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 KYNOBI if this occurs (5.2)
- Syncope and hypotension/orthostatic hypotension may occur; monitor blood pressure (5.4)
- Oral mucosal irritation may occur, which may require pausing or discontinuing treatment (5.5)
- 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 KYNOBI if this 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 KYNOBI 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)

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 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 KYNOBI (2.1, 5.1)

The dose range for KYNOBI is 10 mg to 30 mg per dose, administered sublingually, as needed (2.2)

KYNOBI 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 should be separated by at least 2 hours. If a single dose of KYNOBI is ineffective for a particular “off” episode, a second dose should not be given (2.2)

Doses should be separated by at least 2 hours. If a single dose of KYNOBI 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 (2.2)

Do not administer more than 5 doses per day. The maximum single dose of KYNOBI 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 KYMOBI, the “off” state was achieved by instructing patients not to 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 could be resumed and titration with KYMOBI 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

KYMOBI sublingual film is a blue to green rectangular film with a white printed number identifying the strength (e.g., “10” is 10 mg). KYMOBI 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

KYMOBI is contraindicated in patients:

- Using concomitant SHT3 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 SHT3 antagonist.
- With hypersensitivity/allergic reaction to apomorphine or to any of the ingredients of KYMOBI. Angioedema or anaphylaxis may occur [see Warnings and Precautions (5.3)].

5 WARNINGS AND PRECAUTIONS

5.1 Nausea and Vomiting

KYMOBI may cause nausea and vomiting when administered at recommended doses. Because of the high incidence of nausea and vomiting with KYMOBI when administered at recommended doses, an antieptic, e.g., trimethobenzamide 300 mg three times a day, is recommended beginning 3 days prior to the initial dose of KYMOBI. Treatment with the antieptic should only be continued as long as necessary to control nausea and vomiting, and generally no longer than 2 months after initiation of treatment with KYMOBI [see Dosage and Administration (2.1)].

In Study 1 [see Clinical Studies (14)], treatment with an antieptic (e.g., trimethobenzamide hydrochloride; 300 mg by mouth three times daily) was required beginning 3 days before starting KYMOBI; 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 KYMOBI, while vomiting was reported as an adverse reaction by 4% of patients treated with KYMOBI. During the maintenance phase of Study 1, nausea was reported as an adverse reaction by 28% of patients treated with KYMOBI, 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 KYMOBI, 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 KYMOBI during the titration phase and 2% of patients treated with KYMOBI during the maintenance phase.

Concomitantly administered antieptic drugs other than trimethobenzamide have not been studied. SHT3 antagonist antieptics are contraindicated [see Contraindications (4)]. Antieptics with anti-dopaminergic actions (e.g., biperiden, clozapramine, 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 tired 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 KYMOBI. During the maintenance phase of Study 1, somnolence was reported as an adverse reaction in 13% of patients treated with KYMOBI, 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 KYMOBI, advise patients of the risk of drowsiness and ask them about factors that could increase the risk with KYMOBI, 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.), KYMOBI should be discontinued. If a decision is made to continue KYMOBI, 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 an adverse reaction in 15% of patients treated with KYMOBI during the maintenance phase of Study 1, compared with 0% of patients who received placebo; 11% of patients discontinued KYMOBI because of this event. Swelling of the face, oral allergy syndrome, hypersensitivity, or urticaria were reported as adverse reactions in 6% of patients treated with KYMOBI during the maintenance phase of Study 1, compared with 0% of patients who received placebo; 4% of patients discontinued KYMOBI because of this event.

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

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

Sulfite Sensitivity

KYMOBI 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

KYMOBI 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 KYMOBI, compared with 0% of patients who received placebo. Patients treated with KYMOBI 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 KYMOBI may be increased by the concomitant use of alcohol, antihypertensive medications, and vasodilators (especially nitrate). Patients should avoid alcohol when using KYMOBI [see Drug Interactions (7.3), Clinical Pharmacology (12.3)]. Patients taking KYMOBI 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/or 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 KYMOBI. During the maintenance phase of Study 1, oral mucosal ulceration or stomatitis were reported as adverse reactions in 7% of patients treated with KYMOBI, compared with 0% of patients who received placebo [see Adverse Reactions (6.1)].

During the titration phase of Study 1, oral soft tissue pain or paresthesia were reported as adverse reactions in 2% of patients treated with KYMOBI. During the maintenance phase of Study 1, oral soft tissue pain or paresthesia were reported as adverse reactions in 13% of patients treated with KYMOBI, compared with 2% of patients who received placebo. In general, oral mucosal irritation reactions were mild to moderate in severity, and usually resolved with treatment discontinuation.
KYMNOMI rechallenge is not generally recommended after discontinuation as oral adverse reactions may recur and be more severe than the initial reaction. Hypersensitivity adverse reactions may also occur during treatment with KYMNOMI [see Warnings and Precautions (5.3)].

5.6 Falls

Patients with Parkinson’s disease are at risk of falling because of underlying postural instability, possible autonomic instability, and syncope caused by the blood pressure-lowering effects of the drugs used to treat Parkinson’s disease [see Clinical Pharmacology (12.2)]. KYMNOMI might increase the risk of falling by simultaneously lowering blood pressure and altering mobility [see Warnings and Precautions (5.4)]. During the titration period of Study 1, falls were reported as an adverse reaction in 4% of patients treated with KYMNOMI. During the maintenance period of Study 1, falls were reported as an adverse reaction in 6% of patients treated with KYMNOMI, compared with 2% of patients who received placebo.

5.7 Hallucinations/Psychotic-Like Behavior

During the maintenance phase of Study 1, hallucinations, delusions, disorientation, or confusion were reported as adverse reactions in 6% of patients treated with KYMNOMI, compared with 2% of patients who received placebo. No patient developed hallucinations or psychotic-like behavior during the titration phase.

