CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204553Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

EXCLUSIVITY SUMMARY

NDA # **204553** SUPPL # NA HFD #

Trade Name **COLPREP KIT**

Generic Name **sodium sulfate, potassium sulfate and magnesium sulfate for oral solution**

Applicant Name **GATOR PHARMACEUTICALS**

Approval Date, If Known **12.27.2016**

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)(2)

b) 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.

NA

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:

NA

c) Did the applicant request exclusivity?

YES ☐ NO ☒

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

d) 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).

Sodium Sulfate:

NDA# 021881	Moviprep
NDA# 018983	Colyte, Colyte – Flavored, and Colyte with Flavor Packs
NDA# 019011	Golytely
NDA# (b) (4)	Sulfur-35 Solution
NDA#203595	Suclear
NDA# 022372	Suprep

Magnesium Sulfate:

NDA#020577	Elliot's B Solution
NDA#019316	Magnesium Sulfate
NDA#020488	Magnesium Sulfate in Dextrose 5% in Plastic Container
NDA#203595	Suclear
NDA#018508	TIS-U-SOL
NDA# (b) (4)	Magnesium Sulfate
NDA#018336	TIS-U-SOL
NDA#020309	Magnesium Sulfate in PVC Flexible Container
NDA# 022372	Suprep

Potassium Sulfate:

NDA#203595	Suclear
NDA#022372	Suprep

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: James Carr, MPAS, PA-C
Title: Regulatory Project Manager
Date: 12.28.2016

Name of Division Director signing form: Joyce Korvick, M.P.H., M.D.
Title: Deputy Director, Safety

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/

JAMES B CARR
01/06/2017

JOYCE A KORVICK
01/06/2017

ACTION PACKAGE CHECKLIST

APPLICATION INFORMATION[1]

NDA # **204553** BLA #	NDA Supplement # BLA Supplement #	If NDA, Efficacy Supplement Type: *(an action package is not required for SE8 or SE9 supplements)*
Proprietary Name: **COLPREP KIT** Established/Proper Name: **sodium sulfate, potassium sulfate and magnesium sulfate** Dosage Form: **oral solution**		Applicant: **GATOR PHARMACEUTICALS, INC.** Agent for Applicant (if applicable): **N/A**
RPM: **JAMES CARR**		Division: DGIEP

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: 11.09.2016

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 **12.28.2016**	☒ AP ☐ TA ☐ CR
• Previous actions *(specify type and date for each action taken)*	☐ None 10.04.2013 TA
❖ 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):
(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

❖ 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)*	Action(s) and date(s) AP- 12.27.2017 TA- 10.04.2017
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
❖ 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)*	11.01.2013 10.31.2013
❖ Labeling reviews *(indicate dates of reviews)*	RPM: ☒ None 4.17.2013 DMEPA: 12.12.2016, 9.5.2013 DMPP/PLT (DRISK): 9.03.2013 OPDP: 9.03.2013 SEALD: ☒ None CSS: ☒ None Product Quality ☒ 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	2.01.2013 11.08.2016
❖ 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 o If yes, Center Director's Exception for Review memo *(indicate date)* o If yes, OC clearance for approval *(indicate date of clearance communication)*	☐ Yes ☒ No ☐ Not an AP action
❖ Pediatrics *(approvals only)* • Date reviewed by PeRC _____ 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)*	
❖ 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)*	
❖ 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 12.27.2016
Division Director Summary Review *(indicate date for each review)*	☐ None 12.27.2016
Cross-Discipline Team Leader Review *(indicate date for each review)*	☒ None
PMR/PMC Development Templates *(indicate total number)*	☐ None 12.27.2016
Clinical	

❖ Clinical Reviews	
• Clinical Team Leader Review(s) *(indicate date for each review)*	☒ No separate review
• Clinical review(s) *(indicate date for each 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)*	
❖ 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
❖ 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)*	☒ No separate review 8.21.2013
Clinical Pharmacology Team Leader Review(s) *(indicate date for each review)*	☐ No separate review
Clinical Pharmacology review(s) *(indicate date for each review)*	☐ None
❖ 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 ☐ None	
❖ Pharmacology/Toxicology Discipline Reviews	
• ADP/T Review(s) *(indicate date for each review)*	☒ No separate review 8.16.2013
• 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
❖ 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[6]	
• Tertiary review (*indicate date for each review*)	☐ None 8.1.2013
• Secondary review (e.g., Branch Chief) *(indicate date for each review)*	☐ None 9.27.2013
• Integrated Quality Assessment (contains the Executive Summary and the primary reviews from each product quality review discipline) *(indicate date for each review)*	☒ None
❖ Reviews by other disciplines/divisions/Centers requested by product quality review team *(indicate date of each review)*	BIOPHARM 6.28.2013
❖ 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)*	8.7.2013
☐ Review & FONSI *(indicate date of review)*	
☐ Review & Environmental Impact Statement *(indicate date of each review)*	
❖ Facilities Review/Inspection	
☐ Facilities inspections (indicate date of recommendation; within one week of taking an approval action, confirm that there is an acceptable recommendation) *(only original applications and efficacy supplements that require a manufacturing facility inspection(e.g., new strength, manufacturing process, or manufacturing site change)*	☒ Acceptable Re-evaluation date: ☐ 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

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204553

ACKNOWLEDGE -
CLASS 1 COMPLETE RESPONSE

Gator Pharmaceuticals, Inc.
Attention: Mr. Paul Burlaga
Director
194 Inlet Drive
St Augustine, FL 32080

Dear Mr. Burgala:

We acknowledge receipt on October 28, 2016, of your October 28, 2016, resubmission to your new drug application submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for ColPrep Kit (Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Powder for Oral Solution) 17.5 g/3.13 g/1.6 g.

