CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

210875Orig1s000

OTHER REVIEW(S)

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:	May 19, 2020
Requesting Office or Division:	Division of Neurology 1 (DN 1)
Application Type and Number:	NDA 210875
Product Name and Strength:	Kynmobi (apomorphine hydrochloride) film, 10 mg, 15 mg, 20 mg, 25 mg and 30 mg
Applicant/Sponsor Name:	Sunovion Pharmaceuticals Inc
OSE RCM #:	2019-2408-1
DMEPA Safety Evaluator:	Ebony Whaley, PharmD, BCPPS
DMEPA Team Leader:	Lolita White, PharmD

1 PURPOSE OF MEMORANDUM

The Applicant submitted revised carton labeling, Instructions for Use (IFU), and Integrated IFU received on May 18, 2020 for Kynmobi. The Division of Neurology 1 (DN 1) requested that we review the revised carton labeling, IFU, and Integrated IFU for Kynmobi (Appendix A) to determine if they are 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 Applicant implemented our recommendations and we have no additional recommendations at this time.

10 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

[a] Whaley E. Human Factors Study Results and Label and Labeling Review for Kynmobi (NDA 210875). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 APR 20. RCM No.: 2019-2407 and 2019-2408.

This is a representation of an electronic record that was signed electronically. Following this are manifestations of any and all electronic signatures for this electronic record.

/s/

EBONY A WHALEY
05/19/2020 12:01:41 PM

LOLITA G WHITE
05/19/2020 12:28:48 PM

Memorandum

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS

Date: May 13, 2020

From: Interdisciplinary Review Team for Cardiac Safety Studies

Through: Christine Garnett, PharmD
Clinical Analyst
DCN

To: Jack Dan, RPM
DN1

Subject: QT Consult to NDA 210875 (SDN 044)

Note: Any text in the review with a light background should be inferred as copied from the sponsor's document.

This memo responds to your consult to us dated 5/11/2020 regarding the sponsor's QT related language in the proposed product label. We reviewed the following materials:

- Previous IRT reviews for NDA 210875 dated 09/25/2018 in DARRTS;
- Previous IRT reviews for NDA 21264 dated 07/09/2019 in DARRTS; and
- Proposed label (Submission 0044).

1 Responses for the Division

During our review of the TQT study (CTH-201), we found the results to be inconclusive and cannot be used to exclude a 10-ms mean increase in the QTc interval at the maximum recommended dose of 35 mg (QT-IRT review dated 09/25/2018 in DARRTS). The maximum therapeutic exposure in the current submission is comparable to that in the previous submission. Therefore, we disagree with the sponsor's proposed QT-related language in Section 12.2:

12 CLINICAL PHARMACOLOGY

12.2 Pharmacodynamics

Cardiac Electrophysiology

(b) (4)

One of the major issues with the TQT study was that the selected doses did not cover the exposures associated with clinical dosing regimen. The final dose levels were achieved through individual titrations based on tolerability rather than by randomized treatment assignment. The higher dose groups did not result in higher exposures compared to lower dose groups as would have been expected with linear PK. The mean Cmax across dose levels is ~4 ng/mL, which is inadequate to cover Cmax of the maximum recommended therapeutic dose of 30 mg (~9 ng/ml) [based on Clinical Pharmacology review in DARRTS dated 05/02/2020] that is being considered in the current resubmission. Furthermore, higher exposures are expected in patients with renal impairment (50% higher Cmax with renal impairment). Note that there were too few patients receiving 15 mg and doses above 20 mg (2 for 25 mg, 3 for 35 mg and 1 for 50 mg) to be able to adequately characterize the change in QTc interval at those dose levels.

We note that the RLD, APOKYN, was shown to prolong the QTc interval in a TQT study (see QT-IRT review under NDA 21264 dated 07/09/2019 in DARRTS) and has Warning and Precautions for QT Prolongation in the label. Even though a positive exposure-response was observed in the TQT study submitted under NDA 21264, ΔΔQTc at a given concentration may not be well predicted. Therefore, we cannot use TQT study submitted under APOKYN to exclude a small effect for KYNMOBI.

Thank you for requesting our input into the development of this product. We welcome more discussion with you now and in the future. Please feel free to contact us via email at cderdcrpqt@fda.hhs.gov

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