CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022544Orig1s027

Trade Name: GRALISE®

Generic or Proper Name: gabapentin

Sponsor: Almatica Pharma LLC

Approval Date: 09/16/2021

Indication: GRALISE® is indicated for the management of Postherpetic Neuralgia (PHN). Important Limitation: GRALISE is not interchangeable with other gabapentin products because of differing pharmacokinetic profiles that affect the frequency of administration.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 022544/S-027

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 022544/S-027

APPROVAL LETTER

NDA 022544/S-027

APPROVAL LETTER

Almatica Pharma LLC
Attention: Ayse Baker
Vice President of Regulatory Affairs
44 Whippany Road, Suite 300
Morristown, NJ 07960

Dear Ms. Baker:

Please refer to your Supplemental New Drug Application (sNDA) dated and received March 18, 2021, and your amendment, pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Gralise (gabapentin) Tablets.

This "Changes Being Effected in 30 days" supplemental new drug application provides for the addition of (b) (4) as an alternate drug product manufacturing facility for Gralise (gabapentin) Tablets, 300 mg and 600 mg.

APPROVAL & LABELING

We have completed our review of this supplemental application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the prescribing information) with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications that include labeling changes for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes, and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

CARTON AND CONTAINER LABELS

Submit final printed carton and container labels that are identical to enclosed carton and container labels, as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry *Providing Regulatory Submissions in Electronic Format – Certain Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications*. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved NDA 022544/S-027.**" Approval of this submission by FDA is not required before the labeling is used.

We remind you that you must comply with reporting requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Teicher Agosto, Regulatory Business Process Manager, at (240) 402 - 3777.

Sincerely,

{See appended electronic signature page}

Gurpreet Gill-Sangha, Ph.D
Branch Chief, B3
Division of Post-Marketing Activities I
Office of Lifecycle Drug Products
Office of Pharmaceutical Quality
Center for Drug Evaluation and Research

Enclosure(s):
Carton and Container Labeling

Gurpreet
Gill Sangha

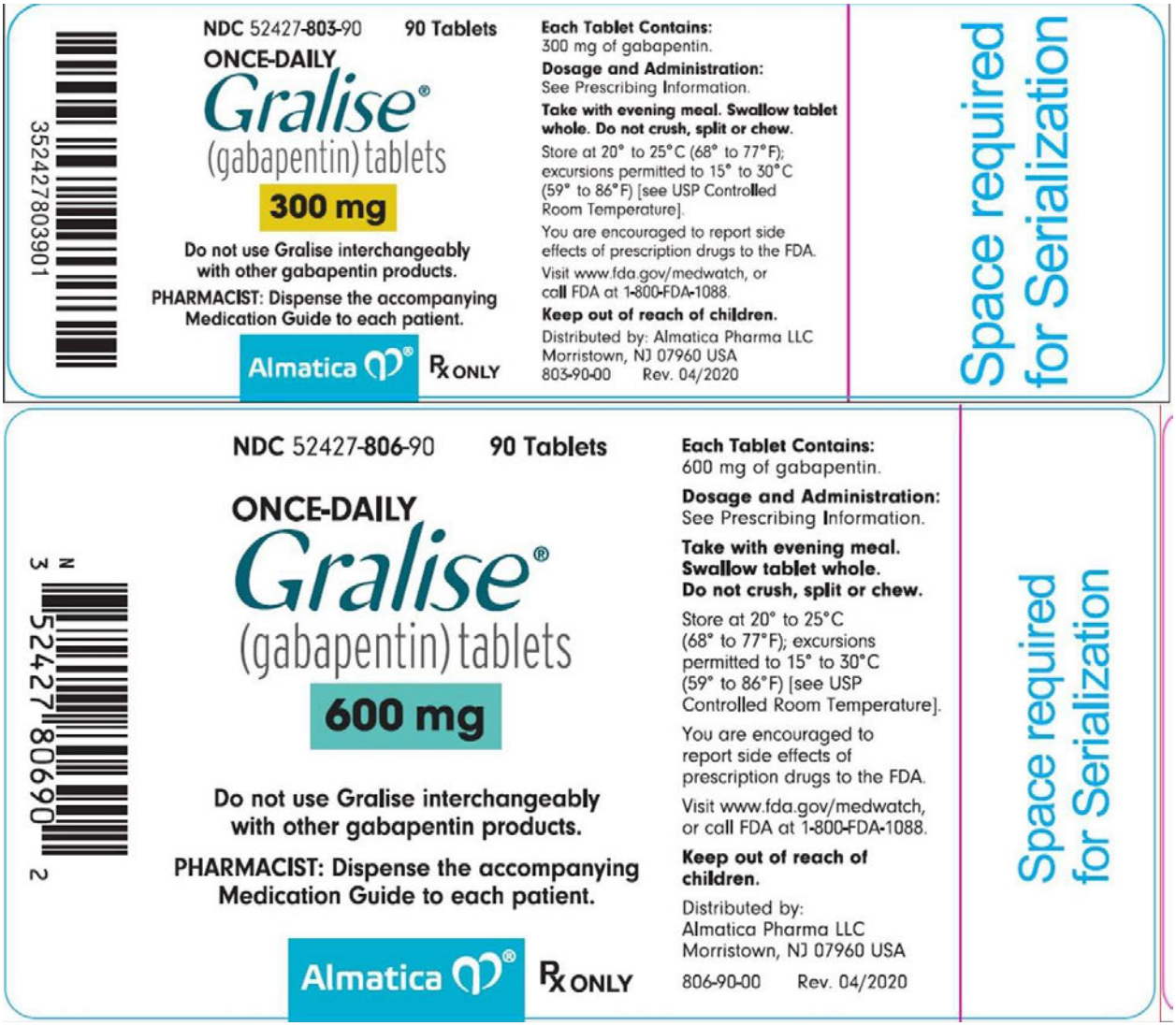
Digitally signed by Gurpreet Gill Sangha
Date: 9/16/2021 03:05:18PM
GUID: 5135f2ad000117842392c50c36c7f28a