We consider this resubmission a complete, class 1 response to our action letter. Therefore, the user fee goal date is December 28, 2016.

If you have any questions, call me at (240) 402-6624.

Sincerely,

{See appended electronic signature page}
CDR James Carr, MPAS, PA-C
Regulatory Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
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/

JAMES B CARR
11/03/2016

From:	Carr, James
To:	"pj@gatorpharma.com"
Subject:	FW: NDA 204553 ColPrep Kit- Gator Pharmaceuticals Information Request 10.14.2016
Date:	Friday, October 14, 2016 8:31:00 AM
Attachments:	image001.png

Mr. Burlaga

This is an information request, respond as soon as possible and no later than next Friday (10/21/2016).

- **Submit the outcome of Braintree's patent infringement lawsuit against Gator Pharmaceuticals regarding your 505(b)(2) product (sodium sulfate, potassium sulfate, magnesium sulfate, powder for oral solution, 17.5g/3.13g/1.6g). We note that you submitted a court order pertaining to Braintree's patent infringement lawsuit against Breckinridge regarding Breckinridge's generic product. Clarify how the submitted court order applies to Braintree's patent infringement lawsuit against Gator Pharmaceuticals.**

Jay

CDR James B Carr, USPHS
Regulatory Health Project Manager
FDA/CDER/OND/ODEIII
Division of Gastroenterology and Inborn Errors Products

(240) 402-6624 (office)
(3101 796-9904 (fax)
James.Carr@fda.hhs.gov

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

/s/

JAMES B CARR
10/14/2016

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Silver Spring, MD 20993

NDA 204553

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Gator Pharmaceuticals, Inc.
c/o KVK-TECH, INC.
110 Terry Drive, Suite 200
Newton, PA 18940

ATTENTION: Ashvin Panchal
Manager – Quality

Dear Mr. Panchal:

Please refer to your New Drug Application (NDA) resubmission dated November 30, 2012, received December 4, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Powder for Oral Solution, 17.5 g/3.13 g/1.6 g per bottle.

We also refer to your correspondence, dated and received September 5, 2013, requesting review of your proposed proprietary name, ColPrep Kit. We have completed our review of the proposed proprietary name, ColPrep Kit and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your September 5, 2013 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 Phong Do, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4795. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Matthew Scherer, at (301) 796-2307.

Sincerely,

{See appended electronic signature page}

Kellie 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
11/01/2013

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 204553

PROPRIETARY NAME REQUEST
UNACCEPTABLE

Gator Pharmaceuticals, Inc.
c/o KVK-TECH, INC.
110 Terry Drive, Suite 200
Newton, PA 18940

ATTENTION: Ashvin Panchal
Manager – Quality Assurance

Dear Mr. Panchal:

Please refer to your New Drug Application (NDA) dated November 30, 2012, received December 4, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Powder for Oral Solution, 17.5 g/3.13 g/1.6 g per bottle.

We also refer to your June 19, 2013, correspondence, received June 28, 2013, requesting review of your proposed proprietary name, PrepEase Kit. We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

(b) (4)

Please note that 21 CFR 201.10(c)(3) states that labeling or advertising can misbrand a product if misleading representations are made, whether through a proprietary name or otherwise; this includes suggestions that a drug is better, more effective, useful in a broader range of conditions or patients, safer, has fewer, or lower incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n); 21 CFR 202.1(e)(6)(i)].

We note that you have not proposed an alternate proprietary name. 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 Phong Do, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4795. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Matthew Scherer, at (301) 796-2307.

Sincerely,

{See appended electronic signature page}

Carol Holquist, 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

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/s/

CAROL A HOLQUIST
07/23/2013

Tran-Zwanetz, Catherine

From: Tran-Zwanetz, Catherine
Sent: Wednesday, July 10, 2013 4:38 PM
To: 'Ashvin Panchal'
Cc: Scherer, Matthew
Subject: NDA 204553 CMC IR #3

Attachments: CS ChemDraw Drawing; Picture (Metafile)

HI Ashvin,

Here is our latest information request:

1. Include an upper limit for pH of the reconstituted solution for the drug product specification. The upper limit should be based on your batch data.