A total of 4% of patients treated with KYMNOMI discontinued treatment because of disorientation, confusional state, or delusions, compared with 2% of patients who received placebo. Postmarketing reports with subcutaneous apomorphine indicate that patients may experience new or worsening mental status and behavioral changes, which may be severe, including psychotic-like behavior after starting or increasing the dose of apomorphine. Other drugs prescribed to improve the symptoms of Parkinson’s disease can have similar effects on thinking and behavior. This abnormal thinking and behavior can consist of one or more of a variety of manifestations, including paranoid ideation, delusions, hallucinations, confusion, disorientation, aggressive behavior, agitation, and delirium.

Patients with a major psychotic disorder should ordinarily not be treated with apomorphine because of the risk of exacerbating psychosis. In addition, certain medications used to treat psychosis may exacerbate the symptoms of Parkinson’s disease and may decrease the effectiveness of KYMNOMI [see Drug Interactions (7.4)].

5.8 Impulse Control/Compulsive Behaviors

Case reports suggest that patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money uncontrollably, and other intense urges and the inability to control these urges while taking one or more medications, including KYMNOMI, that increase central dopaminergic tone. In some cases, although not all, these urges were reported to have stopped when the dose was reduced, or the medication was discontinued. Because patients may not recognize these behaviors as abnormal, it is important for prescribers to spend time with patients or their caregivers about the development of new or increased gambling urges, sexual urges, uncontrolled spending, binge eating or other urges while being treated with KYMNOMI. Physicians should consider dose reduction or stopping the medication if a patient develops such urges while taking KYMNOMI.

5.9 Withdrawal-Emergent Hyperpyrexia and Confusion

A symptom complex resembling the neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, elevated serum creatine kinase, and autonomic instability), with no other obvious etiology, has been reported in association with rapid dose reduction, withdrawal of, or changes in antiparkinsonian therapy.

5.10 QTc Prolongation and Potential for Proarrhythmic Effects

At exposures achieved with therapeutic doses of subcutaneous apomorphine, a dose-related prolongation of QTc has been observed [see Clinical Pharmacology (12.2)]. Although the extent of the exposure and the Cmax of apomorphine are lower following the maximum recommended dose of KYMNOMI (30 mg) than following the maximum recommended dose of subcutaneous apomorphine (6 mg), QTc prolongation with KYMNOMI cannot be excluded.

Drugs that prolong the QTc interval have been associated with torsades de pointes and sudden death. The relationship of QTc prolongation to torsades de pointes is clearer for larger increases (20 msec and greater), but it is possible that smaller QTc prolongations may also increase risk, or increase in susceptible individuals, such as those with hypokalemia, hypomagnesemia, bradycardia, concomitant use of other drugs that prolong the QTc interval, or genetic predisposition (e.g., congenital prolongation of the QT interval). Although torsades de pointes has not been observed in association with the use of KYMNOMI at recommended doses in clinical studies, experience is too limited to rule out an increased risk. Palpitations and syncope may signal the occurrence of an episode of torsades de pointes.

The risks and benefits of KYMNOMI treatment should be considered prior to initiating treatment with KYMNOMI in patients with risk factors for prolonged QTc.

5.11 Fibrotic Complications

Cases of retroperitoneal fibrosis, pulmonary infiltrates, pleural effusion, pleural thickening, and cardiac valvulopathy have been reported in some patients treated with ergot-derived dopaminergic agents. While these complications may resolve when the drug is discontinued, complete resolution does not always occur. Although these adverse reactions are believed to be related to the ergoline structure of these dopamine agonists, whether another, non-ergot-derived dopamine agonists, such as KYMNOMI, can cause these reactions is unknown.

5.12 Priapism

Apomorphine may cause prolonged painful erections in some patients. Severe priapism may require surgical intervention.

5.13 Retinal Pathology in Albino Rats

In a 2-year carcinogenicity study of apomorphine in albino rat, retinal atrophy was detected at all subcutaneous doses tested (up to 0.8 mg/kg/day or 2 mg/kg/day in males or females, respectively). Retinal atrophy/degeneration has been observed in albino rats treated with other dopamine agonists for prolonged periods (generally during 2-year carcinogenicity studies). Retinal findings were not observed in a 39-week subcutaneous toxicity study of apomorphine in monkey at doses up to 1.5 mg/kg/day. The clinical significance of the finding in the albino rat cannot be disregarded because disruption of a mechanism that is universally present in vertebrates (e.g., disk shedding) may be involved.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed in more detail in the Warnings and Precautions section of labeling:

• Nausea and Vomiting [see Warnings and Precautions (5.1)]
• Falling Asleep During Activities of Daily Living and Somnolence [see Warnings and Precautions (5.2)]
• Hypersensitivity [see Warnings and Precautions (5.3)]
• Syncope/Hypotension/Orthostatic Hypotension [see Warnings and Precautions (5.4)]
• Oral Mucosal Irritation [see Warnings and Precautions (5.5)]
• Falls [see Warnings and Precautions (5.6)]
• Hallucinations/Psychotic Behavior [see Warnings and Precautions (5.7)]
• Impulse Control/Compulsive Behaviors [see Warnings and Precautions (5.8)]
• Withdrawal-Emergent Hyperpyrexia and Confusion [see Warnings and Precautions (5.9)]
• QTc Prolongation and Potential for Proarrhythmic Effects [see Warnings and Precautions (5.10)]
• Fibrotic Complications [see Warnings and Precautions (5.11)]
• Priapism [see Warnings and Precautions (5.12)]
• Retinal Pathology in Albino Rats [see Warnings and Precautions (5.13)]

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to the rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

KYMNOMI safety data presented below is derived from a randomized, double-blind, placebo-controlled study in patients with Parkinson’s disease (Study 1) [see Clinical Studies (14)]. Study 1 included a titration phase, in which 141 patients received at least one dose of KYMNOMI, followed by a placebo-controlled 12-week maintenance phase. The mean age of patients in Study 1 was 63 years (range 43 to 86 years); 63% of patients were male, and 93% were Caucasian.

