Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting
June 9, 2021

Location: Please note that due to the impact of the COVID-19 pandemic, all meeting participants joined this advisory committee meeting via an online teleconferencing platform.

Topic: The committee discussed the following four bulk drug substances nominated for inclusion on the 503A Bulks List: choline chloride, oxitriptan (also known as 5-hydroxytryptophan or 5-HTP), melatonin, and methylcobalamin. The chart below identifies the use(s) FDA reviewed for each of the four bulk drug substances discussed at this advisory committee meeting. The nominators of these substances or another interested party were invited to make a short presentation supporting the nomination.

Bulk Drug Substance	Uses Evaluated
Choline Chloride	Liver diseases (including non-alcoholic fatty liver disease) and hepatic steatosis
	Atherosclerosis
	Fetal alcohol spectrum disorder
	Supplementation in long term total parenteral nutrition
Melatonin	Treatment of sleep disorders in patients with autism spectrum disorder (specifically children and adolescents)
Methylcobalamin	Amyotrophic lateral sclerosis (also known as ALS)
	Pain management
	Peripheral neuropathy (including diabetic neuropathy)
	Inborn errors of metabolism (also known as genetic metabolic disorders) (including methylenetetrahydrofolate reductase deficiency (also known as MTHFR))
	Hyperhomocysteinemia (including conjunctive therapy in hemodialysis patients)
	Vitamin B12 deficiency
	Autism spectrum disorder
Oxitriptan (5-HTP)	Treatment for patients with tetrahydrobiopterin (BH4) deficiency

The committee also discussed revisions FDA is considering to the Withdrawn or Removed List. FDA now is considering whether to amend the rule to add one more entry to the list: Neomycin Sulfate: All parenteral drug products containing neomycin sulfate (except for ophthalmic or otic use, or when combined with polymyxin B sulfate for irrigation of the intact bladder). As previously explained in the Federal Register of July 2, 2014 (79 FR 37687 at 37689 through 37690), the list may specify that a drug may not be compounded in any form, or, alternatively, may expressly exclude a particular formulation, indication, dosage form, or route of administration from an entry on the list. Moreover, a drug may be listed only with regard to certain formulations, indications, routes of administration, or dosage forms because it has been found to be unsafe or not effective in those particular formulations, indications, routes of administration, or dosage forms. FDA sought the committee's advice concerning the inclusion of this drug product on the list.

These summary minutes for the June 9, 2021 meeting of Pharmacy Compounding Advisory Committee (PCAC) of the Food and Drug Administration were approved on 7/12/2021.

I certify that I attended the June 9, 2021 meeting of the PCAC meeting of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/
Takyiah Stevenson, PharmD
Designated Federal Officer, PCAC

/s/
Padma Gulur, MD, FASA
Chairperson, PCAC

Final Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting
June 9, 2021

The Pharmacy Compounding Advisory Committee (PCAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on June 9, 2021. The meeting presentations were heard, viewed, captioned, and recorded through an online teleconferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA. The meeting was called to order by Padma Gulur, MD, FASA (Chairperson). The conflict of interest statement was read into the record by Takyiah Stevenson, PharmD (Designated Federal Officer). There were approximately 226 people online. There were three Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda: The committee discussed the following four bulk drug substances nominated for inclusion on the 503A Bulks List: choline chloride, oxitriptan (also known as 5-hydroxytryptophan or 5-HTP), melatonin, and methylcobalamin. The chart below identifies the use(s) FDA reviewed for each of the four bulk drug substances discussed at this advisory committee meeting. The nominators of these substances or another interested party were invited to make a short presentation supporting the nomination.