2. Please provide all raw data (clearly labeled) for method validation for calcium content in sodium sulfate drug substance (Document No QC-13-MVR-048). Please show how the recovery of (b) (4)% in the precision/accuracy study (page 5 of QC-13-MVR-048) was obtained using the raw data and the equation shown below as provided in page 10 of the validation protocol (QC-13-MVP-036).

$$\text{calcium recovered (ppm)} = \frac{(\text{Abs} + Y_{\text{intercept}})}{\text{Slope}} + C_{y=0}$$

Where Abs = Average absorbance for the solution
$C_{y=0}$ = the absolute value of the calcium concentration (µg/mL) for the x-intercept of the linearity plot (MSA result)
Slope/$Y_{\text{intercept}}$ = from linear regression line equation from MSA linearity plot

It seems that the correct equation should be the one shown below, not the one shown above.

$$\text{calcium recovered (ppm)} = \frac{(\text{Abs} - Y_{\text{intercept}})}{\text{Slope}}$$

3. To date, you have not provided any response to address Items 7 and 8 described in the FDA Information Request Letter dated April 11, 2013. Please provide an updated mock-up container label and carton labeling to address issues described in Item 7of the letter. Please either provide an updated Structured Product Labeling (SPL) or commit to address the issues described in Item 8 of the letter. Please note that proprietary name should be included in Product Data Elements in SPL only if an approved one is available.

Please let me know if you have any questions and reply by July 24.

Thanks!
Cathy

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/s/

CATHERINE A TRAN-ZWANETZ
07/12/2013

Tran-Zwanetz, Catherine

From: Ashvin Panchal [ap@kvktech.com]
Sent: Wednesday, June 19, 2013 4:53 PM
To: Tran-Zwanetz, Catherine
Cc: Scherer, Matthew
Subject: RE: Second IR for NDA 204553

Hi Cathy,

This is to confirm we are targeting to submit next amendment before Monday, July 1!

Can I ask compliance status of the NDA?

Thanks

Ashvin Panchal

From: Tran-Zwanetz, Catherine [mailto:Catherine.TranZwanetz@fda.hhs.gov]
Sent: Wednesday, June 19, 2013 4:34 PM
To: Ashvin Panchal
Cc: Scherer, Matthew
Subject: RE: Second IR for NDA 204553

HI Ashvin,

Could you please confirm that the next amendment will be in by Monday, July 1?

Thanks!
Cathy

From: Ashvin Panchal [mailto:ap@kvktech.com]
Sent: Wednesday, June 19, 2013 4:35 PM
To: Tran-Zwanetz, Catherine
Cc: Scherer, Matthew
Subject: RE: Second IR for NDA 204553

Hi Catherine,

I got you email and will respond in next amendment.

Thanks

Ashvin

From: Tran-Zwanetz, Catherine [mailto:Catherine.TranZwanetz@fda.hhs.gov]
Sent: Wednesday, June 19, 2013 4:10 PM
To: Ashvin Panchal
Cc: Scherer, Matthew
Subject: Second IR for NDA 204553

Hello Mr. Panchal,

Per our conversation earlier today, here is an additional Information Request.

Please commit to perform [redacted] (b) (4) for all three drug substances prior to use for the manufacture of the drug product once they pass the [redacted] (b) (4) retest date after the initial testing. The retest date of [redacted] (b) (4) for drug substances is applicable only after the initial testing. Because the drug substances are expected to be chemically stable, only testing for [redacted] (b) (4) is required.
Add testing for pH of the reconstituted solution in the drug product specification.

We look forward to receiving your response to both IR (today and from April 11, 2013) by Monday, July 1.

Please let me know if you have any questions.
Cathy Tran-Zwanetz
Regulatory Project Manager
(301) 796-3877

KVK-Tech, Inc. email notice: The information contained in this email (including attachments) is confidential, may be privileged, may constitute inside information and is intended only for the use of the intended addressee and any others who have been specifically authorized by the sender to receive it; it may not be forwarded without permission of the sender. Employees, advisors, agents and representatives of KVK-Tech, Inc. do not provide scientific, technical, business, management, strategic, human resource, legal, accounting or tax advice. Any statement in this email (including any attachments) regarding scientific, technical, business, management, strategic, human resource, legal, accounting or tax matters was written in connection with the explanation of the matters described herein and was not intended or written to be relied upon or distributed by any person. Unauthorized dissemination, distribution, disclosure, or other use of the contents of this email, whether intended or unintended, is strictly prohibited, may be unlawful and will result in KVK-Tech, Inc. pursuing legal recourse against you to the fullest extent of the law. If you have received this email in error, please notify us immediately by return email or by calling (215) 579-1842 and destroy this message and all copies thereof, including any attachments.

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/s/

CATHERINE A TRAN-ZWANETZ
06/20/2013

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 204553

PROPRIETARY NAME REQUEST
UNACCEPTABLE

KVK-TECH, INC.
On behalf of Gator Pharmaceuticals, Inc.
Attention: Ashvin Panchal
Manager – Quality Assurance
110 Terry Drive, Suite 200
Newton, PA 18940

Dear Mr. Panchal:

Please refer to your New Drug Application (NDA) dated November 30, 2012, received December 4, 2012, submitted under section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Sodium Sulfate, Potassium Sulfate and Magnesium Sulfate Powder for Oral Solution, 17.5 g/3.13 g/1.6 g.