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

Adverse reactions led to discontinuation of KYMNOMI in 9% of patients in the titration phase, and 28% of patients in the maintenance phase, compared with 7% of patients on placebo (in the maintenance phase).

The most common adverse reactions leading to discontinuation during the maintenance phase were oral/pharyngeal soft tissue swelling, oral mucosal erythema, and nausea/vomiting.

Table 1 presents the adverse reactions that occurred in at least 5% of patients treated with KYMNOMI during the maintenance phase of Study 1, and with an incidence greater than in patients who received placebo.
Table 1: Adverse Reactions Reported by at Least 5% of Patients Treated with KYNMOBI during the Maintenance Phase of Study 1, and with an Incidence Greater Than Placebo

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Titration KYNMOBI (N=141)</th>
<th>Maintenance KYNMOBI (N=54)</th>
<th>Placebo (N=55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>21</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>Oral/pharyngeal soft tissue swelling1</td>
<td>1</td>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>Oral/pharyngeal soft tissue pain and paraesthesia2</td>
<td>2</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Oral ulceration and stomatitis3</td>
<td>2</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Oral mucosal erythema</td>
<td>4</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Vomiting</td>
<td>4</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Dry mouth</td>
<td>1</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Nervous system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Somnolence</td>
<td>11</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Dizziness</td>
<td>11</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>8</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Respiratory, thoracic, and mediasternal disorders</td>
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<td></td>
</tr>
<tr>
<td>Rhinorrhea</td>
<td>6</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>General disorders and administration site conditions</td>
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<td></td>
</tr>
<tr>
<td>Fatigue</td>
<td>3</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Injury, poisoning, and procedural complications</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fall</td>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Laceration</td>
<td>1</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Skin and subcutaneous tissue disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hyperhidrosis</td>
<td>4</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Immune system disorders</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypersensitivity4</td>
<td>0</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

1 Includes lip swelling, lip edema, oropharyngeal swelling, gingival edema, edema mouth, swollen tongue, and pharyngeal edema
2 Includes throat irritation, glossodynia, oral pain, oral paresthesia, oropharyngeal pain, gingival pain, and oral hypoesthesia
3 Includes lip ulceration, oral mucosal blisters, stomatitis, cheilitis, and tongue ulceration
4 Includes hypersensitivity, swelling face, oral allergy syndrome and urticaria

Less Common Adverse Reactions

Other adverse reactions, including hallucinations, delusions, and impulse control disorder, have been reported in patients treated with KYNMOBI [see Warnings and Precautions (5.7, 5.8)]. Vital Sign Changes

Blood Pressure

Decreases in blood pressure have been observed in patients treated with KYNMOBI. During the titration phase of Study 1, syncope, pre-syncope, hypotension, or orthostatic hypotension were reported as adverse reactions in 4% of patients treated with KYNMOBI. 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 [see Warnings and Precautions (5.4) and Clinical Pharmacology (12.2)].

7 DRUG INTERACTIONS

7.1 SHT3 Antagonists

Based on reports of profound hypotension and loss of consciousness when subcutaneous apomorphine was administered with ondansetron, the concomitant use of KYNMOBI with SHT3 antagonists, including antiemetics (e.g., ondansetron, granisetron, palonosetron) and alosetron, is contraindicated [see Warnings and Precautions (5.4)].

7.2 Antihyperensive Medications and Vasodilators

In a study of healthy subjects, concomitant administration of 0.4 mg sublingual nitroglycerin with subcutaneous apomorphine caused greater decreases in blood pressure than with subcutaneous apomorphine alone [see Clinical Pharmacology (12.3)]. Patients taking KYNMOBI should lie down before and after taking sublingual nitroglycerin [see Warnings and Precautions (5.4)].

7.3 Alcohol

In a study of healthy subjects, concomitant administration of high-dose (0.6 g/kg) or low-dose (0.3 g/kg) ethanol with subcutaneous apomorphine caused greater decreases in blood pressure than with subcutaneous apomorphine alone [see Clinical Pharmacology (12.3)]. Patients should avoid drinking alcohol after using KYNMOBI [see Warnings and Precautions (5.4)].

7.4 Dopamine Antagonists

Since KYNMOBI is a dopamine agonist, it is possible that concomitant use of dopamine antagonists, such as the neuroleptics (e.g., phenothiazines, butyrophenones, thioxanthines) or metoclopramide, may diminish the effectiveness of KYNMOBI. Antiemetics with anti-dopaminergic action should be avoided [see Warnings and Precautions (5.1)]. Patients with major psychotic disorders receiving neuroleptics should be treated with dopamine agonists only if the potential benefits outweigh the risks [see Warnings and Precautions (6.7)].

7.5 Drugs Prolonging the QT/QTc Interval

Caution should be exercised when prescribing KYNMOBI concomitantly with drugs that prolong the QT/QTc interval [see Warnings and Precautions (5.10) and Clinical Pharmacology (12.3)].

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate data on the developmental risk associated with use of KYNMOBI in pregnant women. In animal reproduction studies, apomorphine had adverse developmental effects in rats (increased neonatal deaths) and rabbits (increased incidence of malformation) when administered during pregnancy at clinically relevant doses. These doses were also associated with maternal toxicity [see Data]. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. The background risk of major birth defects and miscarriage for the indicated population is unknown.