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Attendance:

PCAC Members Present (Voting): Robin H. Bogner, PhD; Seemal R. Desai, MD, FAAD; Timothy D. Fensky, RPh, DPh, FACA (National Association of Boards of Pharmacy Representative); Sandra J. Fusco-Walker (Consumer Representative); Padma Gulur, MD, FASA (Chairperson); Anita Gupta, DO, MPP, PharmD; Kathleen M. Gura PharmD, BCNSP, FASHP, FASPEN; Linda F. McElhiney, PharmD, RPh, MSP, FAPC, FACA, FASHP, DPLA; Kuldip R. Patel, PharmD, FASHP; Elizabeth Rebello, RPh, MD, FASA, CPPS; Jeanne H. Sun, PharmD, JD (United States Pharmacopeia Representative); Allen J. Vaida, BSc, PharmD, FASHP

PCAC Members Not Present (Voting): None

PCAC Member Present (Non-Voting): Gus Bassani, PharmD (Industry Representative for neomycin sulfate topic only), Michael D. Bui, DDS, MPH, JD (Industry Representative)

Acting Industry Representative to the Committee (Non-Voting): Richard L. Green, BS Pharm, RPh, BCNP, FAPhA (Melatonin, Methylcobalamin, Choline Chloride and Oxitriptan Topics Only)

Temporary Members (Voting): Jonathan Emens, MD, FAASM, DFAPA (Melatonin Topic Only); Joanna Katzman, MD, MSPH (Methylcobalamin Topic Only); Jennifer C. Lai, MD, MBA (Choline Chloride Topic Only); Suthat Liangpunsakul, MD, MPH (Choline Chloride Topic Only); Friedhelm Sandbrink, MD (Methylcobalamin Topic Only)

FDA Participants (Non-Voting): Frances Gail Bormel, RPh, JD; Gabrielle Cosel; Rosilend Lawson, VMD, JD; Charles Ganley, MD; Susan Johnson, PharmD, PhD; Suhail Kasim, MD, MPH; Madeline Wolfert, MD (Oxitriptan Topic Only); Jae Ho Hong, MD (Neomycin Topic Only)

Designated Federal Officers (Non-Voting): Takyiah Stevenson, PharmD

Open Public Hearing Speakers:

- Melatonin (Topic 1) – No OPH speakers
- Methylcobalamin (Topic 2): James Neubrander, MD; Heather E. Volk, PhD, MPH
- Choline Chloride (Topic 3) – No OPH speakers
- Oxitriptan (Topic 4) – No OPH speakers
- Neomycin sulfate (Topic 5): Michael A. Carome, MD (Public Citizen)

The agenda was as follows:

Call to Order	**Padma Gulur, MD, FASA** Chairperson, PCAC
Introduction of Committee and Conflict of Interest Statement	**Takyiah Stevenson, PharmD** Designated Federal Officer, PCAC
FDA INTRODUCTORY REMARKS	**Frances Gail Bormel, RPh, JD** Director Office of Compounding Quality and Compliance (OCQC) Office of Compliance (OC), CDER, FDA

SECTION 503A BULK DRUG SUBSTANCES LIST – MELATONIN

Melatonin	**Suhail Kasim, MD, MPH** Lead Physician Pharmacy Compounding Review Team Office of Specialty Medicine (OSM) Office of New Drugs (OND), CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

SECTION 503A BULK DRUG SUBSTANCES LIST – METHYLCOBALAMIN

Methylcobalamin	**Susan Johnson, PharmD, PhD** Clinical Reviewer Pharmacy Compounding Review Team OSM, OND, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS	**A.J. Day, PharmD** National Community Pharmacists Association and Alliance for Pharmacy Compounding
	Richard E. Frye, MD, PhD Professional Compounding Centers of America

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

LUNCH

SECTION 503A BULK DRUG SUBSTANCES LIST – CHOLINE CHLORIDE

Choline Chloride	**Suhail Kasim, MD, MPH** Lead Physician Pharmacy Compounding Review Team OSM, OND, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATIONS	**Paul S. Anderson, ND** American Association of Naturopathic Physicians

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

SECTION 503A BULK DRUG SUBSTANCES LIST – OXITRIPTAN

Oxitriptan	**Madeline Wolfert, MD** Physician Pharmacy Compounding Review Team OSM, OND, CDER, FDA

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

Conflict of Interest Statement	**Takyiah Stevenson, PharmD** Designated Federal Officer, PCAC
WITHDRAWN OR REMOVED LIST PROCESS	**Gabrielle Cosel** Director (Acting) Division of Compounding Policy and Outreach OCQC, OC, CDER, FDA