We also refer to your April 1, 2013, correspondence, received April 1, 2013, requesting review of your proposed proprietary name, UltraPrep Kit. We have completed our review of this proposed proprietary name and have concluded that this name is unacceptable for the following reasons:

Please note that the Federal Food Drug and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made, whether through a proposed proprietary name or otherwise; this includes suggestions that a drug is better, more effective, useful in a broader range of conditions or patients, safer, has fewer, or lower incidence of, or less serious side effects or contraindications than has been demonstrated by substantial evidence or substantial clinical experience. [21 U.S.C. 321(n); see also 21 U.S.C. 352(a) & (n); 21 CFR 202.1(e)(5)(i); (e)(6)(i)].

We note that you have not proposed an alternate proprietary name for application. 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 Phong Do, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4795. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Matthew Scherer, at (301) 796-2307.

Sincerely,

{See appended electronic signature page}

Carol Holquist, 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

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/s/

CAROL A HOLQUIST
05/02/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204553 **INFORMATION REQUEST**

KVK-TECH, INC
On behalf of Gator Pharmaceuticals, Inc.
Attention: Ashvin Panchal
Manager – Quality Assurance
110 Terry Drive, Suite 200
Newton, PA 18940

Dear Mr. Panchal,

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for sodium sulfate, potassium sulfate, and magnesium sulfate powder for oral solution.

We also refer to your August 2, 2013, submission, containing your proposed labeling.

During our preliminary review of your submitted labeling, we have identified the following labeling format issues. We request a submitted response by May 15, 2013, in order to continue our evaluation of your NDA.

Highlights

1. Highlights (HL) must be in two-column format, with ½ inch margins on all sides and in a minimum of 8-point font.
2. The length of HL must be less than or equal to one-half page (the HL Boxed Warning does not count against the one-half page requirement) unless a waiver has been granted.
3. All headings in HL must be presented in the center of a horizontal line, in UPPER-CASE letters and **bolded**.
4. White space must be present before each major heading in HL.
5. Remove the [redacted] (b) (4) before Highlights heading and insert the drug name after the Highlights Limitation Statement, but above the placeholder for Initial US Approval.
6. A horizontal line must separate HL and Table of Contents (TOC).
7. The **bolded** HL Limitation Statement must be on the line immediately beneath the HL heading and must state: "**These highlights do not include all the information needed to use (insert name of drug product in UPPER CASE) safely and effectively. See full prescribing information for (insert name of drug product in UPPER CASE)**."

8. Initial U.S. Approval in HL must be placed immediately beneath the product title, **bolded,** and include the verbatim statement "**Initial U.S. Approval:**" followed by the **4-digit year**.
9. The Patient Counseling Information Statement for a product with a medication guide must include the following **bolded** verbatim statement (without quotation marks):

   "See 17 for PATIENT COUNSELING INFORMATION and Medication Guide."

   Remove (b) (4) from your Patient Counseling Information Statement.

Contents: Table of Contents

10. A horizontal line must separate TOC from the full prescribing information (FPI).
11. All subsection headings must be indented, not bolded, and in title case. Your subsection headings are not indented. Subsection heading 17.1 is bolded.

Full Prescribing Information

12. Revise your Patient Counseling Information reference expected FDA-approved patient labeling, to read:

    "See FDA-approved patient labeling (Medication Guide)".

We strongly recommend that you reference FDA's website for Physician Labeling Rule (PLR) requirements for prescribing information (http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/LawsActsandRules/ucm084159.htm).

If you have any questions, call Matthew Scherer, Regulatory Project Manager, at (301) 796-2307.

Sincerely,

{See appended electronic signature page}

R. Wesley Ishihara
Chief, Project Management Staff
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

RICHARD W ISHIHARA
05/01/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204553

INFORMATION REQUEST

KVK-TECH, INC.
Attention: Ashvin Panchal
Manager- Quality Assurance
110 Terry Drive, Suite 200
Newtown, PA 18940

Dear Mr. Panchal:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for [redacted] (b) (4) (sodium sulfate, potassium sulfate and magnesium sulfate) for Oral Solution Kit.

We are reviewing the Chemistry, Manufacturing and Controls section of your submission and have the following comments and information requests. We request a prompt written response in order to continue our evaluation of your NDA.

1. Regarding sodium sulfate [redacted] (b) (4) drug substance specification including the analytical procedures:

[redacted] (b) (4)

ii. Revise the equation for calculation [redacted] (b) (4) as following:

[redacted] (b) (4)

b. Please provide updated method validation data for the revised [redacted] (b) (4) test. Because the equation for calculation [redacted] (b) (4) as provided in the 11/30/2012 submission is incorrect, the validity of the method validation data is questionable.

c. Please provide analytical procedures and the corresponding method validation data [redacted] if non-compendial analytical procedures are used. If compendial analytical procedures are used, please indicate so by referencing the corresponding compendial chapters.

Please note that complete information on the regulatory specification for each drug substance, including a list of tests, acceptance criteria, and the corresponding analytical procedures, should be provided. Even though some of these tests are performed by the drug substance manufacturers or their contract laboratories, the reliability of the supplier's analyses for each component of the drug product should be established by the drug product manufacturer (or their contract laboratory) through appropriate validation of the supplier's test results at appropriate intervals per 21 CFR 211.84(d)(2).

