Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting
June 8, 2022

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 list of bulk drug substances that can be used to compound drug products in accordance with section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act), although they are neither the subject of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph nor components of FDA-approved drugs (503A Bulks List): ammonium tetrathiomolybdate, enclomiphene citrate, ferric subsulfate, and glutathione. 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**
Ammonium Tetrathiomolybdate	Wilson disease, use as copper (Cu) chelation therapy for the treatment of breast cancer, kidney cancer, prostate cancer, colorectal cancer, esophageal cancer, and malignant pleural mesothelioma.
Enclomiphene Citrate	To increase serum testosterone, luteinizing hormone (LH), and follicle-stimulating hormone (FSH) to normal levels in the treatment of secondary hypogonadism.
Ferric Subsulfate	For use as an astringent and hemostatic agent during minor surgical procedures.
Glutathione	Skin lightening, cystic fibrosis, asthma, chronic obstructive pulmonary disease, chronic lung disease, oxidative stress, reduction of the side effects of chemotherapy, inhibition of chemical induced carcinogenesis, prevention of radiation injury, treatment of heavy metal poisoning (cadmium and mercury), acetaminophen toxicity, autism spectrum disorder, Alzheimer's disease, Parkinson's disease, major depressive disorder, schizophrenia, helicobacter pylori infection, human immunodeficiency virus infection, tuberculosis, otitis media, peripheral obstructive arterial disease, anemia, diabetes, and septic shock.

The committee also discussed revisions FDA is considering to the list of drugs that have been withdrawn or removed from the market because such drug products or components of such drug products have been found to be unsafe or not effective (Withdrawn or Removed List). FDA now is considering whether to amend the rule to add one more entry to the list: "Lorcaserin Hydrochloride: All drug products containing lorcaserin hydrochloride." As previously explained in the Federal Register of July 2, 2014 (79 FR 37687), 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 on the list.

These summary minutes for the June 8, 2022 meeting of Pharmacy Compounding Advisory Committee (PCAC) of the Food and Drug Administration were approved on August 19, 2022.

I certify that I attended the June 8, 2022 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/
Allen J. Vaida, BSc, PharmD, FASHP
Acting Chairperson, PCAC

Final Summary Minutes of the Pharmacy Compounding Advisory Committee Meeting
June 8, 2022

The Pharmacy Compounding Advisory Committee (PCAC) of the Food and Drug Administration (FDA), Center for Drug Evaluation and Research met on June 8, 2022. The meeting presentations were heard, viewed, captioned, and recorded through an online teleconferencing platform. Prior to the meeting, the members and temporary members were provided the briefing materials from the FDA. The meeting was called to order by Allen J. Vaida, BSc, PharmD, FASHP (Acting Chairperson). The conflict of interest statement was read into the record by Takyiah Stevenson, PharmD (Designated Federal Officer). There were approximately 230 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 list of bulk drug substances that can be used to compound drug products in accordance with section 503A of the Federal Food, Drug, and Cosmetic Act (FD&C Act), although they are neither the subject of an applicable United States Pharmacopeia (USP) or National Formulary (NF) monograph nor components of FDA-approved drugs (503A Bulks List): ammonium tetrathiomolybdate, enclomiphene citrate, ferric subsulfate, and glutathione. 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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Hydrochloride: All drug products containing lorcaserin hydrochloride." As previously explained in the Federal Register of July 2, 2014 (79 FR 37687), 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 on the list.

Attendance:

PCAC Members Present (Voting): Robin H. Bogner, PhD; Timothy D. Fensky, RPh, DPh, FACA (National Association of Boards of Pharmacy Representative); Sandra J. Fusco-Walker (Consumer Representative); 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, CMQ; Brian Serumaga, PhD (United States Pharmacopeia Representative); Allen J. Vaida, BSc, PharmD, FASHP (Acting Chairperson)

PCAC Members Not Present (Voting): Seemal R. Desai, MD, FAAD**;** Padma Gulur, MD, FASA (Chairperson)

PCAC Member Present (Non-Voting): Michael D. Bui, DDS, MPH, JD (Industry Representative)

PCAC Member Not Present (Non-Voting): Gus Bassani, PharmD

Acting Industry Representative to the Committee (Non-Voting): Richard L. Green, BS Pharm, RPh, BCNP, FAPhA

