categories: Internal, 1Sponsor

Good Morning Ms. Geissler,

We acknowledge your 19 MAY 2017 email response to the 18 MAY 2017 request to change the dosage form designation from '(b) (4) to 'extended release' and recognize the need to distinguish this product from products for shorter duration. However it is not possible to do so based on the nonproprietary name. The Nomenclature Guidelines referenced by USP <1121> states that "Expressions such as "prolonged-release", "repeat-action", "controlled-release", "sustained-release", and their corresponding acronyms should not be used to describe such dosage forms." Therefore we request that you revise all labeling to reflect 'extended release' dosage form designation

Grafton Adams, RN, M.S.,
CDR, U.S. Public Health Service Commissioned Corps
Senior Regulatory Business Process Manager
Office of Program and Regulatory Operations | Office of Pharmaceutical Quality
Center for Drug Evaluation and Research | U.S. Food and Drug Administration
•0903 New Hampshire Ave | Bldg. 75 Rm. 4609 | Silver Spring, MD 20993
•240-402-7765 | grafton.adams@fda.hhs.gov

FDA U.S. FOOD & DRUG ADMINISTRATION

From: Geissler, Mary [mailto:mgeissler0@shire.com]
Sent: Friday, May 19, 2017 4:44 PM
To: Adams, Grafton
Cc: Sung, Peggy; Wilson, Latrice
Subject: RE: Request for information NDA 022063

Good afternoon Grafton,
Please find a response to your request for information related to NDA 022063, which was received yesterday.
I look forward to your feedback to support Shire's submission of the labels to the NDA next week.

Kind Regards,
Mary

FDA Request 1: Revise the description '(b) (4) Capsule" to "Extended-Release Capsules" to meet USP guidelines.

With regards to revising the product description in the USPI, Shire would like to respectfully request reconsideration of the change to Extended-Release Capsules based on the following reasons:

- Reference is made to the approvable letter for SHP465 (NDA No. 22-063) received by Shire dated 18 May 2007, wherein FDA requested Shire to develop a plan to educate health care providers to distinguish between mixed amphetamine salt formulations (MAS), Adderall, Adderall XR and SPD465, for the lifecycle of the product. Reference is also made to the 25 April 2014 FDA written response only (WRO) meeting, where Shire reviewed plans to address the request for an educational plan for consumers and healthcare professionals (HCPs) and obtained FDA's agreement on Shire's approach (WRO Question 6). On 12 May 2017, Shire submitted a Request for Advisory Comments on Educational Materials Requested by FDA Review Division – Professional and Consumer Booklet (Serial 0031). As discussed in the April 2014 WRO meeting, one of the key objectives of the proposed educational materials is to describe the formulation of SHP465 (MAS [redacted] (b) (4), (b) (4)) and how it differs from currently marketed MAS formulations (MAS immediate release [IR] and MAS extended release [ER]) . The [redacted] (b) (4), description helps distinguish SHP465 from the other MAS formulations in a manner consistent with FDA's request.
- Acknowledging the main difference between SHP465 and other products (e.g. Adderall XR) is the third bead which is a [redacted] (b) (4), bead, Shire believes the [redacted] (b) (4), description most accurately reflects SHP465 formulation.
- In light of the above and considering precedent for US approved products with [redacted] (b) (4), description in the approved USPI, Shire respectfully requests reconsideration of the FDA's request to revise the SHP465 description from '[redacted] (b) (4), to 'extended release.'

FDA Request 2: Revise the storage condition to be consistent with USP controlled room temperature: "Store at room temperature, 20°C to 25°C (68°F to 77°F). Excursions permitted between 15°C to 30°C (59°F to 86°F)."

Shire accepts the request to revise the storage condition text. This change will be reflected in the labels which will be submitted to NDA 022063.

Shire will await feedback regarding the request for reconsideration (per Response to FDA Request 1) prior to submitting the revised USPI, Medication Guide and container labels for SHP465.

From: Adams, Grafton [mailto:Grafton.Adams@fda.hhs.gov]
Sent: Thursday, May 18, 2017 8:39 PM
To: Geissler, Mary
Cc: Sung, Peggy; Wilson, Latrice
Subject: Request for information NDA 022063

Good Evening Ms. Geissler,

Below is a Request for information for NDA 022063. Please provide an email response by Close of Business tomorrow May 19, 2017. The revised labels can be submitted to the application as soon as possible after that.

1. Revise the description "[redacted] (b) (4), Capsule" to "Extended-Release Capsules" to meet USP guidelines.
2. Revise the storage condition to be consistent with USP controlled room temperature: "Store at room temperature, 20°C to 25°C (68°F to 77°F). Excursions permitted between 15°C to 30°C (59°F to 86°F)."

Please acknowledge receipt of this communication.

Thank you.

Grafton Adams, RN, M.S.,
CDR, U.S. Public Health Service Commissioned Corps
Senior Regulatory Business Process Manager
Office of Program and Regulatory Operations | Office of Pharmaceutical Quality

Center for Drug Evaluation and Research | U.S. Food and Drug Administration
10903 New Hampshire Ave | Bldg. 75 Rm. 4609 | Silver Spring, MD 20993
O+240-402-7765 | grafton.adams@fda.hhs.gov

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022063

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Shire Development LLC
300 Shire Way
Lexington, MA 02421-2101

ATTENTION: Peggy Sung, M.A., RAC
Manager, Global Regulatory Affairs

Dear Ms. Sung:

Please refer to your New Drug Application (NDA) dated and received December 20, 2016, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for SHP465 (Mixed Salts of a Single-Entity Amphetamine) Extended-Release Capsules 12.5mg, 25mg, 37.5mg and 50mg.

