HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use KYNMOBI safely and effectively. See full prescribing information for KYNMOBI.

KYNMOBI™ (apomorphine hydrochloride) sublingual film
Initial U.S. Approval: 2004

INDICATIONS AND USAGE

KYNMOBI is a non-ergoline dopamine agonist indicated for the acute, intermittent treatment of "off" episodes in patients with Parkinson's disease (1)

DOSAGE AND ADMINISTRATION

- For sublingual administration only (2.1)
- Dose initiation should be supervised by a healthcare provider (2.1, 2.3)
- Treatment with a concomitant antiemetic, e.g. trimethobenzamide, is recommended, beginning 3 days prior to initial dose of KYNMOBI (2.1, 5.1)
- The dose range for KYNMOBI is 10 mg to 30 mg per dose, administered sublingually, as needed (2.2)
- KYNMOBI doses should be separated by at least 2 hours (2.2)
- Maximum of 5 doses per day; maximum single dose is 30 mg (2.2, 2.3)

DOSAGE FORMS AND STRENGTHS

KYNMOBI sublingual film: 10 mg, 15 mg, 20 mg, 25 mg, and 30 mg of apomorphine hydrochloride (3, 16)

CONTRAINDICATIONS

- Concomitant use of KYNMOBI with 5HT3 antagonists (4)
- Hypersensitivity to apomorphine or any of its ingredients including sodium metabisulfite (4)

WARNINGS AND PRECAUTIONS

- Nausea and vomiting may occur (2.1, 5.1)
- Falling asleep during activities of daily living and daytime somnolence may occur, discontinue KYNMOBI if occurs (5.2)
- Syncope and hypotension/orthostatic hypotension may occur, monitor blood pressure (5.3)
- Oral mucosal irritation may occur, which may require pausing or discontinuing treatment (5.4)
- Falls may occur, or increase (5.6)
- May cause hallucinations and psychotic-like behavior (5.7)
- May cause impulse control and impulsive behaviors; consider dose reduction or discontinuing KYNMOBI if occurs (5.8)
- Withdrawal-emergent hyperpyrexia and confusion may occur with rapid dose reduction or withdrawal (5.9)
- May prolong QTc and cause torsades de pointes or sudden death; consider risk factors prior to initiation (5.10)

ADVERSE REACTIONS

Most common adverse reactions (incidence at least 10% in patients treated with KYNMOBI and with an incidence greater than placebo) were nausea, oral/pharyngeal soft tissue swelling, oral/pharyngeal soft tissue pain and paraesthesia, dizziness, and somnolence (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact Sunovion Pharmaceuticals Inc. at 1-877-737-7226 or FDA at 1-800-FDA-1088 or *www.fda.gov/medwatch*.

DRUG INTERACTIONS

- Concomitant use of antihypertensive medications and vasodilators may increase risk for hypotension, myocardial infarction, falls and injuries (7.2)
- Dopamine antagonists may diminish the effectiveness of KYNMOBI (7.4)

USE IN SPECIFIC POPULATIONS

- Pregnancy: Based on animal data, may cause fetal harm (8.1)

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 5/2020

FULL PRESCRIBING INFORMATION: CONTENTS*

***Sections or subsections omitted from the full prescribing information are not listed.**

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

KYNMOBI is indicated for the acute, intermittent treatment of "off" episodes in patients with Parkinson's disease (PD).

2 DOSAGE AND ADMINISTRATION

2.1 Important Administration Instructions

Dose initiation should be supervised by a healthcare provider *[see Dosage and Administration (2.3)]*.

KYNMOBI must be administered whole. Do not to cut, chew, or swallow KYNMOBI. KYNMOBI will disintegrate in about 3 minutes.

Because of the high incidence of nausea and vomiting with KYNMOBI when administered at recommended doses, an antiemetic (e.g., trimethobenzamide 300 mg three times a day), beginning 3 days prior to the initial dose of KYNMOBI, is recommended. Treatment with the antiemetic should only be continued as long as necessary to control nausea and vomiting, and generally no longer than two months after initiation of treatment with KYNMOBI *[see Contraindications (4) and Warnings and Precautions (5.1)]*.

Based on reports of profound hypotension and loss of consciousness when apomorphine was administered with ondansetron, the concomitant use of apomorphine with drugs of the 5HT3 antagonist class including antiemetics (for example, ondansetron, granisetron, dolasetron, palonosetron) and alosetron are contraindicated *[see Contraindications (4)]*.