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 022544/S-027

LABELING


NDC 52427-803-90 90 Tablets
ONCE-DAILY
Gralise®
(gabapentin) tablets
300 mg
Do not use Gralise interchangeably with other gabapentin products.
PHARMACIST: Dispense the accompanying Medication Guide to each patient.
Almatica
Rx ONLY
Each Tablet Contains:
300 mg of gabapentin.
Dosage and Administration:
See Prescribing Information.
Take with evening meal. Swallow tablet whole. Do not crush, split or chew.
Store at 20° to 25°C (68° to 77°F); excursions permitted to 15° to 30°C (59° to 86°F) [see USP Controlled Room Temperature].
You are encouraged to report side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch, or call FDA at 1-800-FDA-1088.
Keep out of reach of children.
Distributed by: Almatica Pharma LLC
Morristown, NJ 07960 USA
803-90-00 Rev. 04/2020
Space required for Serialization
NDC 52427-806-90 90 Tablets
ONCE-DAILY
Gralise®
(gabapentin) tablets
600 mg
Do not use Gralise interchangeably with other gabapentin products.
PHARMACIST: Dispense the accompanying Medication Guide to each patient.
Almatica
Rx ONLY
Each Tablet Contains:
600 mg of gabapentin.
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Take with evening meal. Swallow tablet whole. Do not crush, split or chew.
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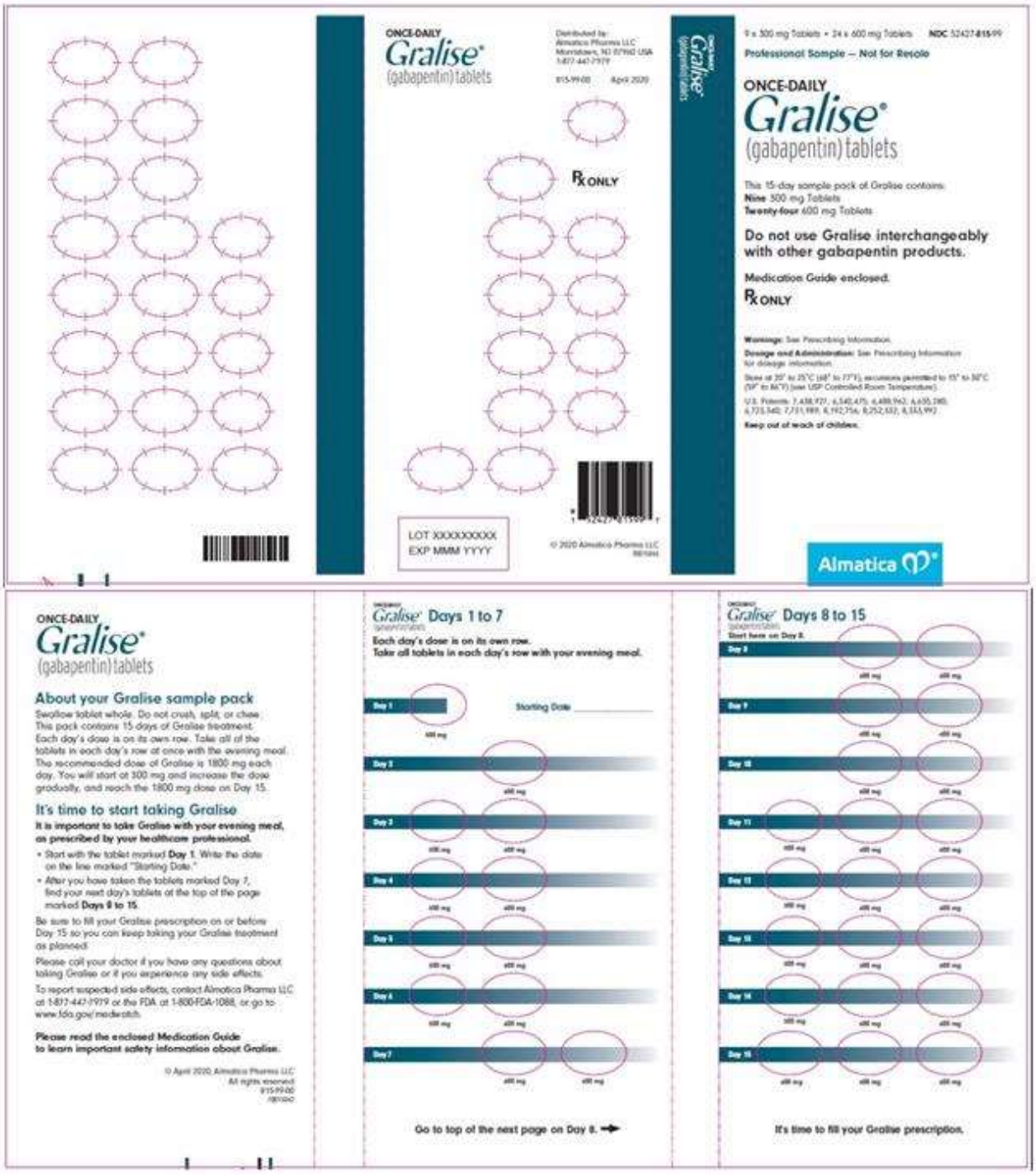
You are encouraged to report side effects of prescription drugs to the FDA.
Visit www.fda.gov/medwatch, or call FDA at 1-800-FDA-1088.
Keep out of reach of children.
Distributed by:
Almatica Pharma LLC
Morristown, NJ 07960 USA
806-90-00 Rev. 04/2020
Space required for Serialization


ONCE-DAILY
Gralise®
(gabapentin) tablets
Distributed by:
Almatica Pharma LLC
Morristown, NJ 07960 USA
1-877-447-7979
915-99-00 April 2020
℞ ONLY
LOT XXXXXXXX
EXP MMM YYYY
© 2020 Almatica Pharma LLC
9 x 300 mg Tablets • 24 x 600 mg Tablets NDC 52427-815-99
Professional Sample — Not for Resale
ONCE-DAILY
Gralise®
(gabapentin) tablets
This 15-day sample pack of Gralise contains:
Nine 300 mg Tablets
Twenty-four 600 mg Tablets
Do not use Gralise interchangeably with other gabapentin products.
Medication Guide enclosed.
℞ ONLY
Warnings: See Prescribing Information.
Dosage and Administration: See Prescribing Information for dosage information.
Keep out of reach of children.
Almatica
ONCE-DAILY
Gralise®
(gabapentin) tablets
About your Gralise sample pack
Swallow tablet whole. Do not crush, split, or chew.
This pack contains 15 days of Gralise treatment.
Each day's dose is on its own row. Take all of the tablets in each day's row at once with the evening meal.
The recommended dose of Gralise is 1800 mg each day. You will start at 300 mg and increase the dose gradually, and reach the 1800 mg dose on Day 15.
It's time to start taking Gralise
It is important to take Gralise with your evening meal, as prescribed by your healthcare professional.
• Start with the tablet marked Day 1. Write the date on the line marked "Starting Date."
• After you have taken the tablets marked Day 7, find your next day's tablets at the top of the page marked Days 8 to 15.
Be sure to fill your Gralise prescription on or before Day 15 so you can keep taking your Gralise treatment as planned.
Please call your doctor if you have any questions about taking Gralise or if you experience any side effects.
To report suspected side effects, contact Almatica Pharma LLC at 1-877-447-7979 or the FDA at 1-800-FDA-1088, or go to www.fda.gov/medwatch.
Please read the enclosed Medication Guide to learn important safety information about Gralise.
© April 2020, Almatica Pharma LLC
All rights reserved
915-99-00
Gralise® Days 1 to 7
Each day's dose is on its own row.
Take all tablets in each day's row with your evening meal.
Starting Date
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Go to top of the next page on Day 8.
Gralise® Days 8 to 15
Start here on Day 8.
Day 8
Day 9
Day 10
Day 11
Day 12
Day 13
Day 14
Day 15
It's time to fill your Gralise prescription.

Gurpreet
Gill Sangha

Digitally signed by Gurpreet Gill Sangha
Date: 9/16/2021 03:05:18PM
GUID: 5135f2ad000117842392c50c36c7f28a

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 022544/S-027

CHEMISTRY REVIEW(S)

Office of Lifecycle Drug Products
Division of Post-Marketing Activities I
Review of Chemistry, Manufacturing, and Controls

1. NDA Supplement Number: NDA 022544 /S-27

2. Submission(s) Being Reviewed:

Submission	Type	Submission Date	CDER Stamp Date	Assigned Date	PDUFA Goal Date	Review Date
Original	CBE-30	3/18/2021	3/18/2021	3/24/2021	9/18/2021	9/2/2021
Amendment IR		4/5/2021	4/5/2021			

3. Provides For: Addition of (b) (4), as an alternate drug product manufacturing facility for Gralise (gabapentin) Tablets, 300 mg and 600 mg.