Temporary Members (Voting): David N. Assis, MD (Ammonium Tetrathiomolybdate Topic Only); William J. Calhoun MD, FACP, FCCP, FAAAAI (Glutathione Topic Only), John N. Caviness, MD (Ammonium Tetrathiomolybdate Topic Only); Srinivasan Dasarathy, MD (Ammonium Tetrathiomolybdate Topic Only); Roger R. Dmochowski, MD, MMHC (Enclomiphene Citrate Topic Only); David L. Eisenberg, MD, MPH, FACOG (Ferric Subsulfate Topic Only); Scott E. Evans, MD, FCCP, ATSF (Glutathione Topic Only); Jorge A. Garcia, MD, FACP (Ammonium Tetrathiomolybdate Topic Only); Brian P. Green, DO, FAAD (Glutathione Topic Only); Vivian Lewis, MD, FACOG (Enclomiphene Citrate Topic Only); Michael K. Lindsay, MD, MPH (Ferric Subsulfate Topic Only); David J. Margolis, MD, PhD (Glutathione Topic Only); Jorge J. Nieva, MD (Ammonium Tetrathiomolybdate Topic Only)

FDA Participants (Non-Voting): Frances Gail Bormel, RPh, JD; Kathleen Anderson, PharmD; Gabrielle Cosel, MSc; Rosilend Lawson, VMD, JD; Lori Bickel, JD (Investigational New Drug/Expanded Access Presentation Only); Charles Ganley, MD; Daiva Shetty, MD; Emily Kneeream, PharmD (Glutathione Topic Only); Marianne San Antonio, DO (Lorcaserin Hydrochloride Topic Only); Raquel Tapia, MD (Ammonium Tetrathiomolybdate Topic Only);

Anam Tariq, DO, MHS (Ferric Subsulfate Topic Only); Madeline Wolfert, MD (Enclomiphene Citrate Topic Only)

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

Open Public Hearing Speakers:

- Enclomiphene Citrate (Topic 1) – No OPH speakers
- Glutathione (Topic 2): Paul Anderson, MD (American Association of Naturopathic Physicians (AANP))
- Ammonium Tetrathiomolybdate (Topic 3) – No OPH speakers
- Ferric Subsulfate (Topic 4) – No OPH speakers
- Lorcaserin Hydrochloride (Topic 5): Michael A. Carome, MD (Public Citizen); Nina Zeldes, PhD (National Center for Health Research)

The agenda was as follows:

June 8, 2022, AM Session

Call to Order	**Allen J. Vaida, BSc, PharmD, FASHP** Acting 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
FDA Investigational New Drug (IND)/Expanded Access Presentation	**Lori Bickel, JD** Regulatory Counsel Division of Medical Policy Development (DMPD) Office of Medical Policy (OMP), CDER, FDA

SECTION 503A BULK DRUG SUBSTANCES LIST – ENCLOMIPHENE CITRATE

FDA PRESENTATION	**Madeline Wolfert, MD** Physician Pharmacy Compounding Review Team Office of Specialty Medicine (OSM) Office of New Drugs (OND), CDER, FDA
Clarifying Questions from the Committee	
NOMINATOR PRESENTATIONS	**Marwa Elsaied, PharmD, RPh and Thomas Masterson III, MD** Empower Pharmacy

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

SECTION 503A BULK DRUG SUBSTANCES LIST – GLUTATHIONE

FDA PRESENTATION	**Emily Kneeream, PharmD** Clinical Analyst Pharmacy Compounding Review Team OSM, OND, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATION	**A.J. Day, PharmD** Professional Compounding Centers of America and National Community Pharmacists Association

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

LUNCH

June 8, 2022, PM Session

SECTION 503A BULK DRUG SUBSTANCES LIST – AMMONIUM TETRATHIOMOLYBDATE (ATTM)

FDA PRESENTATION	**Raquel Tapia, MD** Physician Pharmacy Compounding Review Team OSM, OND, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATION	**Mark Rosenberg, MD** Pharmacy Solutions