Data

Animal Data

No adverse developmental effects were observed when apomorphine (0.3, 1, or 3 mg/kg/day) was administered by subcutaneous injection to pregnant rats throughout organogenesis. Administration of apomorphine (0.3, 1, or 3 mg/kg/day) by subcutaneous injection to pregnant rabbits throughout organogenesis resulted in an increased incidence of malformations of the heart and/or great vessels at the mid and high doses; maternal toxicity was observed at the highest dose tested. Apomorphine (0.3, 1, or 3 mg/kg/day), administered by subcutaneous injection to females throughout gestation and lactation, resulted in increased offspring mortality at the highest dose tested, which was associated with maternal toxicity. There were no effects on developmental parameters or reproductive performance in surviving offspring.

8.2 Lactation

Risk Summary

There are no data on the presence of apomorphine in human milk, the effects of apomorphine on the breastfed infant, or the effects of apomorphine on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for KYNMOBI and any potential adverse effects on the breastfed infant from KYNMOBI or from the underlying maternal condition.

8.4 Pediatric Use

The safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use

Clinical studies of KYNMOBI did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. In Study 1, 78 patients below 65 years of age and 63 patients 65 years of age or older received at least one dose of KYNMOBI. Clinical experience with subcutaneous use of apomorphine has shown that the following adverse reactions were reported more frequently in patients 65 years of age or older compared to patients less than 65 years of age: confusion; hallucinations; serious adverse reactions (life-threatening events or events resulting in hospitalization and/or increased disability); falls (experiencing bone and joint injuries); cardiovascular events; gastrointestinal events; and discontinuation of treatment as a result of one or more adverse reactions. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosage range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.
Although the extent of the exposure and the Cmax of apomorphine are QT study also identified a significant exposure-response relationship QTcF of 10 msec (90% upper confidence interval of 16 msec). The thorough apomorphine dosing (i.e., 6 mg), apomorphine resulted in a prolongation of similar to those achieved with the recommended subcutaneous In a thorough QT study with subcutaneous apomorphine at exposures 12.2 Pharmacodynamics the caudate-putamen in the brain.

12.1 Mechanism of Action KYNMOBI (apomorphine hydrochloride) sublingual film contains apomorphine hydrochloride, a non-ergoline dopamine agonist. Apomorphine hydrochloride is chemically designated as (S)-Apomorphine-10,11-diol hydrochloride hemihydrate with a molecular formula of C_{17}H_{21}NO_3.HCl.H_2O. Its structural formula and molecular weight are:

Figure 1: Structural Formula and Molecular Weight of Apomorphine Hydrochloride

HNO

\[ \text{HCl} \cdot 1/2 \text{H}_2\text{O} \]

The molecular weight is 312.79 (hydrochloride hemihydrate salt). Apomorphine hydrochloride is white to grayish glistening crystals or white powder that is sparingly soluble in water and alcohol at ambient temperature.

KYNMOBI is intended for sublingual administration only and is available in 5 dosage strengths. Each film contains 10 mg, 15 mg, 20 mg, 25 mg, or 30 mg of apomorphine hydrochloride (equivalent to 8.8 mg, 13.2 mg, 17.6 mg, 22.0 mg, and 26.4 mg of apomorphine, respectively). Each film also contains the following inactive ingredients: disodium EDTA dihydrate, FD&C Blue #1, glycercylic glycerin monostearate, hydroxyethyl cellulose, hydroxypropyl cellulose, maltodextrin, (-)-menthol, pyridoxine hydrochloride, sodium hydroxide, sodium metabisulfite, sucrose, and white ink.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action KYNMOBI is a non-ergoline dopamine agonist with high in vitro binding affinity for the dopamine D_{2} receptor, and moderate affinity for the dopamine D_{2}, D_{3}, and D_{4} and adrenergic α_{1}D, α_{2}B, α_{2}C receptors. The precise mechanism of action of KYNMOBI as a treatment for “off” episodes associated with Parkinson’s disease is unknown, although it is believed to be due to stimulation of post-synaptic dopamine D_{2}-type receptors within the caudate-putamen in the brain.

12.2 Pharmacodynamics Cardiac Electrophysiology In a thorough QT study with subcutaneous apomorphine at exposures similar to those achieved with the recommended subcutaneous apomorphine dosing (i.e., 6 mg), apomorphine resulted in a prolongation of QTcF of 10 msec (90% upper confidence interval of 16 msec). The thorough QT study also identified a significant exposure-response relationship between apomorphine concentration and QTc.

Although the extent of the exposure and the Cmax of apomorphine are lower following the maximum recommended dose of KYNMOBI (30 mg) than following the maximum recommended dose of subcutaneous apomorphine (6 mg), QTc prolongation with KYNMOBI cannot be excluded.

Decreases in Blood Pressure In 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, compared to 36% of patients who received placebo [see Warnings and Precautions (5.4) and Drug Interactions (7.2, 7.3)].