2.2 Dosing Information

The dose range for KYNMOBI is 10 mg to 30 mg per dose, administered sublingually, as needed, for the acute, intermittent treatment of "off" episodes.

Doses should be separated by at least 2 hours. If a single dose of KYNMOBI is ineffective for a particular "off" episode, a second dose should not be given for that "off" episode. The efficacy or safety of administering a second dose for a single "off" episode has not been studied.

Do not administer more than 5 doses per day.

The maximum single dose of KYNMOBI is 30 mg.

2.3 Dose Titration

The initial dose is 10 mg. Dose initiation should occur when the patient is in an "off" state and in a setting where a healthcare provider can monitor blood pressure and pulse. In clinical studies of KYNMOBI, the "off" state was achieved by instructing patients to not take their regular morning dose of carbidopa/levodopa or any other adjunctive Parkinson's disease medications, and to take their last dose of carbidopa/levodopa and any other adjunctive Parkinson's disease medications no later than midnight the night before *[see Clinical Studies (14)]*.

If the patient tolerates the 10 mg dose, and responds adequately, the starting dose should be 10 mg, used on an as needed basis, up to 5 times per day, to treat “off” episodes. If the dose is tolerated but the response is insufficient, the patient’s usual Parkinson’s disease medications should be resumed and up-titration with KYNMOBI continued generally within 3 days. Increase dosage by increments of 5 mg and assess response. Continue to titrate in a similar manner, under the supervision of a healthcare provider, until an effective and tolerable dose is achieved *[see Dosage and Administration (2.2) and Clinical Studies (14)]*.

3 DOSAGE FORMS AND STRENGTHS

KYNMOBI sublingual film is a blue to green rectangular film with a white printed number identifying the strength (e.g., “10” is 10 mg). KYNMOBI comes in dosage strengths of 10 mg, 15 mg, 20 mg, 25 mg, and 30 mg. Each sublingual film is individually packaged in a sealed foil pouch.

4 CONTRAINDICATIONS

KYNMOBI is contraindicated in patients:

- Using concomitant 5HT3 antagonists, including antiemetics (e.g., ondansetron, granisetron, dolasetron, palonosetron) and alosetron *[see Drug Interactions (7.1)]*. There have been reports of profound hypotension and loss of consciousness when subcutaneous apomorphine was administered with a 5HT3 antagonist.
- With hypersensitivity/allergic reaction to apomorphine or to any of the ingredients of KYNMOBI. Angioedema or anaphylaxis may occur *[see Warnings and Precautions (5.3)]*.

5 WARNINGS AND PRECAUTIONS

5.1 Nausea and Vomiting

KYNMOBI may cause nausea and vomiting when administered at recommended doses. Because of the high incidence of nausea and vomiting with KYNMOBI when administered at recommended doses, an antiemetic, e.g., trimethobenzamide 300 mg three times a day, is recommended beginning 3 days prior to the initial dose of KYNMOBI. Treatment with the antiemetic should only be continued as long as necessary to control nausea and vomiting, and generally no longer than two months after initiation of treatment with KYNMOBI *[see Dosage and Administration (2.1)]*.

In Study 1 *[see Clinical Studies (14)]*, treatment with an antiemetic (i.e., trimethobenzamide hydrochloride; 300 mg by mouth three times daily) was required beginning 3 days before starting KYNMOBI; however, it could be discontinued during the maintenance phase. During the titration phase of Study 1, nausea was reported as an adverse reaction by 21% of patients treated with KYNMOBI, while vomiting was reported as an adverse reaction by 4% of patients treated with KYNMOBI. During the maintenance phase of Study 1, nausea was reported as an adverse reaction by 28% of patients treated with KYNMOBI, compared with 4 % of patients who

received placebo. During the maintenance phase of Study 1, vomiting was reported as an adverse reaction by 7% of patients treated with KYNMOBI, compared with 0 % of patients who received placebo. Nausea or vomiting was the reason for withdrawal from the study in 2% of patients treated with KYNMOBI during the titration phase and 2% of patients treated with KYNMOBI during the maintenance phase.

Concomitantly administered antiemetic drugs other than trimethobenzamide have not been studied. 5HT3 antagonist antiemetics are contraindicated *[see Contraindications (4)]*. Antiemetics with anti-dopaminergic actions (e.g., haloperidol, chlorpromazine, promethazine, prochlorperazine, metoclopramide) have the potential to worsen symptoms in patients with Parkinson's disease and should be avoided *[see Drug Interactions (7.4)]*.