DRUGS TO BE CONSIDERED FOR THE WITHDRAWN OR REMOVED LIST – NEOMYCIN SULFATE

Neomycin sulfate

Jae Ho Hong, MD
Medical Officer
Division of Anti-Infectives
Office of Infectious Diseases
OND, CDER, FDA

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

ADJOURNMENT

Questions to the Committee:

Questions for PCAC Regarding Whether to Include Certain Bulk Drug Substances on the 503A Bulk List

1. **VOTE:** FDA is proposing that melatonin for oral administration be INCLUDED on the 503A Bulks List. Should melatonin for oral administration be placed on the list?

   Vote Result: Yes: 13 No: 0 Abstain: 0

   Committee Discussion: *The committee unanimously agreed that melatonin for oral administration be included on the 503A Bulks List. Please see the transcript for details of the Committee's discussion.*

2. **VOTE**: FDA is proposing that methylcobalamin NOT be included on the 503A Bulks List. Should methylcobalamin be placed on the list?

   Vote Result: Yes: 9 No: 5 Abstain: 0

   Committee Discussion: *A majority of committee members voted in favor of adding methylcobalamin to the 503A Bulks List. Members who voted "Yes" expressed concern with limiting access to care for patients who are treated by compounded formulations containing methylcobalamin for those uses being evaluated, particularly autism spectrum disorder (ASD). Members noted the high number of written submissions to the docket related to compounded formulations of this product. Other committee members stated there is not enough evidence that methylcobalamin is unsafe in compounded drugs.*

   Committee members who voted "No" agreed that there is a lack of scientific evidence establishing safety and effectiveness of compounded formulations containing methylcobalamin in the conditions evaluated. A few committee members stated that more studies need to be done and hope that this question can be addressed again when more data are available. One member stated that it is not always easy to discern adverse reactions in

patients already afflicted with diseases such as ASD. It was acknowledged that the vote on this question will not affect access to methylcobalamin commercially available as dietary supplements.

Please see the transcript for details of the Committee's discussion.

3. **VOTE:** FDA is proposing that choline chloride NOT be included on the 503A Bulks List. Should choline chloride be placed on the list?

   Vote Result: Yes: 2 No: 11 Abstain: 1

   Committee Discussion: *The majority of the committee members voted against placing choline chloride on the 503A Bulks List. The two committee members who voted for placing choline chloride on the 503A Bulks List expressed that the data and information presented did not convince them to vote against adding choline chloride on the 503A Bulks List. Those two committee members also stated concerns over taking away access to care for patients who are treated by compounded formulations containing choline chloride. One member stated their abstention was due to technical issues. Please see the transcript for details of the Committee's discussion.*

4. **VOTE:** FDA is proposing that oxitriptan for oral administration be INCLUDED on the 503A Bulks List. Should oxitriptan for oral administration be placed on the list?

   Vote Result: Yes: 11 No: 0 Abstain: 1

   Committee Discussion: *The majority of the committee agreed that oxitriptan for oral administration be included on the 503A Bulks List. One member stated their abstention was due to technical issues. Please see the transcript for details of the Committee's discussion.*

Question for PCAC Regarding Whether to Include an Entry on the Withdrawn or Removed List

5. **VOTE**: FDA is proposing that "Neomycin sulfate: All parenteral drug products containing neomycin sulfate (except when used for ophthalmic or otic use or in combination with polymyxin B sulfate for irrigation of the intact bladder)" be ADDED to the Withdrawn or Removed List under sections 503A and 503B of the FD&C Act. Do you agree?

   Vote Result: Yes: 12 No: 0 Abstain: 0

   Committee Discussion: *The committee unanimously agreed that all parenteral drug products containing neomycin sulfate (except when used for ophthalmic or otic use or in combination with polymyxin B sulfate for irrigation of the intact bladder) should be added to the Withdrawn or Removed list. Please see the transcript for details of the Committee's discussion.*

The meeting was adjourned at approximately 6:08 p.m. Eastern Time.