12.3 Pharmacokinetics Absorption Following sublingual administration of 15 mg of apomorphine, the time to maximum concentration (T_{max}) ranged from 0.5 to 1 hour. Apomorphine exhibits less than dose-proportional increase in exposures over a dose range of 10 mg to 35 mg (1.2 times the highest recommended dosage) following a single sublingual administration of KYNMOBI in patients with Parkinson’s disease. Distribution Following sublingual administration of 15 mg of apomorphine, the geometric mean (CV%) of the apparent volume of distribution was 3630 L (66%). Elimination Metabolism The major metabolic pathways for sublingual apomorphine are sulfation by multiple sulfotransferase (SULT) enzymes; glucuronidation by multiple glucuronyltransferase (UGT) enzymes; N-demethylation catalyzed by multiple enzymes, including CYP2B6, CYP2C8, and CYP3A4/5, followed by conjugation. Metabolism of sublingual apomorphine results in 3 major inactive metabolites: apomorphine sulfate, apomorphine glucuronide, and norapomorphine glucuronide. Excretion Following sublingual administration of 15 mg of apomorphine, the geometric mean (CV%) of the apparent clearance was 1440 L/h (68%), and the geometric mean of the terminal elimination half-life is about 1.7 hours (range about 0.8 hour to 3 hours).

Specific Populations The apparent clearance of apomorphine does not appear to be influenced by age, gender, race, weight, duration of Parkinson’s disease, levodopa dose, use of antiemetic, or duration of therapy. Renal Impairment The clinical studies of KYNMOBI included patients with mild renal impairment (Clcr of ≥60 mL/min and <90 mL/min). There were no differences in apomorphine exposure after administration of KYNMOBI in patients with mild renal impairment as compared to patients with normal renal function (Clcr of ≥90 mL/min). Studies with KYNMOBI in patients with moderate to severe renal impairment have not been conducted. In a study with subcutaneous apomorphine comparing patients with moderate renal impairment (as determined by estimated creatinine clearance) to healthy matched volunteers, the AUC_{0-∞} and Cmax values were increased by approximately 16% and 50%, respectively, following a single administration. The mean time to peak concentrations and the mean terminal half-life of apomorphine were unaffected by the renal status of the individual. Since the Cmax and AUC_{0-∞} of apomorphine following the sublingual administration are lower as compared to the subcutaneous route of administration and the KYNMOBI dose is titrated individually, these changes are not expected to be clinically significant for patients with mild or moderate renal impairment [see Use in Specific Populations (8.6)]. Hepatic Impairment Studies with KYNMOBI in patients with hepatic impairment have not been conducted. In a study with subcutaneous apomorphine comparing patients with moderate hepatic impairment (as determined by the Child-Pugh classification method) to healthy matched volunteers, the AUC_{0-∞} and Cmax values were increased by approximately 10% and 25%, respectively, following a single administration. These changes are not expected to be clinically significant for patients with mild or moderate hepatic impairment [see Use in Specific Populations (8.7)]. Drug Interaction Studies Carbipoda/levodopa Levodopa pharmacokinetics were unchanged when subcutaneous apomorphine and levodopa were co-administered in patients. However, motor response differences were significant. The threshold levodopa concentration necessary for an improved motor response was reduced significantly, leading to an increased duration of effect without a change in the maximal response to levodopa therapy.
Nitroglycerin

Co-administration of nitroglycerin (0.4 mg) with subcutaneous apomorphine in healthy subjects did not have a significant impact on the pharmacokinetics of apomorphine. However, concomitant administration of nitroglycerin (0.4 mg) with subcutaneous apomorphine caused greater decreases in blood pressure than with subcutaneous apomorphine alone (see Warnings and Precautions (5.4) and Drug Interactions (7.2)).

When nitroglycerin and subcutaneous apomorphine were concomitantly administered to healthy subjects, the mean largest decrease (the mean of each subject’s largest drop in blood pressure measured within the 6-hour period following administration of subcutaneous apomorphine) in supine systolic and diastolic blood pressure (measured over 6 hours) was 9.7 mm Hg and 9.3 mm Hg, respectively. The mean largest decrease in standing systolic and diastolic blood pressure was 14.3 mm Hg and 13.5 mm Hg, respectively. Some individuals experienced very large decreases in standing systolic and diastolic blood pressure, up to a maximum decrease of 65 mm Hg and 43 mm Hg, respectively. In comparison, the mean largest decrease in supine systolic and diastolic blood pressure when subcutaneous apomorphine was administered alone was 6.1 mm Hg and 7.3 mm Hg, respectively, and in standing systolic and diastolic blood pressure was 6.7 mm Hg and 8.4 mm Hg, respectively.

A similar study has not been performed with KYNMOBI.

Ethanol

Co-administration of low-dose ethanol (0.3 g/kg) with subcutaneous apomorphine in healthy subjects did not have a significant impact on the pharmacokinetics of apomorphine, but high-dose ethanol (0.6 g/kg), equivalent to approximately 3 standardized alcohol-containing beverages, the pharmacokinetics of apomorphine, but high-dose ethanol (0.6 g/kg), equivalent to approximately 3 standardized alcohol-containing beverages, increased the Cmax of apomorphine by about 63%.

When high-dose ethanol (0.6 g/kg) and subcutaneous apomorphine were concomitantly administered to healthy subjects, the mean largest decrease (the mean of each subject’s largest drop in blood pressure measured within the 6-hour period following administration of subcutaneous apomorphine) for supine systolic and diastolic blood pressure was 9.1 mm Hg and 10.5 mm Hg, respectively. The mean largest standing systolic and diastolic blood pressure decrease was 11.3 mm Hg and 12.6 mm Hg, respectively. In some individuals, the decrease was as high as 61 mm Hg and 51 mm Hg, respectively, for standing systolic and diastolic blood pressure.

When low-dose ethanol (0.3 g/kg) and subcutaneous apomorphine were concomitantly administered, the mean largest decrease in supine systolic and diastolic blood pressure was 10.2 mm Hg and 9.9 mm Hg, respectively. The mean largest decrease in standing systolic and diastolic blood pressure was 8.4 mm Hg and 7.1 mm Hg, respectively. In comparison, the mean largest decrease in supine systolic and diastolic blood pressure when subcutaneous apomorphine was administered alone was 6.1 mm Hg and 7.3 mm Hg, respectively, and in standing systolic and diastolic blood pressure was 6.7 mm Hg and 8.4 mm Hg, respectively.