5.2 Falling Asleep During Activities of Daily Living and Somnolence

Patients treated with dopaminergic medications, including apomorphine, have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles, which sometimes has resulted in accidents. Patients may not perceive warning signs, such as excessive drowsiness, or they may report feeling alert immediately prior to the event.

During the titration phase of Study 1, somnolence was reported as an adverse reaction in 11% of patients treated with KYNMOBI. During the maintenance phase of Study 1, somnolence was reported as an adverse reaction in 13% of patients treated with KYNMOBI, compared with 2% of patients who received placebo.

Prescribers should reassess patients for drowsiness or sleepiness, especially since some of the events occur well after the start of treatment. Prescribers should also be aware that patients may not acknowledge drowsiness or sleepiness until directly questioned about drowsiness or sleepiness during specific activities.

Before initiating treatment with KYNMOBI, advise patients of the risk of drowsiness and ask them about factors that could increase the risk with KYNMOBI, such as concomitant sedating medications and the presence of sleep disorders. If a patient develops significant daytime sleepiness or falls asleep during activities that require active participation (e.g., conversations, eating, etc.), KYNMOBI should ordinarily be discontinued. If a decision is made to continue KYNMOBI, patients should be advised not to drive and to avoid other potentially dangerous activities. There is insufficient information to determine whether dose reduction will eliminate episodes of falling asleep while engaged in activities of daily living.

5.3 Hypersensitivity

Oral soft tissue swelling (lips, tongue, gingiva, and mouth) was reported as adverse reaction in 15% of patients treated with KYNMOBI during the maintenance phase of Study 1, compared with 0% of patients who received placebo; 11% of patients discontinued KYNMOBI because of this event.

Swelling of the face, oral allergy syndrome, hypersensitivity, or urticaria were reported as an adverse reaction in 6% of patients treated with KYNMOBI during the maintenance phase of Study 1, compared with 0% of patients who received placebo; 4% of patients discontinued KYNMOBI because of this event.

It is not known whether these events are related to apomorphine, sodium metabisulfite, or another KYNMOBI excipient.

KYNMOBI rechallenge is not generally recommended after discontinuation as oral adverse reactions may recur and may be more severe than the initial reaction.

Sulfite Sensitivity

KYNMOBI contains sodium metabisulfite, a sulfite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

5.4 Syncope / Hypotension / Orthostatic Hypotension

KYNMOBI may cause syncope, hypotension, or orthostatic hypotension. During the titration phase of Study 1, syncope, pre-syncope, hypotension, or orthostatic hypotension were reported as adverse reactions in 4% of patients. During the maintenance phase of Study 1, syncope, pre-syncope, hypotension, or orthostatic hypotension were reported as adverse reactions in 2% of patients treated with KYNMOBI, compared with 0% of patients who received placebo.

During the maintenance phase of Study 1, systolic orthostatic hypotension (reduction of 20 mmHg or more in standing minus supine/sitting systolic blood pressure) or diastolic hypotension (10 mmHg or more for standing minus supine/sitting diastolic blood pressure) occurred in 43% of patients treated with KYNMOBI, and in 36% of patients who received placebo.

Patients treated with KYNMOBI should receive an assessment for hypotension / orthostatic hypotension, especially if they have a history of hypotension or cardiovascular disease, or if they are currently using antihypertensive medication. Inform patients of the risk of orthostatic hypotension.

The hypotensive effects of KYNMOBI may be increased by the concomitant use of alcohol, antihypertensive medications, and vasodilators (especially nitrates). Patients should avoid alcohol when using KYNMOBI *[see Drug Interactions (7.3), Clinical Pharmacology (12.3)]*. Patients taking KYNMOBI should lie down before and after taking sublingual nitroglycerin *[see Drug Interactions (7.2), Clinical Pharmacology (12.3)]*.

Monitor patients taking concomitant antihypertensive medications for hypotension and orthostatic hypotension *[see Drug Interactions (7.2, 7.3)]*.

5.5 Oral Mucosal Irritation

During the titration phase of Study 1, oral mucosal ulceration or stomatitis were reported as adverse reactions in 2% of patients treated with KYNMOBI. During the maintenance phase of Study 1, oral mucosal ulceration or stomatitis were reported as adverse reactions in 7% of patients treated with KYNMOBI, compared with 0% of patients who received placebo *[see Adverse Reactions (6.1)]*.

During the titration of Study 1, oral soft tissue pain or paresthesia were reported as adverse reactions in 2% of patients treated with KYNMOBI. During the maintenance phase of Study 1,

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