CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

215025Orig1s000

OTHER REVIEW(S)

FOOD AND DRUG ADMINISTRATION
Center for Drug Evaluation and Research
Office of Prescription Drug Promotion

****Pre-decisional Agency Information****

Memorandum

Date: May 26, 2021

To: Michael White, PhD, Chief, Project Management
Division of Rare Diseases and Medical Genetics (DRDMG)

From: Adewale Adeleye, Pharm.D., MBA, Regulatory Review Officer
Office of Prescription Drug Promotion (OPDP)

Subject: OPDP Labeling Comments for SODIUM PHENYLACETATE AND SODIUM BENZOATE injection, for intravenous use

NDA: 215025

In response to DRDMG consult request dated September 21, 2020, OPDP has reviewed the proposed product labeling (PI) for the original NDA submission for SODIUM PHENYLACETATE AND SODIUM BENZOATE injection, for intravenous use.

Labeling: OPDP's comments on the proposed labeling are based on the draft labeling available in SharePoint on May 25, 2021, at 1:06 pm and are provided below.

Thank you for your consult. If you have any questions, please contact Adewale Adeleye at (240) 402-5039 or adewale.adeleye@fda.hhs.gov.

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/s/

ADEWALE A ADELEYE
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DEPARTMENT OF HEALTH & HUMAN SERVICES

MEMORANDUM

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

TO: Nicolas Kong, Regulatory Project Manager
Division of Regulatory Operations for Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (ORPURM)
Rare Diseases & Medical Genetics (DRDMG)

FROM: Tinya Sensie, MHA, Senior Regulatory Project Manager
Division of Regulatory Operations for Rare Diseases, Pediatrics, Urologic and Reproductive Medicine (ORPURM)
Pediatric and Maternal Health (DPMH)

SUBJECT: New NDA 215025 for sodium phenylacetate and sodium benzoate with PLLR updates

NDA: 215025

DRUG: sodium phenylacetate and sodium benzoate

On September 21, 2020, DPMH received a consult for new NDA 215025/sodium phenylacetate and sodium benzoate with PLLR updates. DPMH attended the mid-cycle meeting on January 11, 2021 and a labeling meeting on February 9, 2021. The sponsor aligned their labeling with the listed drug, Ammonul (NDA 020645) and we have no additional comments. DPMH input was provided for the Ammonul PLLR labeling approved in December 2020.

This memorandum will close out the consult request.

DPMH RPM- Tinya Sensie
DPMH RPM Team Leader- George Greeley
DPMH Maternal Health Reviewer- Christos Mastroyannis
DPMH Maternal Health Team Leader- Tamara Johnson
DPMH Division Director- Lynne P. Yao

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/s/

TINYA J SENSIE
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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	April 14, 2021
Requesting Office or Division:	Division of Rare Diseases and Medical Genetics (DRDMG)
Application Type and Number:	NDA 215025
Product Name and Strength:	Sodium Phenylacetate and Sodium Benzoate injection, 10%/10%
Applicant/Sponsor Name:	MAIA Pharmaceuticals, Inc
OSE RCM #:	2021-568-2
DMEPA Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA Team Leader:	Idalia E. Rychlik, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label and carton labeling received on April 9, 2021 for Sodium Phenylacetate and Sodium Benzoate. Division of Rare Diseases and Medical Genetics (DRDMG) requested that we review the revised container label and carton labeling for Sodium Phenylacetate and Sodium Benzoate (Appendix A) to determine if it is acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a]

2 CONCLUSION

The revised carton labeling is acceptable from a medication error perspective. We do not have any recommendations at this time.

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[a] Vee S. Label and Labeling Review for Sodium Phenylacetate and Sodium Benzoate (NDA 215025). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 APR 07. RCM No.: 2021-568-1.