A similar study has not been performed with KYNMOBI.

COMT Interactions

A pharmacokinetic interaction of apomorphine with catechol-O-methyl transferase (COMT) inhibitors or drugs metabolized by this route is unlikely since apomorphine appears not to be metabolized by COMT.

In vitro studies

Based on in vitro studies, the potential for KYNMOBI to interact with concomitant medications to cause a CYP metabolism or transporter-based drug-drug interaction is considered low.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Lifetime carcinogenicity studies of apomorphine were conducted in male (0.1, 0.3, or 0.8 mg/kg/day) and female (0.3, 0.8, or 2 mg/kg/day) rats. Apomorphine was administered by subcutaneous injection for 22 months or 23 months, respectively. In males, there was an increase in Leydig cell tumors at the highest dose tested. This finding is of questionable significance because the endocrine mechanisms believed to be involved in the production of Leydig cell tumors in rats are not relevant to humans. No drug-related tumors were observed in females.

In a 26-week carcinogenicity study in F344-KO knockout transgenic mice, there was no evidence of carcinogenic potential when apomorphine was administered by subcutaneous injection at doses up to 20 mg/kg/day (male) or 40 mg/kg/day (female).

Mutagenesis

Apomorphine was mutagenic in the in vitro bacterial reverse mutation (Ames) and the in vitro mouse lymphoma tk assays. Apomorphine was clastogenic in the in vitro chromosomal aberration assay in human lymphocytes and in the in vitro mouse lymphoma tk assay. Apomorphine was negative in the in vivo micronucleus assay in mice.
16.1 How Supplied
KYNMOBI sublingual film is a blue to green rectangular film with a white printed number identifying the strength (e.g., “10” is 10 mg). Each sublingual film is individually packaged in a sealed foil pouch. Films are supplied in the following strengths and package configurations (Table 3):

**Table 3: Package Configuration for KYNMOBI sublingual film**

<table>
<thead>
<tr>
<th>Single Film Strength (NDC Code)</th>
<th>Package Configuration</th>
<th>NDC Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 mg (63402-010-01)</td>
<td>Each titration kit carton will contain a total of 10 individually packaged films of:</td>
<td>63402-088-10</td>
</tr>
<tr>
<td>15 mg (63402-015-01)</td>
<td>2 – single 10 mg films</td>
<td></td>
</tr>
<tr>
<td>20 mg (63402-020-01)</td>
<td>2 – single 15 mg films</td>
<td></td>
</tr>
<tr>
<td>25 mg (63402-025-01)</td>
<td>2 – single 20 mg films</td>
<td></td>
</tr>
<tr>
<td>30 mg (63402-030-01)</td>
<td>2 – single 25 mg films</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 – single 30 mg films</td>
<td></td>
</tr>
<tr>
<td><strong>Trade Product</strong></td>
<td>10 mg (63402-010-01)</td>
<td>63402-010-30</td>
</tr>
<tr>
<td></td>
<td>15 mg (63402-015-01)</td>
<td>63402-015-30</td>
</tr>
<tr>
<td></td>
<td>20 mg (63402-020-01)</td>
<td>63402-020-30</td>
</tr>
<tr>
<td></td>
<td>25 mg (63402-025-01)</td>
<td>63402-025-30</td>
</tr>
<tr>
<td></td>
<td>30 mg (63402-030-01)</td>
<td>63402-030-30</td>
</tr>
</tbody>
</table>

16.2 Storage and Handling
Store at 20°C to 25°C (68°F to 77°F); excursions permitted between 15°C to 30°C (59°F to 86°F) [see USP controlled room temperature].

Keep KYNMOBI in the foil pouch until ready to use.

17 PATIENT COUNSELING INFORMATION
Advertise the patient to read the FDA-approved patient labeling (Patient Information and Instructions for Use).

Administration of KYNMOBI
Advertise patients that KYNMOBI is for sublingual use only [see Dosage and Administration (2.1)].

KYNMOBI must be administered whole. Advise patients not to cut, chew, or swallow KYNMOBI.

Nausea and Vomiting
Advertise patients that KYNMOBI may cause nausea and vomiting when it is administered at recommended doses. Treatment with an antiemetic (e.g., trimethobenzamide) may be used, as needed, if nausea or vomiting occurs. Inform patients that they should discuss with their healthcare provider when the antiemetic can be discontinued [see Warnings and Precautions (5.1)].

 cfguring Activities of Daily Living and Somnolence
Alert patients to the potential sedating effects of KYNMOBI, including somnolence and falling asleep while engaged in activities of daily living. Instruct patients not to drive a car or engage in other potentially dangerous activities until they have gained sufficient experience with KYNMOBI to gauge whether or not it affects their mental and/or motor performance adversely. Advise patients that if increased somnolence or episodes of falling asleep during activities of daily living (e.g., watching television, passenger in a car, etc.) occur, they should not drive or participate in potentially dangerous activities until they have discussed this with their healthcare provider. Because of possible additive effects of alcohol use, advise patients to limit their alcohol intake [see Warnings and Precautions (5.2)].

Hypersensitivity/Allergic Reactions
Advertise patients that hypersensitivity/allergic reaction (e.g., swelling of the lips, tongue and mouth, flushing, and, infrequently, urticaria and throat tightness) may occur because of apomorphine, sodium metabisulfite, or any KYNMOBI excipients. Inform patients with a sulfi ne that KYNMOBI contains sodium metabisulfite, a sulfite that may cause allergic-type reactions, including anaphylactic symptoms and life-threatening or less severe asthmatic episodes [see Warnings and Precautions (5.3)]. Advise patients who experience any hypersensitivity/allergic reaction to KYNMOBI that they should avoid taking KYNMOBI again [see Contraindications (4)].