2. Regarding potassium sulfate [redacted] drug substance specification including analytical procedures:
   a. Provide analytical procedures and the corresponding method validation data [redacted] if non-compendial procedures are used. If compendial analytical procedures are used, please indicate so by referencing the corresponding compendial chapters.
   b. Clarify the limit of [redacted]. A limit of [redacted] mg/kg is provided in Section 3.2.S.3.2 whereas a limit of NMT [redacted] ppm (i.e. [redacted] mg/kg) is provided in Section 3.2.S.4.1.
   c. Please revise the analytical procedure [redacted] test to use 1.0 g of sample instead of [redacted] g. The procedure described in the 11/30/2012 submission corresponds to a [redacted] limit of [redacted]% [[redacted] mol/L x [redacted] mL x [redacted] L/mL x [redacted] g/mol)/[redacted] g x 100% = [redacted]%], instead of [redacted]%.
3. Numerical results, instead of "complies" as reported in KVK-Tech's certificates of analysis, for the following tests should be provided unless they are limit tests.
   a. Sodium sulfate [redacted]
   b. Potassium sulfate [redacted]
4. Please provide a statement to certify that the [redacted] bags used for packaging each of the drug substances, i.e. sodium sulfate [redacted], potassium sulfate [redacted], and magnesium sulfate [redacted], comply with the FDA requirements for contact with food products by reference to the food additive regulations.
5. Please confirm that the retest date for all three drug substances is [redacted], which is shown in the certificates of analysis provided by KVK-Tech.
6. Regarding elemental impurities of the drug product:
   a. Include testing for elemental impurities in the drug product specification. The acceptance criterion for each elemental impurity should comply with USP <232>. A maximum daily dose of two bottles (total 45.4 g) of the drug product should be used for setting the limit of each elemental impurity. For example, the limits for [redacted] and lead should be NMT [redacted] ppm and NMT [redacted] ppm, respectively.
   b. Provide the analytical procedure for elemental impurities.
   c. Provide additional method validation data for lead and arsenic to demonstrate that the analytical procedure is commensurate with the recommended acceptance criteria. Furthermore, clarify the results for "intermediate precision" and "specificity false

negative" evaluation for [redacted] (b) (4), both of which are listed as "%RSD of Test Samples [redacted] (b) (4) ppm".

d. Please define the term "PQL" used in the analytical report for elemental impurities for Batches D0374, D0375, and D0376. Provide data to support the PQL for each elemental impurity listed in the analytical report. Except for [redacted] (b) (4), the PQLs are well below the levels examined in the method validation study as provided in Section 3.2.P.5.3.

For your convenience, the recommended limits for each elemental impurity per USP <232> and the information provided in your NDA are summarized in the following table.

Elements	Recommended Limits per USP <232>	Information Provided in the NDA		
		Proposed Acceptance Criteria (ppm)	Range Examined in Method Validation Study (ppm)	PQL
[redacted] (b) (4)				

7. Address the following issues for the container and carton labels and provide the updated container and carton labels:

a. Revise the established name of your drug product, which should include names of drug substances, dosage form, and route of administration. For example, the proprietary name and established name may be expressed as:

[redacted] (b) (4)
(sodium sulfate, potassium sulfate, and magnesium sulfate)
Powder for Oral Solution

Furthermore, the font size of the established name should be at least half as large as that of the proprietary name per 21 CFR 201.10(g)(2).

b. Revise the storage condition from [redacted] to "Store at 20° - 25°C (68° - 77°F); excursions permitted between 15° and 30 °C (59° and 86°F) [see USP Controlled Room Temperature]".

8. Address the following issues for Product Data Elements in Structured Product Labeling:
   a. Provide proprietary name
   b. Revise the established name of the drug substances and dosage form from [redacted]" to "sodium sulfate, potassium sulfate, and magnesium sulfate powder, for solution"
   c. Revise [redacted] Product Characteristics from [redacted] to "white"
   d. Revise marketing category and application number from "[redacted] to "NDA".

If you have any questions, call Cathy Tran-Zwanetz, Regulatory Project Manager, at (301) 796-3877.

Sincerely,

{See appended electronic signature page}

Moo-Jhong Rhee, Ph.D.
Branch Chief, Branch IV
Division of New Drug Quality Assessment II
Office of New Drug Quality Assessment
Center for Drug Evaluation and Research

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/s/

MOO JHONG RHEE
04/11/2013
Chief, Branch IV

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204553

FILING COMMUNICATION

KVK-TECH, INC
On behalf of Gator Pharmaceuticals, Inc.
Attention: Ashvin Panchal
Manager – Quality Assurance
110 Terry Drive, Suite 200
Newton, PA 18940

Dear Mr. Panchal:

Please refer to your New Drug Application (NDA) dated November 30, 2012, received December 4, 2012, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for (b) (4) (sodium sulfate, potassium sulfate, magnesium sulfate) 17.5g/3.13g/1.6g.

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 October 4, 2013.

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 September 6, 2013.

During our filing review of your application, we identified the following potential review issue:

> You have not submitted an adequate justification to support a waiver for PREA studies. You did not provide information to support your position that (b) (4) does not represent a meaningful therapeutic benefit over existing treatments for pediatric patients and is not likely to be used by a substantial number of pediatric patients. We note that

(b) (4) might reduce the amount of liquid that children need to consume for bowel cleansing for colonoscopy.