4. Review: **1**

5. Clinical Review Division: Division of Anesthesiology, Addiction Medicine, and Pain Medicine

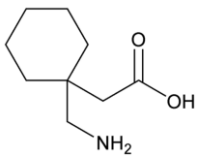
6. Name and Address of Applicant:

Name: Golf Acquiror LLC
Address: 44 Whippany Road
Suite 300
Morristown, NJ 07960
Attn: Ayse Baker, Vice-President
Tel: 1-973-452-4874
Fax: 973-796-3430
Email: ayse.baker@almatica.com

7. Drug Product:

Drug Name	Dosage Form	Strength	Route of Administration	Rx or OTC	Special Product	Orphan Number
GRALISE® (gabapentin) tablets, for oral use	Tablet	300 mg and 600 mg	Oral	Rx	No	06-2365

8. Chemical Name and Structure of Drug Substance:



USAN: Gabapentin
Chemical name: (1) Cyclohexaneacetic acid, 1-(aminomethyl)-; (2) 1-(Aminomethyl)cyclohexaneacetic acid.
Molecular formula: $C_9H_{17}NO_2$
M_W: 171.24 G/Mole

9. Indication: Anticonvulsant. Indicated for the management of Postherpetic Neuralgia (PHN).

10. Supporting/Relating Documents: Drug Product Review for NDA 022544 /S-21 submitted by Ping Jiang-Baucom, Ph.D., on 9/5/2013. Approved.

11. Consults:

Consults	Recommendation	Date	Reviewer
OPMA/Facility	Compliant- Approval	04/19/2021	Yong Wu
Biopharmaceutics	Recommended for Approval	8/27/2021	Kalpana S. Paudel, Ph.D.

12. Executive Summary: Managed by OPQ.

In this supplement, the applicant proposes the addition of (b) (4) as an alternate drug product manufacturing facility for Gralise (gabapentin) Tablets, 300 mg and 600 mg. The applicant refers to NDA 022544 /S-21 approved on 9/5/2013, for the addition of alternate manufacturing site (b) (4) for Gralise 300 and 600 mg tablets per an approved comparability protocol.

The applicant provides adequate information to support the drug product manufacture at the proposed (b) (4) manufacture. Moreover, the OPM and Biopharmaceutic reviewers recommend the approval of this supplement. Refer to section 11 for the relevant disciplines supporting this supplemental NDA.

13. Conclusions & Recommendations:
This supplement is recommended for approval from CMC standpoint, based on the review from biopharmaceutics and OPMA.

14. Comments/Deficiencies to be Conveyed to Applicant: None

15. Primary Reviewer:
Daneli López Pérez, Ph.D., CMC reviewer, Branch 3, Division of Post-Marketing Activities I, Office of Lifecycle Drug Products, Office of Pharmaceutical Quality (OPQ).

16. Secondary Reviewer:
Gurpreet Gill-Sangha, Branch Chief, Branch 3, Division of Post-Marketing Activities I, Office of Lifecycle Drug Products, OPQ.

CMC ASSESSMENT

I BACKGROUND INFORMATION

GRALISE is indicated for the management of Postherpetic Neuralgia (PHN). GRALISE contains gabapentin as the drug substance. Currently, the drug substance, gabapentin USP is manufactured and released by (b) (4) as per specifications approved in the application. The manufacture of Gralise (gabapentin) Tablets, 300 mg and 600 mg drug product is currently approved at (b) (4), a part of (b) (4).

II PROPOSED CHANGES

In this supplement, the applicant proposes the addition of (b) (4)) as an alternate drug product manufacturing facility for Gralise (gabapentin) Tablets, 300 mg and 600 mg. The applicant refers to NDA 022544 /S-21 approved on 9/5/2013, for the addition of alternate manufacturing site (b) (4) for Gralise 300 and 600 mg tablets per an approved comparability protocol.

III DATA SUBMITTED TO SUPPORT THE PROPOSED CHANGES

MODULE 2

1. COMPARATIVE DISSOLUTION REPORT (2.7.1)

☑ **Reviewer Evaluation: Acceptable**

The applicant provides a comparative in-vitro dissolution of the drug product manufactured at the proposed (b) (4)

The Biopharmaceutical Reviewer evaluated the data provided in the section and stated: "*The site change is considered a Level 3 change per the SUPAC-IR guidance, which requires multi-point comparative dissolution testing to support the change. The comparative dissolution data submitted from one batch of each strength manufactured at the current* (b) (4) *site and one batch of each strength manufactured at the alternate* (b) (4) *site showed similarity factor (f2) more than* (b) (4) *for 300 mg and* (b) (4) *for 600 mg strength). In addition, the submitted batch analysis data for all the primary registration and process performance qualification (PPQ) batches of both strengths (three batches per strength) manufactured at the alternate site meet the approved dissolution acceptance criteria. Thus, the dissolution profiles of the proposed drug product manufactured at the new* (b) (4)*) facility and the current* (b) (4) *facility are deemed similar.*"

The Biopharmaceutical Reviewer recommends the approval of this supplement. Refer to the Biopharmaceutics Review submitted by Kalpana S. Paudel, Ph.D., 8/27/2021 in Panorama.

MODULE 3 - QUALITY

2. DRUG SUBSTANCE (3.2.S)-GABAPENTIN

A. Manufacture 3.2.S.4

☑ **Reviewer Evaluation: Acceptable**

The applicant states the drug product manufacturer, (b) (4) will conduct testing of drug substance in accordance with approved specifications for the drug substance. No change to supplier specifications is reported in the supplemental NDA.

B. Control of Drug Substance 3.2.S.4

B(i) Specifications (3.2.S.4.1)

Current approved drug substance, Gabapentin specifications from approved (b) (4) supplier.

(b) (4)

Proposed drug substance, Gabapentin specifications performed at proposed (b) (4) facility.

(b) (4)

☑ **Reviewer Evaluation: Acceptable**

The proposed specifications of the drug substance used in the proposed drug product manufacturer (b) (4) remains the same as currently approved for the drug substance supplier (b) (4) The drug substance specifications meet current USP Monograph for Gabapentin USP.

B(i) Analytical Procedures (3.2.S.4.2) and Validation of Analytical Procedures (3.2.S.4.3)

The applicant provides a list of compendial test methods utilized for testing incoming drug substance by the drug product manufacturer, (b) (4) testing facility in the following Table 1.

(b) (4)

☑ **Reviewer Evaluation: Acceptable**

For the analysis of the Gabapentin drug substance by the proposed drug product manufacturer (b) (4) the applicant provides method verification for the (b) (4) tests and compares with the (b) (4)

In the method verification for the (b) (4), the system suitability, specificity, accuracy, and precision were compared to the current USP monograph and demonstrated the corresponding in-house method (b) (4) is suitable for its intended used. The system suitability, specificity, limit of detection, linearity, accuracy, and precision were also verified for the (b) (4) Assay, and (b) (4) Related compounds tests. The methods to analyze the drug substance are suitable for its intended use.

B(ii) Batch Analysis (3.2.S.4.4)

☑ **Reviewer Evaluation: Acceptable**

The applicant provides the Certificate of Analysis of the drug substance batch number 488305, supplied by (b) (4) and analyzed by the proposed (b) (4) drug product manufacturer. The batch complies with current approved specifications for Gabapentin, drug substance.

B(iii) Justification of Specifications (3.2.S.4.5)

Table 1: Drug Substance Specification Comparison between USP Monograph, (b) (4) registered, and proposed (b) (4)

Test	USP Specifications	Supplier Specifications (b) (4)	Registered Specification (Assertio)	Proposed (b) (4) Specifications	Rationale for (b) (4) Specification
Identification-Description	Not Applicable	(b) (4)			
Identification-IR-Spectrum	USP <197> To match with reference standard <197K> or <197A> may be used.				
Identification-HPLC	The retention time of the major peak of the Sample solution corresponds to that of Standard solution, as obtained in the Assay.				
Water Determination-KF	Method I <921> NMT 0.5%				
Assay-HPLC	Not less than 98.0% and not more than 102.0%, calculated on anhydrous basis				
pH	<791> Between 6.5 and 8.0, in a solution (20 mg/mL)				
Residue on ignition	<281> Not more than 0.1%				
Related compounds-HPLC	Early-eluting organic impurities: Gabapentin rel. cmpd E: NMT 0.10% Gabapentin rel. cmpd. A: NMT 0.1% Gabapentin rel. cmpd. B: NMT 0.06% Any other individual impurity: NMT 0.10% Late-eluting organic impurities: Individual impurities: NMT 0.10% Total impurities: NMT 0.5%				
Residual Solvents-GC	N/A				

☑ **Reviewer Evaluation: Acceptable**

No changes in the approved specifications are reported in this supplemental NDA. The specifications for Gabapentin analysis, performed by the proposed (b) (4) meets current Gabapentin USP Monograph.