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/s/

SARAH K VEE
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IDALIA E RYCHLIK
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MEMORANDUM

REVIEW OF REVISED LABEL AND LABELING
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

Date of This Memorandum:	April 7, 2021
Requesting Office or Division:	Division of Rheumatology and Transplant Medicine (DRTM)
Application Type and Number:	NDA 215025
Product Name and Strength:	(Sodium Phenylacetate and Sodium Benzoate) injection, 10%/10%
Applicant/Sponsor Name:	MAIA Pharmaceuticals, Inc
OSE RCM #:	2021-568-1
DMEPA Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA Team Leader:	Idalia E. Rychlik, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised container label and carton labeling received on April 2, 2021 for Sodium Phenylacetate and Sodium Benzoate. Division of Rheumatology and Transplant Medicine (DRTM) requested that we review the revised container label and carton labeling for Sodium Phenylacetate and Sodium Benzoate (Appendix A) to determine if it is acceptable from a medication error perspective. The revisions are in response to recommendations that we made during a previous label and labeling review.[a] We note that MAIA states that they will use the expiration date format of YYYY-MM-DD or YYYY-MM.

2 CONCLUSION

The revised container label and carton labeling is unacceptable from a medication error perspective. The use of (b) (4) for the established name and the strength statements do not provide adequate differentiation.

3 RECOMMENDATIONS FOR MAIA PHARMACEUTICALS, INC

We recommend the following be implemented prior to approval of this NDA:

[a] Vee S. Label and Labeling Review for Sodium Phenylacetate and Sodium Benzoate (NDA 215025). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 MAR 25. RCM No.: 2021-568.

A. We recommend that you use some means of differentiating the established name and the strength statement (e.g., (b) (4), text box, etc.) to ensure that these important information are not missed.

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/s/

SARAH K VEE
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IDALIA E RYCHLIK
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LABEL AND LABELING REVIEW
Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	March 25, 2021
Requesting Office or Division:	Division of Rare Diseases and Medical Genetics (DRDMG)
Application Type and Number:	NDA 215025
Product Name, Dosage Form, and Strength:	Sodium Phenylacetate and Sodium Benzoate injection, 10%/10%
Product Type:	Multi-Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	MAIA Pharmaceuticals, Inc.
FDA Received Date:	August 21, 2020 and March 19, 2021
OSE RCM #:	2021-568
DMEPA Safety Evaluator:	Sarah K. Vee, PharmD
DMEPA Team Leader:	Idalia E. Rychlik, PharmD

1 REASON FOR REVIEW

As part of the approval process for Sodium Phenylacetate and Sodium Benzoate injection, the Division of Rare Diseases and Medical Genetics (DRDMG) requested that we review the proposed Sodium Phenylacetate and Sodium Benzoate prescribing information (PI), container label, and carton labeling for areas of vulnerability that may lead to medication errors.

2 MATERIALS REVIEWED

We considered the materials listed in Table 1 for this review. The Appendices provide the methods and results for each material reviewed.

Table 1. Materials Considered for this Review

Material Reviewed	Appendix Section (for Methods and Results)
Product Information/Prescribing Information	A
Previous DMEPA Reviews	B – N/A
Human Factors Study	C – N/A
ISMP Newsletters*	D – N/A
FDA Adverse Event Reporting System (FAERS)*	E – N/A
Other	F – N/A
Labels and Labeling	G

N/A=not applicable for this review
*We do not typically search FAERS or ISMP Newsletters for our label and labeling reviews unless we are aware of medication errors through our routine postmarket safety surveillance

3 OVERALL ASSESSMENT OF THE MATERIALS REVIEWED

MAIA submitted a 505(b)(2) NDA to obtain marketing approval for sodium phenylacetate and sodium benzoate injection. The listed drug (LD) for this product is Ammonul (sodium phenylacetate and sodium benzoate) injection. Ammonul is currently available in a 50 mL vial. We note that the proposed sodium phenylacetate and sodium benzoate injection has the same dosage regimen and indication as the LD.

We performed a risk assessment of the full prescribing information (PI), container label, and carton labeling to identify deficiencies that may lead to medication errors and areas for improvement. Our review of the container label and carton labeling identified areas where the label and labeling may be improved to promote the safe use of the product. Thus, we provide related recommendations below in Section 4.1 for the Applicant.

4 CONCLUSION & RECOMMENDATIONS

We conclude that the proposed container label and carton labeling may be improved to promote the safe use of the product. We provide recommendations in Section 4.1 for the Applicant.