We are providing the above comment to give you preliminary notice of potential review issues. Our filing review is only a preliminary evaluation of the application and is not indicative of deficiencies that may be identified during our review. Issues may be added, deleted, expanded upon, or modified as we review the application. If you respond to these issues during this review cycle, we may not consider your response before we take an action on your application.

We request that you submit the following information:

1. A completed Form FDA 3397 (PDUFA user fee cover sheet)

2. A request for FDA review of a proposed proprietary name. Refer to the Guidance for Industry: Contents of a Complete Submission for the Evaluation of Proprietary Names available at the following link: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf.

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), and Medication Guide. 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 Medication Guide, and you believe the labeling is close to the final version.

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

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the

product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We acknowledge receipt of your request for a full waiver of pediatric studies for this application. Once we have reviewed your request, we will notify you if the full waiver request is denied and a pediatric drug development plan is required. If the full waiver request is denied, you will need to submit (1) a partial waiver request and a pediatric development plan for the pediatric age groups not covered by the partial waiver request, or (2) a pediatric drug development plan covering the full pediatric age range (birth to 16 years). All waiver requests must include supporting information and documentation. A pediatric drug development plan must address the indication proposed in this application.

If you have any questions, call Matthew Scherer, Regulatory Project Manager, at (301) 796-2307.

Sincerely,

{See appended electronic signature page}

Donna Griebel, MD
Director
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MATTHEW C SCHERER
02/15/2013

DONNA J GRIEBEL
02/15/2013

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204553

NDA ACKNOWLEDGMENT

KVK-TECH, INC
On behalf of Gator Pharmaceuticals, Inc.
Attention: Ashvin Panchal
Manager – Quality Assurance
110 Terry Drive, Suite 200
Newton, PA 18940

Dear Mr. Panchal:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: [redacted] (b) (4) (sodium sulfate, potassium sulfate, magnesium sulfate) 17.5g/3.13g/1.6g

Date of Application: November 30, 2012

Date of Receipt: December 4, 2012

Our Reference Number: NDA 204553

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 February 2, 2013, 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 Gastroenterology and Inborn Errors 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 (301) 796-2307.

Sincerely,

{See appended electronic signature page}

Matthew Scherer
Senior Regulatory Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MATTHEW C SCHERER
01/08/2013

Scherer, Matthew

From: Scherer, Matthew
Sent: Wednesday, September 19, 2012 12:32 AM
To: 'Ashvin Panchal'
Cc: Grewal, Jagjit; Ford, Elizabeth; Barley, Stacy
Subject: RE: Phone call on 9/18/2012 (NDA 204553 ((b) (4) - early filing comments)

Hi Ashvin,

Unfortunately, I will be out of the office September 19 to 30, returning October 1 so I will not be able to discuss with you tomorrow. I will be able to check my email in the evening.

As mentioned on the message, I have done a preliminary review of your NDA and have identified the deficiencies listed below. The deficiencies, if not corrected, may affect the decision whether or not the NDA will be filed. Recall that the filing date for NDA 204553 is October 2, 2012. Please address these items (1-4) as soon as possible and no later than Thursday, September 27 so we have sufficient time to review before the filing date.

1. You did not submit patent information for your product (Form 3542a). This is required per 21 CFR 314.53(c) even if your product is not patented. Submit a completed 3542a.
2. Registration numbers for manufacturing establishments are not included. Provide these numbers.
3. The wording on your Debarment Certification is unacceptable as it implies that (b) (4) is a generic drug. Revise your debarment certification to reference FD&C Act 306 k (1). For example, the follow text is acceptable:

"[Name of applicant] hereby certifies that it did not and will not use in any capacity the services of any person debarred under section 306 of the Federal Food, Drug, and Cosmetic Act in connection with this application."

4. (b) (4) represents a new dosage form and, therefore, triggers PREA. As conveyed to you in the preliminary comments before the Pre-IND meeting (subsequently cancelled), you must submit a pediatric plan to your NDA. Include in the plan any planned or ongoing pediatric studies, the specific age groups that will be studied, and any age groups to be deferred or waived. Also include associated timelines. All age groups (birth through 16 years) must be addressed in the pediatric plan (through existing data, deferral request or waiver request) and certification of the grounds for deferral or waiver of any assessments should be included. Furthermore, evidence that the studies are being conducted or will be conducted with due diligence and at the earliest possible time should be provided in the plan.

You may wish to review the Suprep Approval letter for a description of the required pediatric studies associated with its approval. We will likely require something similar for this application.

Also, as a 505(b)(2) application, the following should be reviewed:

We note the following:

- Gator submitted a paragraph IV claiming Patent No. 6946149 is invalid, unenforceable and/or will not be infringed by the manufacture, use or sale of proposed drug product (b) (4) FOR SOLUTION KIT…
- Gator states that they will comply with the requirements under 21 C.F.R. 314.52(a) with respect to providing a notice…

Please reference 21 C.F.R. 314.52(b) *Sending the notice*. The applicant shall send the notice required by paragraph (a) of this section when it receives from **FDA an acknowledgment letter** stating that its application has been filed.
We have interpreted this **FDA acknowledgment letter** as the 74 day letter for NDAs.
We then give the applicant a *20 day grace* period to properly notify all parties.