C. Reference Standards or Materials 3.2.S.5

C(i) Reference Standards or Materials (3.2.S.5)

☑ **Reviewer Evaluation: Acceptable**

The applicant provides the Certificates of Analysis for the reference standard lots, Gabapentin and (b) (4) used for the analysis of the drug substance, including method verification studies, at proposed (b) (4) facility.

3. DRUG PRODUCT (3.2.P)

A. Pharmaceutical Development 3.2.P.2

A(i) Manufacturing Process Development (3.2.P.2.3)

The applicant provides an Elemental Impurities Risk Assessment reports and a (b) (4) Risk Assessment used in the manufacturing process for Gralise (gabapentin) Tablets at the proposed (b) (4)

A(ii) Elemental Impurities Risk Assessment (3.2.P.2.4)

Table 1: Elemental Impurities to Test in Gralise ® (Gabapentin) Tablets

Element	Class	Intentionally added	Material Elemental Impurities µg/day	Manufacturing Equipment Elemental Impurities	Container Closure Elemental Impurities	Total Elemental Impurity contribution (µg/day)	Control threshold 30% of PDE (µg/day)	Risk Rating
(b) (4)								

Based om the elemental risk analysis presented in the table 1, the applicant analyzed in triplicated samples of the finished products (300 mg and 600 mg tablets) by ICP/MS for Class and (b) (4) impurities. (b) (4)

Table 5: Total Class (b) (4) impurities in Gabapentin Tablets, 300 mg, determined by ICP-MS analysis

(b) (4)

Table 6: Total Class (b) (4) impurities in Gabapentin Tablets, 600 mg, determined by ICP-MS analysis

(b) (4)

☑ **Reviewer Evaluation: Acceptable**

The provided risk assessment complies with the general principles of the (b) (4) and the (b) (4) for (b) (4) Impurities Limits guidelines. The risk assessment: 1) Identifies the known and potential sources of elemental impurities that find their way into the drug product, 2) Evaluates the presence of a particular element impurity in the drug product by determining the observed level of the impurity and comparing with the established (b) (4) and 3) Summarizes and documents if controls built into the presence are sufficient or identify additional controls to be considered to limit elemental impurities in the drug product.

The risk assessment demonstrated the (b) (4) are below the (b) (4) limits. The analyzed samples of the final Gabapentin drug product resulted to be below the quantitation limits.

A(iii) (b) (4) Risk Assessment (3.2.P.2.5)

☑ **Reviewer Evaluation: Acceptable**

The applicant provides a list of potential sources of (b) (4) during the manufacturing process of the drug product in the proposed facility (b) (4) Refer to table 1, below. The applicant states no (b) (4) are formed during the manufacturing process of the drug product.

Table 1: Potential Sources of (b) (4)

Potential Source	Material Number / Code	Intentionally added	Potential sources listed	Risk Rating	Comment
Drug Substance					
Gabapentin	(b) (4)				(b) (4)
Gabapentin					
Excipients		Excipients			
					(b) (4)
Manufacturing Equipment					
					(b) (4)
Container Closure/Packing					
					(b) (4)

B. Manufacturer 3.2.P.1

☑ **Reviewer Evaluation: Acceptable**

The applicant included the (b) (4)) in the drug product manufacturing list. The following responsibilities are proposed for the (b) (4) facility: (b) (4)

The OPMA reviewer found the proposed (b) (4) facility compliant, and recommended approval of the supplement. Refer to the OPMA report submitted by Yong Wu on 4/19/2021 in Panorama.

B(i) Batch Formula (3.2.P.3.2)

Table 1: Batch Formula for Gralise (gabapentin) Tablets, 300 mg and 600 mg

Material / Component	Material Number	Registration and Commercial Scale					
		Unit Dose 300 mg (mg/tablet)	% w/w (300 mg)	300 mg kg/Batch	Unit Dose 600 mg (mg/tablet)	% w/w (600 mg)	600 mg kg/Batch
Intra-granular:[1] Gabapentin, USP	(b) (4)	300.0	(b) (4)	(b) (4)	600.0	(b) (4)	(b) (4)
Copovidone, (b) (4)							
(b) (4)							
Extra-granular: Polyethylene Oxide, (b) (4)							
(b) (4)							
Hypromellose, USP (b) (4)							
Microcrystalline Cellulose, (b) (4) (Avicel PH-101)							
Magnesium Stearate, (b) (4)							
(b) (4)							
(b) (4)	(b) (4)	(b) (4)	(b)	(b) (4)	(b)	(b)	(b) (4)
Opadry II Beige (b) (4)							
Opadry II White (b) (4)							
(b) (4)							

[1] (b) (4)

[3] Microcrystalline Cellulose is not used in the 600 mg formulation.

(b) (4)

☑ **Reviewer Evaluation: Acceptable**

The applicant states the batch formula for registration batches at (b) (4) are representative of commercial scale for Gralise (gabapentin) Tablets, 300 mg with a batch size of (b) (4) corresponding to (b) (4) tablets and for Gralise (gabapentin) Tablets, 600 with a batch size of (b) (4) corresponding to (b) (4). The proposed batch scale for commercial manufacturing in (b) (4) is within the approved batch size for 300 mg tablets between (b) (4) and for 600 mg tablets between (b) (4)

B(ii) Description of Manufacturing Process (3.2.P.3.3)

☑ **Reviewer Evaluation: Acceptable**

No changes in the manufacturing process are reported in the supplemental NDA.

B(iii) Control of Critical Steps and Intermediates (3.2.P.3.4)

☑ **Reviewer Evaluation: Acceptable**

No changes in the in-process controls and bulk hold time are reported.

B(iv) Process Validation and/or evaluation (3.2.P.3.5)

Table 11: Process Validation Records

Master Production Record	Document Title	Final Document Number
(b) (4)	Gabapentin (b) (4)	(b) (4)
	Gralise (gabapentin) Tablets, 300 mg	
	Gralise (gabapentin) Tablets, 600 mg	

The applicant states: "each registration batch manufactured at (b) (4) of Gralise (gabapentin) Tablets, 300 mg and 600 mg is representative of the commercial process and manufacturing scale. The registration batch also serves as the first process validation batch of Gralise (gabapentin) Tablets, 300 mg (b) (4) and Gralise (gabapentin) Tablets, 600 mg (b) (4) to support this supplement for requalification of (b) (4) facility as the drug product manufacturer as provided in Module 3.2.P. 3.3." The manufacturing process records are provided in the section.

☑ **Reviewer Evaluation: Acceptable**

The applicant has provided adequate data to support the validation of the drug product manufactured at (b) (4).

C. Control of Excipients 3.2.P.4:

Table 1: Specifications for the Excipients used in the manufacture of Gralise (gabapentin) Tablets, 300 mg and 600 mg.