Hypotension/Orthostatic Hypotension
Advertise patients that they may develop postural (orthostatic) hypotension with or without symptoms, such as dizziness, nausea, syncope, and sweating. Instruct patients to rise slowly after sitting or lying down after taking KYNMOBI. Instruct patients to limit their alcohol intake because it may potentiate the hypotensive effect of KYNMOBI. Instruct patients to lie down before and after taking sublingual nitroglycerin because it may potentiate the hypotensive effect of KYNMOBI [see Warnings and Precautions (5.4)].

Oral Mucosal Irritation
Inform patients that KYNMOBI may result in oral mucosal adverse reactions such as irritation, erythema, lip swelling, mouth ulceration, dry mouth, stomatitis, glossodynia, or oropharyngeal pain, swollen tongue, ageusia, oral pain, lip ulceration, oral disorder and hypoaesthesia oral [see Warnings and Precautions (5.5) and Adverse Reactions (6.1)].

Falls
Alert patients that they may have increased risk for falling when using KYNMOBI [see Warnings and Precautions (5.6)].

Hallucinations and/or Psychotic-Like Behavior
Inform patients that KYNMOBI may cause hallucinations or other manifestations of psychotic-like behavior. Advise patients to inform their healthcare provider if they have a major psychotic disorder or are taking any treatments for psychosis [see Warnings and Precautions (5.7)].

Impulse Control/Compulsive Behaviors
Patients and their caregivers should be alerted to the possibility that they may experience intense urges to spend money uncontrollably, intense urges to gamble, increased sexual urges, binge eating and/or other intense urges and the inability to control these urges while taking KYNMOBI [see Warnings and Precautions (5.8)].

Withdrawal-Emergent Hyperpyrexia and Confusion
Advertise patients to contact their healthcare provider if they wish to discontinue KYNMOBI or decrease the dose of KYNMOBI [see Warnings and Precautions (5.9)].

QTc Prolongation and Potential for Proarrhythmic Effects
Alert patients that KYNMOBI may cause QTc prolongation and might produce proarrhythmic effects that could cause torsades de pointes and sudden death. Palpitations and syncope may signal the occurrence of an episode of torsades de pointes [see Warnings and Precautions (5.10)].

Priapism
Advertise patients that KYNMOBI may cause prolonged painful erections and that if this occurs that they should seek medical attention immediately [see Warnings and Precautions (5.12)].

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Patient Information
KYNMOBI® (kin-moe’-bee)
apomorphine hydrochloride
sublingual film

Read this Patient Information before you start taking KYNMOBI and each time you get a refill. There may be new information. This Patient Information does not take the place of talking to your healthcare provider about your medical condition or treatment.

What is KYNMOBI?
KYNMOBI is a prescription medicine used to treat short-term (acute), intermittent “off” episodes in people with Parkinson’s disease (PD). It is not known if KYNMOBI is safe and effective in children.

Do not take KYNMOBI if you are:
- taking certain medicines to treat nausea called 5HT3 antagonists, including ondansetron, granisetron, dolasetron, palonosetron, and alosetron. People taking ondansetron together with apomorphine, the active ingredient in KYNMOBI, have had very low blood pressure and lost consciousness or “blacked out.”
- allergic to apomorphine hydrochloride or to any of the ingredients in KYNMOBI. See the end of the Patient Information leaflet for a complete list of ingredients in KYNMOBI.

KYNMOBI also contains a sulfite called sodium metabisulfite. Sulfites can cause severe, life-threatening allergic reactions in some people. An allergy to sulfites is not the same as an allergy to sulfa. People with asthma are more likely to be allergic to sulfites.

Call your healthcare provider or get emergency help right away if you get any of the following symptoms of a severe life-threatening allergic reaction:
- hives
- swelling of the lips, tongue, and mouth
- rash
- redness of your face (flushing)
- throat tightness
- trouble breathing or swallowing

Before you start taking KYNMOBI, tell your healthcare provider about all of your medical conditions, including if you:
- have difficulty staying awake during the daytime.
- have dizziness.
- have fainting spells.
- have low blood pressure.
- have asthma.
- are allergic to any medicines containing sulfites.

- have liver problems.
- have kidney problems.
- have heart problems.
- have had a stroke or other brain problems.
- have a mental problem called a major psychotic disorder.
- drink alcohol.
- are pregnant or plan to become pregnant. It is not known if KYNMOBI will harm your unborn baby.
- are breastfeeding or plan to breastfeed. It is not known if KYNMOBI passes into your breast milk. You and your healthcare provider should decide if you will take KYNMOBI or breastfeed.
- Tell your healthcare provider about all the medicines you take, including prescription medicines and over-the-counter medicines, vitamins, and herbal supplements.

KYNMOBI may affect the way other medicines work, and other medicines can affect how KYNMOBI works. Taking KYNMOBI with other medicines may cause serious side effects.
- If you take nitroglycerin under your tongue (sublingual) while using KYNMOBI, your blood pressure may decrease and cause dizziness. You should lie down before and after taking sublingual nitroglycerin.