Also, please review the following:

21 C.F.R. 314.52(e)
(e)*Documentation of receipt of notice.* The applicant shall amend its application to document receipt of the notice required under paragraph (a) of this section by each person provided the notice. The applicant shall include a copy of the return receipt or other similar evidence of the date the notification was received. FDA will accept as adequate documentation of the date of receipt a return receipt or a letter acknowledging receipt by the person provided the notice. An applicant may rely on another form of documentation only if FDA has agreed to such documentation in advance. A copy of the notice itself need not be submitted to the agency.

21 C.F.R. 314.52(f)

(f)*Approval.* If the requirements of this section are met, the agency will presume the notice to be complete and sufficient, and it will count the day following the date of receipt of the notice by the patent owner or its representative and by the approved application holder as the first day of the 45-day period provided for in section 505(c)(3)(C) of the act. FDA may, if the applicant amends its application with a written statement that a later date should be used, count from such later date.

If an infringement suit is filed, the FDA is barred from approving the application for 30 months (a 30 month stay), or until the ANDA or 505(b)(2) applicant wins the patent litigation, whichever occurs first.

Best regards,
Matt
If necessary, please contact:

Jagjit Grewal (Sept 20, 21, 27, 28)

Elizabeth Ford (Sept 24, 25)

Stacy Barley (Sept 26)

-
Matthew C. Scherer, MBA
Senior Regulatory Project Manager
Division of Gastroenterology and Inborn Errors Products
CDER/OND/ODEIII
Ph: 301-796-2307
Fax: 301-796-9904

10903 New Hampshire Avenue
Building 22, Room 5139
Silver Spring, MD 20993

From: Ashvin Panchal [mailto:ap@kvktech.com]
Sent: Tuesday, September 18, 2012 4:44 PM
To: Scherer, Matthew
Subject: Phone call on 9/18/2012

Dear Mr. Scherer,

I am sorry I missed your call and thanks for leaving voice message. I like to call you tomorrow to further discuss regarding NDA for (b) (4) Can you please let us know date and time to call you back.

Thanks

Ashvin Panchal

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/s/

MATTHEW C SCHERER
10/03/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204553

ACKNOWLEDGE REQUEST TO WITHDRAW PENDING NDA

KVK-TECH, INC
On behalf of Gator Pharmaceuticals, Inc.
Attention: Ashvin Panchal
Manager – Quality Assurance
110 Terry Drive, Suite 200
Newton, PA 18940

Dear Mr. Panchal:

We have received your September 26, 2012 correspondence on September 27, 2012, notifying us that you are withdrawing your new drug application (NDA) for [redacted] (b) (4) (sodium sulfate, potassium sulfate, magnesium sulfate) 17.5g/3.13g/1.6g.

In accordance with 21 CFR 314.65, this application is withdrawn as of September 27, 2012. If you decide to resubmit this application, this withdrawal will not prejudice any future decisions on filing. You may reference information contained in this withdrawn application in any resubmission.

In addition, the resubmitted application should address the following deficiencies identified during our preliminary review of the withdrawn application. Note that this is a list of issues identified to date. It does not necessarily represent a complete list of all issues.

1. Provide the following missing information for all three drug substances:
   a. Description of manufacturing process and process control
   b. Control of materials (starting materials, reagents, solvents, and auxiliary materials)
   c. Control of critical steps and intermediates
2. Provide data for two additional batches of the drug product. Data of only one batch of the drug product were submitted.
3. Revise the drug substance specifications:
   a. Potassium sulfate:
      i. Add an identification test for sulfate
      ii. Revise the sample size and acceptance criterion for [redacted] (b) (4) to [redacted] (b) (4) g and NMT [redacted] (b) (4) mg/kg, respectively, per the current FCC8 monograph.
   b. For magnesium sulfate, add USP <733> loss on ignition with acceptance criteria of loses [redacted] (b) (4) % - [redacted] (b) (4) %
4. Revise the drug product specification:

a. Revise tests for assay and uniformity of dosage units for sodium sulfate, potassium sulfate, and magnesium sulfate to sodium, potassium, and magnesium, respectively. The proposed analytical procedures provide measurements only for the metal contents.
b. Include testing for metal impurities, including [redacted], with acceptance criteria of [redacted] ppm, [redacted] ppm, [redacted] ppm, and [redacted] ppm, respectively. Based on an oral daily dose of 45.4 g, these limits correspond to permitted daily exposure of 15 µg, 25 µg, 10 µg, and 15 µg, respectively, per USP Draft Chapter <232> Metals and Limits published in Pharmacopeial Forum 36 (1). Provide analytical procedure and method validation data for the test.