Excipient	Reference to Quality Standards	(b) (4) Specification	Vendor COA	(b) (4) COA
Copovidone, (b) (4) (b) (4)	(b) (4)	(b) (4)	(b) (4)	(b) (4)
(b) (4) (b) (4)				
Polyethylene Oxide (b) (4) (b) (4)				
Hypromellose (b) (4) (b) (4)				
Microcrystalline Cellulose, (b) (4) (b) (4)				
Magnesium Stearate (b) (4) (b) (4)				
(b) (4)				

☑ **Reviewer Evaluation: Acceptable**

The applicant provides the specifications and the certificates of analysis for all the excipients and the tablet coloring used in the drug product tablets manufacture at the proposed (b) (4) facility. The excipients used in the tablet manufacture at (b) (4) are of (b) (4) of (b) (4) grade. The applicant validates all the methods used in the specifications of

all the materials used in the tablets manufacture. The applicant states there are no (b) (4) excipients or (b) (4) excipients used in manufacture of Gralise (gabapentin) tablets, 300 mg and 600 mg.

D. Control of Drug Product 3.2.P.5:

D(i) Specifications (3.2.P.5.1)

☑ **Reviewer Evaluation: Acceptable**

No changes in the specifications of the drug product are reported in the supplemental NDA.

D(ii) Analytical Procedures (3.2.P.5.2)

☑ **Reviewer Evaluation: Acceptable**

The analytical methods were transferred from the current approved facility to the new proposed (b) (4) facility. No changes in the analytical methods are reported.

D(iii) Validation of Analytical Procedures (3.2.P.5.3)

Table 21: Validation of Analytical Procedures

Analytical Method Validation	Method Transfer Reports	Method No
(b) (4)	(b) (4)	

☑ **Reviewer Evaluation: Acceptable**

The applicant validated the analytical methods used in the analysis of the drug product at the proposed (b) (4) facility.

D(iv) Batch Analysis (3.2.P.5.4)

Table 1. Batch Analysis for Gralise (gabapentin) Tablets, 300 mg and 600 mg for Registration and Process Performance Qualification Batches

Product	Packaged Finished Drug Product Batch	Bulk Finished Drug Product Batch (COA)	Granulation Batch	Date of Manufacture	Use of Batch	Drug Substance Batch
Gralise (gabapentin) Tablets, 300 mg	(b) (4)	(b) (4)	(b) (4)	10/5/20	Registration Stability (b) (4)	(b) (4)
Gralise (gabapentin) Tablets, 600 mg				10/6/20	Registration Stability (b) (4)	
Gralise (gabapentin) Tablets, 300 mg				12/15/20		
Gralise (gabapentin) Tablets, 300 mg				12/16/20	(b) (4)	
Gralise (gabapentin) Tablets, 600 mg				12/16/20		
Gralise (gabapentin) Tablets, 600 mg				12/18/20		

Gralise drug product results for batch number 490153 manufactured at (b) (4)

(b) (4)

CERTIFICATE OF ANALYSIS

Inspection number : (b) (4) Batch-Nb. : (b) (4)
Material : (b) (4) Batch size : (b) (4) KG
Gralise (gabapentin) Tablets, 300mg

Vendor :
Vendor Batch :

Date of Manufacture : 12/15/2020 Expiration date : N/A
Next Inspection date : 03/15/2021

Test Description	Specification	Results
APPEARANCE	white to off white oval shaped tablets	MEETS
APPEARANCE	debossed with "SLV" on one side	MEETS
APPEARANCE	"300" on other side	MEETS
IDENTITY (b) (4)	Positive	Meets
IDENTITY HPLC (b) (4)	Meets	Meets
ASSAY (b) (4)	MIN. (b) (4) MAX.	(b) (4)
DISSOLUTION INDIV 1 H / L1 (b) (4)	MIN. (b) (4) MAX.	(b) (4)

CONTINUATION- Gralise drug product results for batch number 490153 manufactured at (b) (4)

DISSOLUTION 1H/L2 (b) (4)	MIN. MAX.	(b) (4)	(b) (4)
DISSOLUTION MEAN 1H / L2 (b) (4)	MIN. MAX.		(b) (4)
DISSOLUTION INDIV 4H L1 (b) (4)	MIN. MAX.		(b) (4)
DISSOLUTION INDIV 4H L2 (b) (4)	MIN. MAX.		(b) (4)
DISSOLUTION INDIV 4H L2 (b) (4)	MIN. MAX.		(b) (4)
DISSOLUTION INDIV 8H L1 (b) (4)	MIN. MAX.		(b) (4)
DISSOLUTION INDIV 8H L2 (b) (4)	MIN. MAX.		
DISSOLUTION MEAN 8H L2 (b) (4)	MIN. MAX.		(b) (4)
DISSOLUTION INDIV 12 HR L1 (b) (4)	MIN.		(b) (4)
DISSOLUTION INDIV 12 HR L2 (b) (4)	MIN.		(b) (4)
DISSOLUTION MEAN 12 HRS L2 (b) (4)	MIN.		(b) (4)
DISSOLUTION (b) (4)	Meets		(b) (4)
Related Compound 1 (b) (4)	MAX.		(b) (4)
RELATED COMPOUNDS - (b) (4) (b) (4)	MAX.		
REL COMP INDIVIDUAL UNKNOWN IMPURITY (b) (4)	MAX.		
RELATED COMPOUNDS - TOTAL (b) (4)	MAX.		

CONTINUATION- Gralise drug product results for batch number 490153 manufactured at (b) (4)

Inspection number : (b) (4) Batch-Nb. : (b) (4) Material : (b) (4) Batch size : (b) (4) KG Gralise (gabapentin) Tablets, 300mg			
Vendor : Vendor Batch :			
Date of Manufacture : 12/15/2020 Expiration date : N/A Next Inspection date : 03/15/2021			
Test Description		Specification	Results
(b) (4) CONTENT UNIFORMITY INDIV L1 (b) (4)		%labe	(b) (4)
(b) (4) ACCEPTANCE VALUE L1 (b) (4)		MAX. (b) (4)	(b) (4)
(b) (4) CONTENT UNIFORMITY QL1 (b) (4)		Meets	(b) (4)
(b) (4) CONTENT (b) (4)		MAX. (b) (4)	
(b) (4) (b) (4)		MAX. (b) (4)	

☑ **Reviewer Evaluation: Acceptable**

The applicant provides the specifications results for the three registration batches manufactured at the proposed (b) (4) facility. The registration batches represent the proposed commercial batch size for the manufacture of the drug product at the proposed (b) (4) (b) (4) facility. All the provided batch results for the drug product tablets manufactured at complies with the current approved released specifications.

D(v) Characterization of Impurities (3.2.P.5.5)

☑ **Reviewer Evaluation: Acceptable**

The impurity profile remains the same as currently approved for the drug product.

D(vi) Justification of Specifications (3.2.P.5.6)

☑ **Reviewer Evaluation: Acceptable**

No changes in specifications are reported in the supplement.

E. Reference Standards or Materials 3.2.P.6:

☑ **Reviewer Evaluation: Acceptable**

The reference standards used in the manufacture are the same used for the analysis of the drug substance. Refer to section 3.2.S.5 for details.

F. Container Closure System 3.2.P.7:

☑ **Reviewer Evaluation: Acceptable**

The primary packaging components used for the registration batches are the same as those currently proposed for commercial use at (b) (4) Therefore, the extractable and leachable profiles is unlikely to change for the drug product manufactured at the proposed (b) (4) facility.

G. Stability 3.2.P.8:

G(i) Stability Summary and Conclusion (3.2.P.8.1) and Post-Approval Stability Commitment (3.2.P.8.2)

☑ **Reviewer Evaluation: Acceptable**

The currently approved stability protocol and post approval commitments remains the same as proposed for the drug product tablets manufactured at (b) (4) facility. The expiry period of 24 months for the drug product when stored at (b) (4) with excursions permitted between 15° to 30°C (59° to 86°F) remains the same as approved.

G(ii) Stability Data (3.2.P.8.3)

Stability data for the primary registration batches of Gralise (gabapentin) Tablet 300 mg and 600 mg packaged in 90-count configuration manufactured at (b) (4) is described in Table 1.