4.1 RECOMMENDATIONS FOR MAIA PHARMACEUTICALS, INC.

We recommend the following be implemented prior to approval of this NDA:

A. General Comments (Container labels & Carton Labeling)

1. The route of administration is included as an abbreviation, "For IV use only" and "Must be diluted before IV administration". Presenting the route of administration as an abbreviation may lead to misinterpretation. Revise "IV" to the intended meaning, "intravenous" throughout.
2. Revise the statement: [redacted] (b) (4) " to read "Recommended Dosage: See prescribing information" to align with the prescribing information.
3. We recommend the use of some means (e.g., [redacted] (b) (4), text box, etc.) of increasing the prominence of the important information on the principle display panel (PDP) (i.e., established name and strength). As it is currently presented, the use of [redacted] (b) (4) do not provide prominence to this important information from other information on the PDP.
4. As currently presented, the format for the expiration date is not defined. To minimize confusion and reduce the risk for deteriorated drug medication errors, identify the format you intend to use. FDA recommends that the human-readable expiration date on the drug package label include a year, month, and non-zero day. FDA recommends that the expiration date appear in YYYY-MM-DD format if only numerical characters are used or in YYYY-MMM-DD if alphabetical characters are used to represent the month. If there are space limitations on the drug package, the human-readable text may include only a year and month, to be expressed as: YYYY-MM if only numerical characters are used or YYYY-MMM if alphabetical characters are used to represent the month. FDA recommends that a slash or a hyphen be used to separate the portions of the expiration date.

APPENDICES: METHODS & RESULTS FOR EACH MATERIALS REVIEWED

APPENDIX A. PRODUCT INFORMATION/PRESCRIBING INFORMATION

Table 2 presents relevant product information for Sodium Phenylacetate and Sodium Benzoate received on August 21, 2020 from MAIA Pharmaceuticals, Inc..

Table 2. Relevant Product Information for Sodium Phenylacetate and Sodium Benzoate						
Initial Approval Date	N/A					
Active Ingredient	sodium phenylacetate and sodium benzoate					
Indication	as adjunctive therapy for the treatment of acute hyperammonemia and associated encephalopathy in patients with deficiencies in enzymes of the urea cycle					
Route of Administration	Intravenous injection					
Dosage Form	injection					
Strength	10%/10%					
Dose and Frequency						
Patient Population		Components of Infusion Solution Sodium Phenylacetate and Sodium Benzoate Injection must be diluted with sterile 10% Dextrose Injection at ≥25 mL/kg before administration.		Dosage Provided		
		Sodium Phenylacetate and Sodium Benzoate Injection	Arginine HCl Injection, 10%	Sodium Phenylacetate	Sodium Benzoate	Arginine HCl
CPS and OTC Deficiency						
Patients 0 to 20 kg:	Dose Loading: over 90 to 120 minutes Maintenance: over 24 hours	2.5 mL/kg	2 mL/kg	250 mg/kg	250 mg/kg	200 mg/kg
	ASS and ASL Deficiency					
	Dose Loading: over 90 to 120 minutes Maintenance: over 24 hours	2.5 mL/kg	6 mL/kg	250 mg/kg	250 mg/kg	600 mg/kg

Patients > 20 kg:	CPS and OTC Deficiency					
	Dose Loading: over 90 to 120 minutes Maintenance: over 24 hours	55 mL/m^2	2 mL/kg	5.5 g/m^2	5.5 g/m^2	200 mg/kg
	ASS and ASL Deficiency					
	Dose Loading: over 90 to 120 minutes Maintenance: over 24 hours	55 mL/m^2	6 mL/kg	5.5 g/m^2	5.5 g/m^2	600 mg/kg
How Supplied	single-dose vial containing 20 mL of Sodium Phenylacetate and Sodium Benzoate Injection					
Storage	Store at 20°C to 25°C (68°F to 77°F); excursions permitted to 15°C to 30°C (59°F to 86°F).					

APPENDIX G. LABELS AND LABELING

G.1 List of Labels and Labeling Reviewed

Using the principles of human factors and Failure Mode and Effects Analysis,[a] along with postmarket medication error data, we reviewed the following Sodium Phenylacetate and Sodium Benzoate labels and labeling submitted by MAIA Pharmaceuticals, Inc..

- Container label received on March 19, 2021
- Carton labeling received on March 19, 2021
- Prescribing Information (Image not shown) received on August 21, 2020, available from \\CDSESUB1\evsprod\NDA215025\0001

G.2 Label and Labeling Images

(b) (4)

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[a] Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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