5. Delete USP <467> [redacted] from excipients, drug substances, and drug product release specifications if no organic solvents are used in the manufacturing process of the respective materials. The specifications should reflect actual testing and acceptance criteria used for release. If the test is included in the specification, numerical results, instead of [redacted], should be provided.
6. Provide certificates of analysis from the manufacturers of potassium sulfate and magnesium sulfate.
7. Unless data are provided to support the practice of [redacted] re-test period for each drug substance, the drug substances should be tested [redacted] prior to use in the manufacture of the drug product.
8. A stability specification for blend uniformity of [redacted] is provided in Section 3.2.P.5.2. A hold time for [redacted] should be provided if it is held for an extended period of time. Provide stability data, including blend uniformity and [redacted] content, to support the proposed hold time.
9. Provide a statement to certify that the container closure systems for packaging the drug substances and drug product that are in contact with the drug substance or drug product comply with the FDA requirements. A reference to specific sections of the federal regulations for each component should be provided.
10. Address inconsistent information including:
    a. Drug substance manufacturers:
        i. sodium sulfate in Sections 3.2.S.2.1 [redacted] and 3.2.P.5.6 [redacted]
        ii. potassium sulfate in Sections 3.2.S.2.1 [redacted] and 3.2.P.5.6 [redacted]
        iii. magnesium sulfate in Sections 1.1.2 and 3.2.S.2.1 (incorrect name [redacted], instead of [redacted] was provided) and Section 3.2.P.5.6 [redacted]
    b. Manufacturer for citric acid in Sections 1.1.2 [redacted] and 3.2.P.5.6 [redacted]
    c. Packaging information in Sections 3.2.P.7 (one configuration) and 3.2.P.8.2 (smallest and largest configurations)
    d. Drug product information in Section 3.2.R where the "in-process controls" document for [redacted] is provided.
    e. Sampling frequency for in-process controls by production for filled weight in Sections 3.2.P.3.4 (every [redacted] minutes) and master batch records (at least every [redacted] minutes).

Furthermore, ensure that the resubmitted application addresses the administrative deficiencies conveyed to you via email on September 19, 2012.

If you have any questions, call me at (301) 796-2307.

Sincerely,

{See appended electronic signature page}

Matthew Scherer
Senior Regulatory Project Manager
Division of Gastroenterology and Inborn Errors Products
Office of Drug Evaluation III
Center for Drug Evaluation and Research

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/s/

MATTHEW C SCHERER
10/03/2012

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 204553

NDA ACKNOWLEDGMENT

KVK-TECH, INC
On behalf of Gator Pharmaceuticals, Inc.
Attention: Ashvin Panchal
Manager – Quality Assurance
110 Terry Drive, Suite 200
Newton, PA 18940

Dear Mr. Panchal:

We have received your New Drug Application (NDA) submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

Name of Drug Product: [redacted] (b) (4) (sodium sulfate, potassium sulfate, magnesium sulfate) 17.5g/3.13g/1.6g

Date of Application: August 2, 2012

Date of Receipt: August 3, 2012

Our Reference Number: NDA 204553

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 October 2, 2012, 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). Title VIII of FDAAA amended the PHS Act by adding new section 402(j) [42 USC § 282(j)], which expanded the current database known as

ClinicalTrials.gov to include mandatory registration and reporting of results for applicable clinical trials of human drugs (including biological products) and devices.

In addition to the registration and reporting requirements described above, FDAAA requires that, at the time of submission of an application under section 505 of the FDCA, the application must be accompanied by a certification that all applicable requirements of 42 USC § 282(j) have been met. Where available, the certification must include the appropriate National Clinical Trial (NCT) numbers [42 USC § 282(j)(5)(B)].

You did not include such certification when you submitted this application. You may use Form FDA 3674, "Certification of Compliance, under 42 U.S.C. § 282(j)(5)(B), with Requirements of ClinicalTrials.gov Data Bank," [42 U.S.C. § 282(j)] to comply with the certification requirement. The form may be found at http://www.fda.gov/opacom/morechoices/fdaforms/default.html.

In completing Form FDA 3674, you should review 42 USC § 282(j) to determine whether the requirements of FDAAA apply to any clinical trial(s) referenced in this application. Please note that FDA published a guidance in January 2009, "Certifications To Accompany Drug, Biological Product, and Device Applications/Submissions: Compliance with Section 402(j) of The Public Health Service Act, Added By Title VIII of the Food and Drug Administration Amendments Act of 2007," that describes the Agency's current thinking regarding the types of applications and submissions that sponsors, industry, researchers, and investigators submit to the Agency and accompanying certifications. Additional information regarding the certification form is available at: http://www.fda.gov/RegulatoryInformation/Legislation/FederalFoodDrugandCosmeticActFDCAct/SignificantAmendmentstotheFDCAct/FoodandDrugAdministrationAmendmentsActof2007/ucm095442.htm. Additional information regarding Title VIII of FDAAA is available at: http://grants.nih.gov/grants/guide/notice-files/NOT-OD-08-014.html. Additional information for registering your clinical trials is available at the Protocol Registration System website http://prsinfo.clinicaltrials.gov/.

When submitting the certification for this application, **do not** include the certification with other submissions to the application. Submit the certification within 30 days of the date of this letter. In the cover letter of the certification submission clearly identify that it pertains to **NDA 204553** submitted on August 2, 2012, and that it contains the FDA Form 3674 that was to accompany that application.

If you have already submitted the certification for this application, please disregard the above.

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 Gastroenterology and Inborn Errors Products
5901-B Ammendale Road
Beltsville, MD 20705-1266

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MATTHEW C SCHERER
08/17/2012