(b) (4)

The applicant states: "testing at the intermediate stability storage condition, (b) (4), will not be performed unless significant change is observed in test results from the accelerated storage condition, as defined in the (b) (4) guidelines."

(b) (4)

☑ **Reviewer Evaluation: Acceptable**

All the long-term and accelerate 3 months stability data complies with the current approved stability specifications. No out of specifications are observed. The drug product quality and impurity profile manufactured at the proposed (b) (4) facility is comparable to the drug product manufactured at the current approved facility, (b) (4). The stability data provided supports this supplemental NDA.

H. Regional Information 3.2.R

☑ **Reviewer Evaluation: Acceptable**

The applicant provides the method validation, executed batch records for the registration batches manufactured at (b) (4) in support of this supplemental NDA.

IV RISK ASSOCIATED WITH THE PROPOSED CHANGES AND IMPACT TO PRODUCT QUALITY AND PATIENT SAFETY

Low

Daneli Lopez-Perez

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Gurpreet Gill Sangha

Digitally signed by Gurpreet Gill Sangha
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 022544/S-027

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

BIOPHARMACEUTICS REVIEW Office of New Drug Products			
Application No.:	NDA 022544/S-27	**Reviewer:** Kalpana S. Paudel, Ph.D.	
Submission Date:	03/18/2021		
Division:	DAAP	**Acting Team Lead** Haritha Mandula, Ph.D.	
Applicant:	Golf Acquiror LLC	**Acting Supervisor:** Okpo Eradiri, Ph.D.	
Trade Name:	Gralise®	**Date Assigned:**	03/31//2021
Established Name:	Gabapentin Tablets, 300 mg and 600 mg	**Date of Review:**	08/05/2021
Indication:	Management of postherpetic neuralgia	**Type of Submission:** CBE-30	
Formulation/ strengths	Tablets/300 mg and 600 mg		
Route of Administration	Oral		
Type of Review:	Comparative dissolution data to qualify for the addition of (b) (4) as an Alternate Drug Product Manufacturer		

SUMMARY:

Background: Gabapentin (Gralise) tablets were approved by the FDA for the management of Postherpetic Neuralgia under NDA 22544 on January 2011. (b) (4) Gralise Tablets (300 and 600 mg) were approved as an immediate release formulation, (b) (4)

(b) (4) is the currently approved manufacturing site for gabapentin tablets, 300 mg and 600 mg. On 03/18/2021, the Applicant submitted a CBE-30 supplement for the addition of an alternate site, (b) (4), for manufacturing of the gabapentin tablets. The site change is considered a Level 3 change per the SUPAC-IR guidance, which requires multi-point comparative dissolution testing to support the change.

Submission: The Applicant submitted the results of comparative multi-point dissolution testing to demonstrate similarity of the drug product manufactured at the approved (b) (4) site and the proposed alternate (b) (4) site.

Review: The Biopharmaceutics review is focused on the evaluation and acceptability of

the dissolution data to support the approval of the alternate manufacturing site.

The comparative dissolution data submitted from one batch of each strength manufactured at the current (b) (4) site and one batch of each strength manufactured at the alternate (b) (4) site showed similarity factor (f2) more than (b) (4) for 300 mg and (b) (4) for 600 mg strength). In addition, the submitted batch analysis data for all the primary registration and process performance qualification (PPQ) batches of both strengths (three batches per strength) manufactured at the alternate site meet the approved dissolution acceptance criteria. Thus, the dissolution profiles of the proposed drug product manufactured at the new (b) (4) facility and the current (b) (4) facility are deemed similar.

RECOMMENDATION:
From the Biopharmaceutics perspective, NDA 022544/S-27 to support an alternative manufacturing site is recommended for approval.

Signature	**Signature**
Kalpana S. Paudel, Ph.D. Biopharmaceutics Reviewer Office of New Drug Products	Haritha Mandula, Ph.D. Biopharmaceutics Quality Assessment Lead Office of New Drug Products

cc. OEradiri; PSeo.

BIOPHARMACEUTICS ASSESSMENT

The Applicant submitted this CBE-30 supplement for the addition of an alternate site, (b) (4) for manufacturing of gabapentin tablets. The Applicant noted that in 2013, Depomed (the then NDA holder) (b) (4) . This supplement is submitted to (b) (4) as an alternate manufacturing facility for Gralise (gabapentin) Tablets, 300 mg and 600 mg. (b) (4) facility is the currently approved manufacturing site. This site change is considered a Level 3 site change per the SUPAC IR guidance, and the applicant has provided multi-point comparative dissolution data to support this change.

Approved dissolution method and acceptance criteria

The following dissolution method and acceptance criteria are the currently approved method for gabapentin tablets, 300 mg and 600 mg:

USP Apparatus 1 (basket), 100 rpm, 900 ml of pH 1.2 Buffer, modified Simulated Gastric Fluid without pepsin, at 37ºC

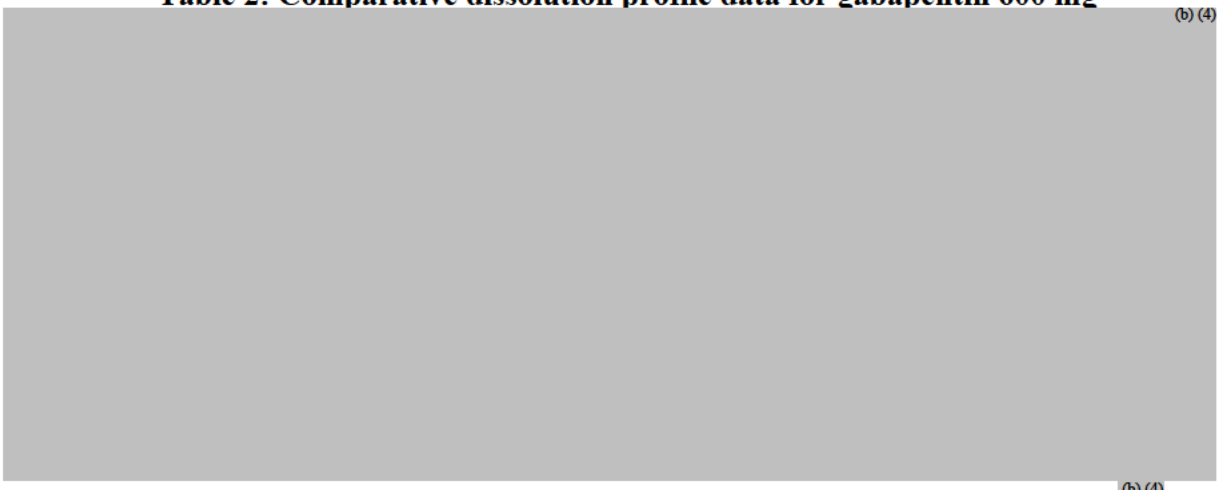
1 hour: (b) (4)
4 hours
8 hours
12 hours: (b) (4)

Comparative Dissolution Assessment:

The Applicant submitted comparative in vitro dissolution data from one batch of each strength manufactured at the current manufacturing site ((b) (4)) and one batch of each strength manufactured at the alternate manufacturing site (b) (4) In addition, the applicant also submitted batch analysis data for all the primary registration and process performance qualification (PPQ) batches of both strengths (three batches per strength) manufactured at the alternate site. Comparative dissolution profile data for the 300 mg and 600 mg strengths are presented in Table 1 and Table 2, respectively. The in vitro dissolution data were determined using the approved dissolution method.

Table 1: Comparative dissolution profile data for gabapentin 300 mg

Table 2: Comparative dissolution profile data for gabapentin 600 mg



This reviewer confirmed that the f2 values were higher than for 300 mg and for 600 mg strength). In addition, all six batches meet the approved dissolution acceptance criteria. Therefore, the proposed alternate manufacturing site, for Gralise tablets, 300 mg and 600 mg is acceptable from Biopharmaceutics perspective.