We also refer to your correspondence dated and received January 17, 2017, requesting review of your proposed proprietary name, Mydayis.

We have completed our review of the proposed proprietary name, Mydayis and have concluded that it is conditionally acceptable.

If any of the proposed product characteristics as stated in your January 17, 2017 submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review. Additionally, if your application receives a complete response, a new request for name review for your proposed name should be submitted when you respond to the application deficiencies.

If you require information on submitting requests for proprietary name review or PDUFA performance goals associated with proprietary name reviews, we refer you to the following:

- Guidance for Industry Contents of a Complete Submission for the Evaluation of Proprietary Names (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf)
- PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2013 through 2017, (http://www.fda.gov/downloads/ForIndustry/UserFees/PrescriptionDrugUserFee/UCM270412.pdf)

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Alycia Anderson, Safety Regulatory Project Manager

in the Office of Surveillance and Epidemiology, at (240) 402-4270. For any other information regarding this application, contact Latrice Wilson, Regulatory Project Manager in the Office of New Drugs, at (240) 402-5317.

Sincerely,

{See appended electronic signature page}

Todd Bridges, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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

/s/

DANIELLE M HARRIS on behalf of TODD D BRIDGES
04/14/2017

Wilson, Latrice

om: Sung, Peggy <psung@shire.com>
ɔent: Monday, March 13, 2017 11:59 AM
To: Wilson, Latrice
Cc: Patel, Hiren; Geissler, Mary
Subject: RE: Pharmacometrics Information Request for NDA 022063 Mydayis
Attachments: cover-letter.pdf

Categories: 1Sponsor

Hi Latrice,

Please be informed that the submission to the Pharmacometrics information request for NDA 22063 was submitted today via the ESG. Attached is the cover letter for your reference.

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Friday, March 10, 2017 12:26 PM
To: Sung, Peggy
Cc: Patel, Hiren; Geissler, Mary
Subject: Pharmacometrics Information Request for NDA 022063 Mydayis

Hi Peggy,

I have a pharmacometrics information request for NDA 022063. It is as follows:

We are unable to locate the input data file for the population PK analyses (SHR0301PK1.csv). Please direct us to the location within GSreview. If it hasn't been submitted, please submit it in the appropriate format (e.g. as a .xpt file).

We are also unable to locate a .txt file for the NONMEM control streams mentioned in the population PK report. While we are aware that the code for the NONMEM control streams is printed in the population PK study report, we ask you please submit the control streams in the appropriate format (e.g. as .txt files). If these text files have already been submitted, please direct us to the location within GSreview.

Please respond within 2 business days.

Sincerely,

Latrice Wilson, PharmD
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center For Drug Evaluation and Research, FDA
Ph: 240.402.5317
Email: latrice.wilson@fda.hhs.gov

****

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022063

ACKNOWLEDGE –
CLASS 2 RESUBMISSION

Shire Development LLC
Attention: Peggy Sung
Manager, Global Regulatory Affairs
300 Shire Way
Lexington, MA 02421

Dear Ms. Sung:

We acknowledge receipt on December 20, 2016, of your December 20, 2016, resubmission to your new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Mydayis® (Mixed Salts of a Single-Entity Amphetamine) extended release capsules in 12.5mg, 25mg, 37.5mg, 50mg.

We consider this a complete, class 2 response to our May 18, 2007 action letter. Therefore, the user fee goal date is June 20, 2017.

If you have any questions, contact me at latrice.wilson@fda.hhs.gov or 240-402-5317.

Sincerely,

{See appended electronic signature page}

Latrice Wilson, PharmD
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

LATRICE WILSON
01/17/2017

Wilson, Latrice

om: Sung, Peggy <psung@shire.com>
ɔent: Tuesday, January 17, 2017 2:43 PM
To: Wilson, Latrice
Cc: Patel, Hiren
Subject: RE: NDA 022063 Biometrics Information Request
Attachments: cover-letter.pdf

Categories: 1Sponsor

Hi Latrice,

Please be informed that the submission to the Biometrics information request for NDA 22063 was submitted today via the ESG. Please find attached the cover letter for your reference.

Kind regards,
Peggy

From: Wilson, Latrice [mailto:Latrice.Wilson@fda.hhs.gov]
Sent: Friday, January 13, 2017 11:01 AM
To: Sung, Peggy
Cc: Patel, Hiren
Subject: NDA 022063 Biometrics Information Request

Good morning Peggy,

The Biometrics reviewers have the following information request for NDA 022063:

1. Regarding the SAS program in ss-t-3-1-1-sas.txt for study 305 and t-3-1-1-sas.txt for study 306, please clarify which dataset you are referring to as *libname*.t_3_1_1, because they could not be located in your submission. If you have submitted them, please specify their locations.
2. Please submit the code for macros you used for your primary analyses for both study 305 and 306 (i.e. all macros used in ss-t-3-1-1-sas.txt for study 305 and t-3-1-1-sas.txt for study 306).

Please provide a response by **12 p.m. EST on Wednesday, Jan 18.**

Sincerely,

Latrice Wilson, PharmD
Regulatory Project Manager
Division of Psychiatry Products
Office of Drug Evaluation I
Center For Drug Evaluation and Research, FDA
Ph: 240.402.5317
Email: latrice.wilson@fda.hhs.gov

****