Know the medicines you take. Keep a list of your medicines with you and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take KYNMOBI?
- Read the step-by-step Instructions for Use that comes with your KYNMOBI prescription.
- Take KYNMOBI exactly as your healthcare provider tells you to take it.
- Your healthcare provider will tell you how much KYNMOBI to take and teach you the right way to take it.
- Your healthcare provider may change your dose if needed.
- Do not change your dose of KYNMOBI or take it more often than prescribed unless your healthcare provider has told you to.
- Do not take more than 1 dose of KYNMOBI to treat an “OFF” episode.
- Do not take another dose of KYNMOBI sooner than 2 hours after the last dose.
- Do not take KYNMOBI more than 5 times a day.
- Do not cut, chew, or swallow KYNMOBI.
- Your healthcare provider may prescribe another medicine for nausea called an antiemetic to take while you are taking KYNMOBI. Antiemetic medicines help to decrease the symptoms of nausea and vomiting that can happen when you take KYNMOBI.
What should I avoid while taking KYNMOBI?

- Do not drink alcohol while you are taking KYNMOBI. It can increase your chance of developing serious side effects.
- Do not take medicines that make you sleepy while you are using KYNMOBI.
- Do not drive, operate machinery, or do other dangerous activities until you know how KYNMOBI affects you.
- Do not change your body position too fast. Get up slowly from sitting or lying. KYNMOBI can lower your blood pressure and cause dizziness or fainting.

What are the possible side effects of KYNMOBI?

KYNMOBI can cause serious side effects, including:

- nausea and vomiting. Nausea is a common side effect of KYNMOBI. Nausea and vomiting can happen with KYNMOBI. Your healthcare provider may prescribe a medicine called an antiemetic, such as trimethobenzamide, to help prevent nausea and vomiting. Some patients can stop taking trimethobenzamide after using KYNMOBI, when advised by your healthcare provider. Some patients may need to keep taking trimethobenzamide to help treat nausea and vomiting. Talk to your healthcare provider before you stop taking trimethobenzamide.

- sleepiness or falling asleep during the day. Sleepiness is a serious and common side effect of KYNMOBI. Some people treated with KYNMOBI may get sleepy during the day or fall asleep without warning while doing everyday activities such as talking, eating, or driving a car.

- allergic reactions. See the “Do not take KYNMOBI if you are” section.

- dizziness. Dizziness is a serious and common side effect of KYNMOBI. KYNMOBI may lower your blood pressure and cause dizziness. Dizziness can happen when KYNMOBI treatment is started or when the KYNMOBI dose is increased. Do not get up too fast from sitting or after lying down, especially if you have been sitting or lying down for a long period of time.

- mouth (oral) irritation. Mouth (oral) irritation is a common side effect of KYNMOBI. You should call your healthcare provider if you develop any of these signs or symptoms:
  - redness
  - swelling
  - mouth sores (ulceration)
  - pain
  - dryness of the mouth, lips, or tongue
  - pain with swallowing

These signs and symptoms may go away if KYNMOBI treatment is stopped.

- falls. The changes that can happen with PD, and the effects of some PD medicines, can increase the risk of falling. KYNMOBI may also increase your risk of falling.

- hallucinations or psychotic-like behavior. KYNMOBI may cause or make psychotic-like behavior worse, including hallucinations (seeing or hearing things that are not real), confusion, excessive suspicion, aggressive behavior, agitation, delusional beliefs (believing things that are not real), and disorganized thinking.

- strong (intense) urges. Some people with PD have reported new or strong uncontrollable urges to gamble, increased sexual urges, increased urges to spend money (compulsive shopping), and other intense urges, while taking PD medicines, including KYNMOBI. If you or your family members notice that you have strong urges, talk to your healthcare provider. The strong urges may go away if your KYNMOBI dose is lowered or stopped.

- high fever and confusion. KYNMOBI may cause a problem that can happen in people who suddenly lower their dose, stop using, or change their dose of KYNMOBI. Symptoms include:
  - very high fever
  - confusion
  - stiff muscles
  - changes in breathing and heartbeat

Do not stop taking KYNMOBI or change your dose unless you are told to do so by your healthcare provider.

- heart problems. If you have shortness of breath, fast heartbeat, chest pain, or feel like you are going to pass out (faint) while taking KYNMOBI, call your healthcare provider or get emergency help right away.

- tissue changes (fibrotic complications). Some people have had changes in the tissues of their pelvis, lungs, and heart valves when taking medicines called non-ergot-derived dopamine agonists like KYNMOBI.

- prolonged painful erections (priapism). KYNMOBI may cause prolonged, painful erections in some people. If you have a prolonged and painful erection you should call your healthcare provider or go to the nearest hospital emergency room right away.

If you have any of these symptoms, stop taking KYNMOBI and call your healthcare provider right away before taking another dose.

The most common side effects of KYNMOBI include:

- nausea
- dizziness
- sleepiness
- mouth swelling, pain, or sores

These are not all of the possible side effects of KYNMOBI. Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.
How should I store KYNMOBI?

- Store KYNMOBI at room temperature between 68°F to 77°F (20°C to 25°C).
- Keep KYNMOBI in the foil pouch until you are ready to take it.

Keep KYNMOBI and all medicines out of the reach of children.

General information about the safe and effective use of KYNMOBI.

Medicines are sometimes prescribed for purposes other than those listed in a Patient Information leaflet. Do not use KYNMOBI for a condition for which it was not prescribed. Do not give KYNMOBI to other people, even if they have the same symptoms that you have. It may harm them. You can ask your pharmacist or healthcare provider for information about KYNMOBI that is written for health professionals.

What are the ingredients in KYNMOBI?

**Active ingredient:** apomorphine hydrochloride

**Inactive ingredients:** disodium EDTA dihydrate, FD&C Blue #1, glycerol, glyceryl monostearate, hydroxyethyl cellulose, hydroxypropyl cellulose, maltodextrin, (-)-menthol, pyridoxine hydrochloride, sodium hydroxide, sodium metabisulfite, sucralose, and white ink.