Recommendation:

The dissolution data to support the addition of a new manufacturing site was reviewed. The dissolution data presented in this submission demonstrate that the proposed drug products manufactured at the new site and currently approved site have similar dissolution profiles. Therefore, the comparative dissolution data support approval of the proposed new drug product manufacturing site at .

Kalpana Paudel

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Haritha Mandula

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 022544/S-027

OTHER REVIEW(S)

REGULATORY BUSINESS PROCESS MANAGER LABELING REVIEW

Office of Program and Regulatory Operations

Application: NDA 022544/S-27

Name of Drug: Gralise (gabapentin) Tablets, 300 mg and 600 mg.

Applicant: Golf Acquiror LLC

Submission and amendment receipt date: March 18, 2021 and April 5, 2021
Material Reviewed:

Material	**Submit Date**	**Receipt Date**	**Compared to last approved labels/labeling**
Prescribing Information	March 18, 2021	March 18, 2021	Last Approved in S-026 dated April 2, 2020
Carton Label	March 18, 2021	March 18, 2021	Last Approved in S-012 dated March 27, 2013
Blister Label	March 18, 2021	March 18, 2021	Last Approved in S-024 dated March 6, 2017

Background and Summary Description:

This supplement submitted as a "Changes Being Effected in 30 days " provides for the addition of (b) (4), as an alternate drug product manufacturing facility for Gralise (gabapentin) Tablets, 300 mg and 600 mg.

CMC review is recommended for approval as of by Daneli López Pérez, Ph.D., and Gurpreet Gill-Sangha, Ph.D.

Review

This comparison was done by visually comparing the proposed to the last submitted or approved labeling on file.

The following are the assessments for each change identified:

Carton Labels:

Last Approved:

Proposed:

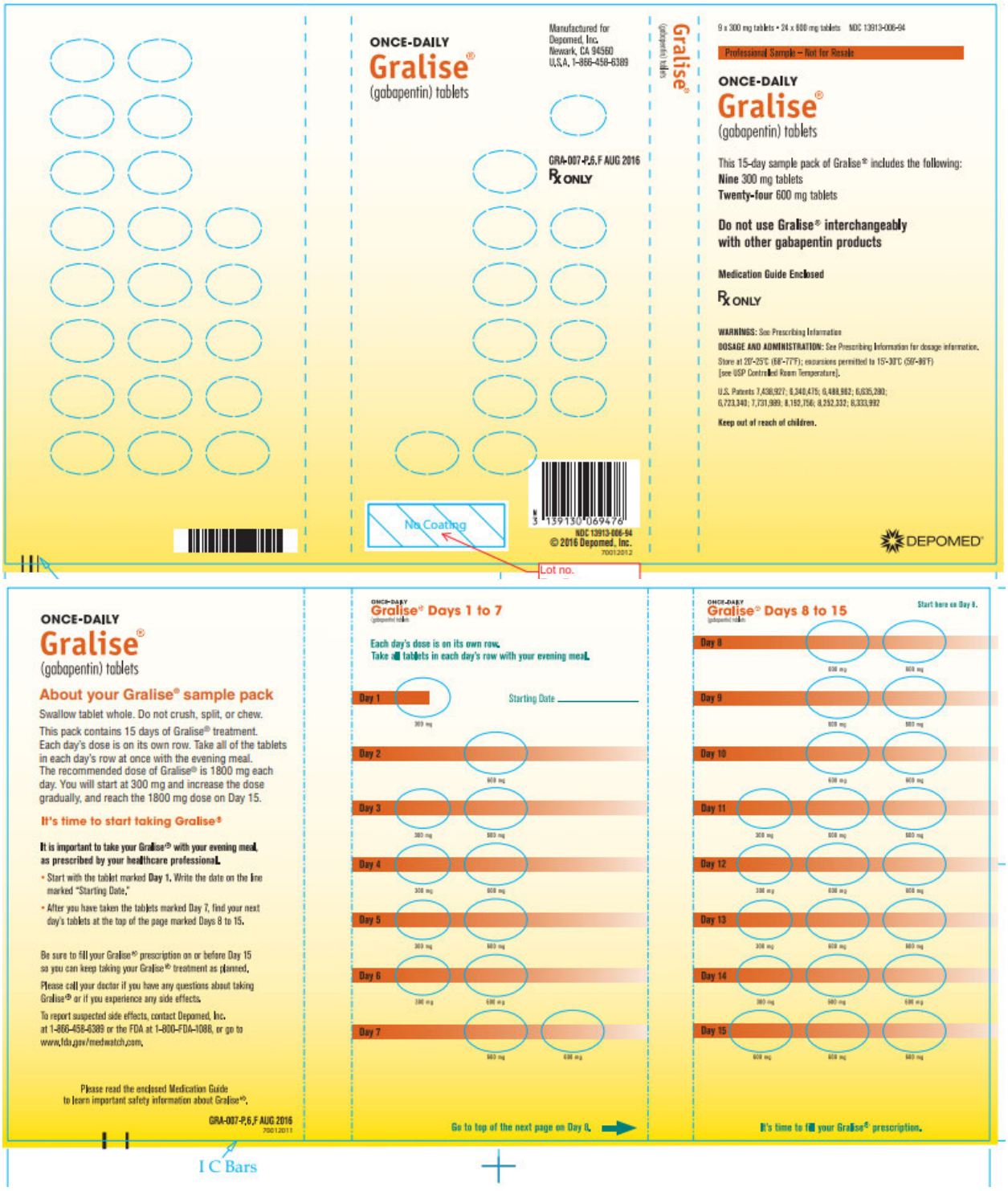
Comment:

- Manufactured for Depomed Inc. was changed to Distributed by : Almatica Pharma LLC
- Attention: Distribute required medication guide to each patient was changed to Pharmacist: Dispense the accompanying medication guide to each patient
- The logo was changed from Depomed to Almatica and so was the NDC
- The format color change from orange- yellow to green-blue

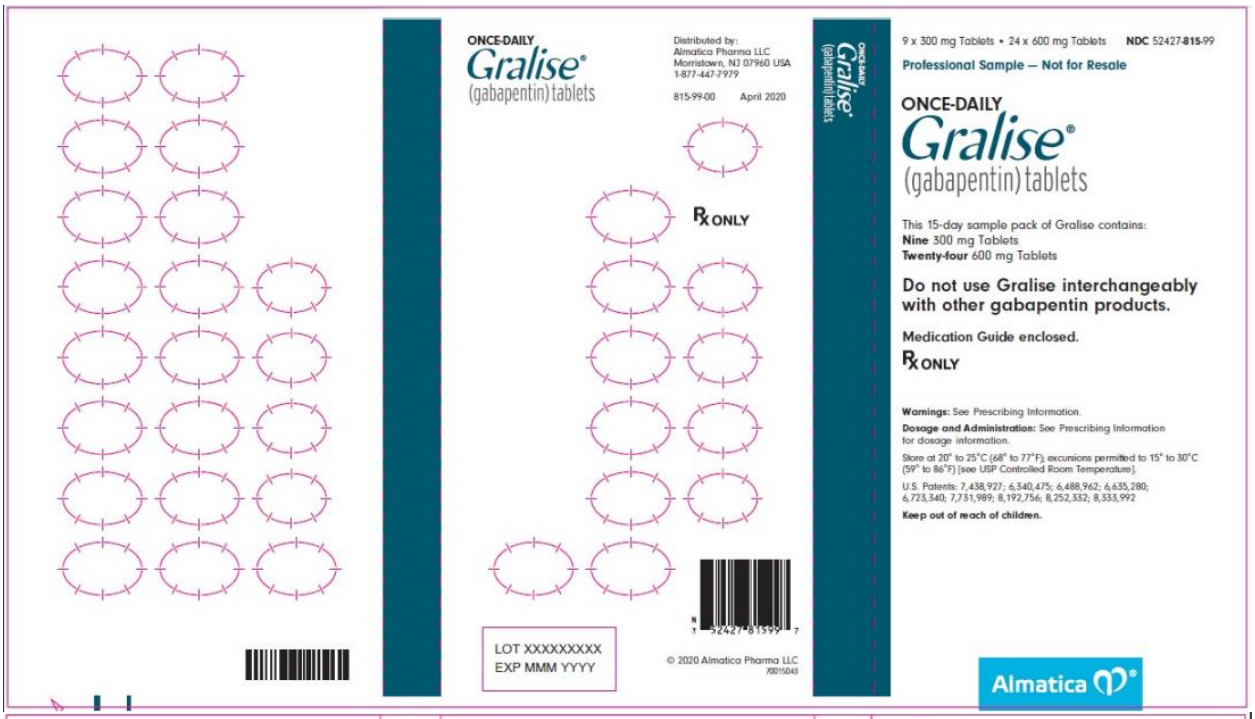
These changes are acceptable per CMC review.