Clarifying Questions from the Committee

OPEN PUBLIC HEARING

COMMITTEE DISCUSSION AND VOTE

BREAK

SECTION 503A BULK DRUG SUBSTANCES LIST – FERRIC SUBSULFATE

FDA PRESENTATION	**Anam Tariq, DO, MHS** Physician Pharmacy Compounding Review Team OSM, OND, CDER, FDA

Clarifying Questions from the Committee

NOMINATOR PRESENTATION

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, MSc** Director Division of Compounding Policy and Outreach OCQC, OC, CDER, FDA

DRUGS TO BE CONSIDERED FOR THE WITHDRAWN OR REMOVED LIST – LORCASERIN HYDROCHLORIDE

FDA PRESENTATION	**Marianne San Antonio, DO** Physician Pharmacy Compounding Review Team OSM, 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 enclomiphene citrate NOT be included on the 503A Bulks List. Should enclomiphene citrate be placed on the list?

   Vote Result: Yes: 4 No: 8 Abstain: 0

   Committee Discussion: *The majority of the committee members voted against placing enclomiphene citrate on the 503A Bulks List. Several committee members who voted "No" noted lack of clinical efficacy evidence. One member stated that more studies need to be conducted.*

   One committee member who voted in favor of placing enclomiphene citrate on the 503A Bulks List stated that United States Pharmacopeia (USP) has a drug substance monograph for clomiphene citrate, a mixture that contains enclomiphene citrate. The member further stated that enough evidence was provided to show the drug substance can be physically and chemically characterized.

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

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

   Vote Result: Yes: 8 No: 5 Abstain: 1

   Committee Discussion: *A majority of committee members voted in favor of adding glutathione to the 503A Bulks List. Several committee members who voted "Yes" expressed concerns about patient access to compounded formulations containing glutathione. Several members stated that the data and information presented demonstrated that glutathione has physical and chemical stability. Other members stated there was no compelling evidence presented to show that there are safety concerns with compounded glutathione products. One committee member discussed evidence presented regarding effectiveness for some uses.*

   Several committee members who voted "No" stated that there is a lack of scientific evidence establishing effectiveness of compounded formulations containing glutathione for the conditions evaluated. Several members stated that more studies need to be conducted. One member stated that glutathione has been used for a wide range of indications without clear evidence of effectiveness despite well-established alternate therapies for those indications.

   The committee member who voted "Abstain," stated that the mixed evidence of effectiveness, in light of the variety of indications under review, was not convincing enough to vote for or against adding glutathione to the 503A Bulks List.

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

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

   Vote Result: Yes: 2 No: 13 Abstain: 0

   Committee Discussion: *The majority of the committee members voted against placing ammonium tetrathiomolybdate (ATTM) on the 503A Bulks List. Committee members who voted "No" agreed that there is a lack of scientific evidence regarding safety and effectiveness of compounded formulations containing ATTM in the conditions evaluated. Several committee members stated that clinical trials with larger patient populations and better monitoring for adverse effects need to be done.*

   The committee members who voted "Yes" noted concerns regarding patient access to compounded formulations containing ATTM for neurological disorders.

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

4. **VOTE:** FDA is proposing that ferric subsulfate solid or powder NOT be included on the 503A Bulks List. Should ferric subsulfate solid or powder be placed on the list?

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

   Committee Discussion: *The committee unanimously agreed that ferric subsulfate solid or powder should not be included on the 503A Bulks List. The committee members stated the data presented regarding the chemical characterization of ferric subsulfate solid or powder showed that the drug substance is not well characterized. Additionally, a couple of committee members acknowledged that there is a USP drug product monograph for ferric subsulfate solution. Please see the transcript for details of the Committee's discussion.*

Questions for PCAC Regarding Whether to Include Certain Entries on the Withdrawn and Removed List

5. **VOTE:** FDA is proposing that "Lorcaserin hydrochloride: All drug products containing lorcaserin hydrochloride" be ADDED to the Withdrawn or Removed List under sections 503A and 503B of the FD&C Act. Do you agree?

   Vote Result: Yes: 10 No: 0 Abstain: 0

   Committee Discussion: *The committee unanimously agreed that an entry for "Lorcaserin Hydrochloride: All drug products containing lorcaserin hydrochloride" should be added to the Withdrawn or Removed List based on safety concerns. Please see the transcript for details of the Committee's discussion.*

The meeting was adjourned at approximately 5:15 p.m.