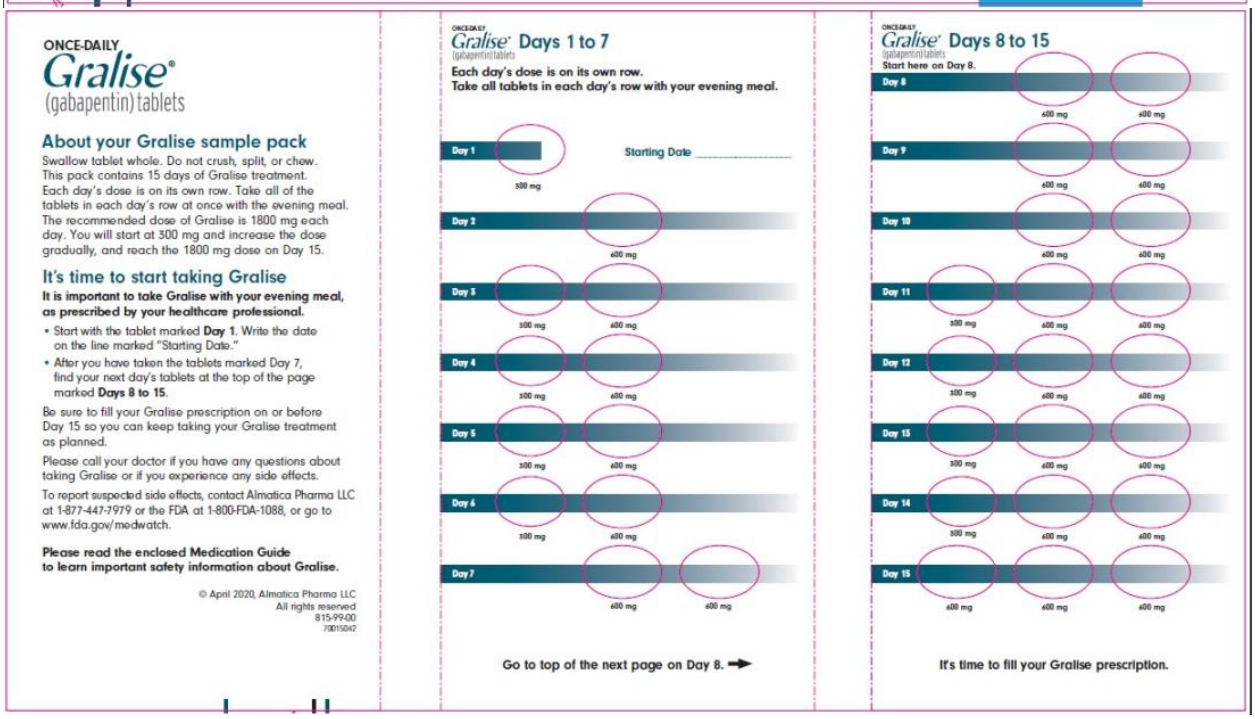
Blister:

Last Approved:


ONCE-DAILY
Gralise®
(gabapentin) tablets
Manufactured for
Depomed, Inc.
Newark, CA 94560
U.S.A. 1-866-458-6389
GRA-007-P,6,F AUG 2016
℞ ONLY
No Coating
Lot no.
NDC 13913-006-94
© 2016 Depomed, Inc.
9 x 300 mg tablets • 24 x 600 mg tablets NDC 13913-006-94
Professional Sample – Not for Resale
This 15-day sample pack of Gralise® includes the following:
Nine 300 mg tablets
Twenty-four 600 mg tablets
Do not use Gralise® interchangeably with other gabapentin products
Medication Guide Enclosed
℞ ONLY
WARNINGS: See Prescribing Information
DOSAGE AND ADMINISTRATION: See Prescribing Information for dosage information.
Store at 20°-25°C (68°-77°F); excursions permitted to 15°-30°C (59°-86°F)
[see USP Controlled Room Temperature].
U.S. Patents 7,438,927; 8,348,475; 8,488,962; 8,635,280;
8,723,340; 7,731,989; 8,192,756; 8,252,332; 8,333,992
Keep out of reach of children.
DEPOMED
About your Gralise® sample pack
Swallow tablet whole. Do not crush, split, or chew.
This pack contains 15 days of Gralise® treatment. Each day's dose is on its own row. Take all of the tablets in each day's row at once with the evening meal. The recommended dose of Gralise® is 1800 mg each day. You will start at 300 mg and increase the dose gradually, and reach the 1800 mg dose on Day 15.
It's time to start taking Gralise®
It is important to take your Gralise® with your evening meal, as prescribed by your healthcare professional.
• Start with the tablet marked Day 1. Write the date on the line marked "Starting Date."
• After you have taken the tablets marked Day 7, find your next day's tablets at the top of the page marked Days 8 to 15.
Be sure to fill your Gralise® prescription on or before Day 15 so you can keep taking your Gralise® treatment as planned.
Please call your doctor if you have any questions about taking Gralise® or if you experience any side effects.
To report suspected side effects, contact Depomed, Inc. at 1-866-458-6389 or the FDA at 1-800-FDA-1088, or go to www.fda.gov/medwatch.com.
Please read the enclosed Medication Guide to learn important safety information about Gralise®.
GRA-007-P,6,F AUG 2016
Gralise® Days 1 to 7
Each day's dose is on its own row.
Take all tablets in each day's row with your evening meal.
Starting Date
Day 1
Day 2
Day 3
Day 4
Day 5
Day 6
Day 7
Go to top of the next page on Day 8.
Gralise® Days 8 to 15
Start here on Day 8.
Day 8
Day 9
Day 10
Day 11
Day 12
Day 13
Day 14
Day 15
It's time to fill your Gralise® prescription.
I C Bars

Proposed:





Comment:

- Manufactured for Depomed Inc. was changed to Distributed by : Almatica Pharma LLC
- The contact information for the side effects has been update to Almatica Pharma 1-877-447-7979
- The logo was changed from Depomed to Almatica and so was the NDC

- The format color change from orange- yellow to blue

These changes are acceptable per CMC review.

Prescribing Information:

No new changes to the submitted PI. The last approved was in S-026 dated April 2, 2020

Enclosures:

Caron and Container Label:
\\CDSESUB1\evsprod\nda022544\0178\m1

Recommendations

The change to the content of labeling is acceptable. The supplement is recommended for approval.

{See appended electronic signature page}

Teicher Agosto, Pharm.D.
Regulatory Business Process Manager
Office of Programs and Regulatory Operations
Office of Pharmaceutical Quality

Date: September 2021

Teicher Agosto

Digitally signed by Teicher Agosto
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