New Targeted Therapy for EGFR Exon 20 Insertion-Positive mNSCLC

Takeda Oncology is pleased to announce that the US Food and Drug Administration (FDA) has approved EXKIVITY™ (mobocertinib), the first oral therapy to target epidermal growth factor receptor
(EGFR) exon 20 insertion mutations in metastatic non-small cell lung cancer (NSCLC).[1]

EXKIVITY is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic NSCLC with EGFR exon 20 insertion mutations, as detected by an FDA-approved test, whose disease has progressed on or after platinum-based chemotherapy. This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trial(s).[1]

EGFR exon 20 insertion-positive NSCLC is a rare subtype of NSCLC.[2] EXKIVITY is a tyrosine kinase inhibitor developed to inhibit EGFR exon 20 insertion mutations.[1]

The most common (>20%) adverse reactions were diarrhea, rash, nausea, stomatitis, vomiting, decreased appetite, paronychia, fatigue, dry skin, and musculoskeletal pain. The most common (≥2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes, increased amylase, increased lipase, decreased potassium, decreased hemoglobin, increased creatinine, and decreased magnesium.[1]

IMPORTANT SAFETY INFORMATION

WARNING: QTc PROLONGATION and TORSADES DE POINTES

See full prescribing information for complete boxed warning.

- **EXKIVITY can cause life-threatening heart rate–corrected QT (QTc) prolongation, including Torsades de Pointes, which can be fatal, and requires monitoring of QTc and electrolytes at baseline and periodically during treatment. Increase monitoring frequency in patients with risk factors for QTc prolongation [see Warnings and Precautions].**
- **Avoid use of concomitant drugs which are known to prolong the QTc interval and use of strong or moderate CYP3A inhibitors with EXKIVITY, which may further prolong the QTc.**
- **Withhold, reduce the dose, or permanently discontinue EXKIVITY based on the severity of QTc prolongation.**

Please see additional Important Safety Information below.

EXKIVITY is now available in the following strength and package size[1]:

Trade Name	Description	NDC
EXKIVITY (mobocertinib)	40-mg capsules (120 count)	63020-040-12

Store at 20°C to 25°C (68°F to 77°F); excursions permitted from 15°C to 30°C (59°F to 86°F) [see USP Controlled Room Temperature].[1]

EXKIVITY is available by prescription through Biologics and Onco360 Specialty Pharmacies. Practices may also arrange for in-office dispensing via ASD Healthcare, Cardinal, and Oncology Supply.

For information about patient access support and financial assistance that your patients may qualify for, call Takeda Oncology Here2Assist™ at 1-844-817-6468, Option 2. **Let's Talk.** We're available Monday-Friday, 8AM–8PM ET, or visit us at **www.Here2Assist.com/hcp** to learn more.

Please share this exciting announcement about EXKIVITY with your society members.

Please click here to review more information on EXKIVITY.

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS

QTc Prolongation and Torsades de Pointes

EXKIVITY can cause life-threatening heart rate–corrected QT (QTc) prolongation and Torsades de Pointes, which can be fatal. In the 250-patient subset of the pooled EXKIVITY safety population who had scheduled and unscheduled electrocardiograms (ECGs), 1.2% of patients had a QTc interval >500 msec and 11% of patients had a change-from-baseline QTc interval >60 msec. Grade 4 Torsades de Pointes occurred in 1 patient (0.4%). Clinical trials of EXKIVITY did not enroll patients with a baseline QTc greater than 470 msec.

Assess QTc and electrolytes at baseline and correct abnormalities in sodium, potassium, calcium, and magnesium prior to initiating EXKIVITY. Monitor QTc and electrolytes periodically during treatment. Increase monitoring frequency in patients with risk factors for QTc prolongation, such as patients with congenital long QT syndrome, heart disease, or electrolyte abnormalities. Avoid use of concomitant drugs which are known to prolong the QTc interval. Avoid concomitant use of strong or moderate CYP3A inhibitors with EXKIVITY, which may further prolong the QTc. Withhold, reduce the dose, or permanently discontinue EXKIVITY based on the severity of the QTc prolongation.

Interstitial Lung Disease (ILD)/Pneumonitis

EXKIVITY can cause ILD/pneumonitis, which can be fatal. In the pooled EXKIVITY safety population, ILD/pneumonitis occurred in 4.3% of patients, including Grade 3 events in 0.8% of patients and fatal events in 1.2% of patients. Monitor patients for new or worsening pulmonary symptoms indicative of ILD/pneumonitis. Immediately withhold EXKIVITY in patients with suspected ILD/pneumonitis, and permanently discontinue EXKIVITY if ILD/pneumonitis is confirmed.

Cardiac Toxicity

EXKIVITY can cause cardiac toxicity (including decreased ejection fraction, cardiomyopathy, and congestive cardiac failure) resulting in cardiac failure. In the pooled EXKIVITY safety population, cardiac failure occurred in 2.7% of patients, including Grade 3 reactions in 1.2% of patients, Grade 4 reactions in 0.4% of patients, and one (0.4%) fatal case of cardiac failure.

EXKIVITY can cause QTc prolongation resulting in Torsades de Pointes. Atrial fibrillation (1.6%), ventricular tachycardia (0.4%), first-degree atrioventricular block (0.4%), second-degree atrioventricular block (0.4%), left bundle branch block (0.4%), supraventricular extrasystoles (0.4%), and ventricular extrasystoles (0.4%) also occurred in patients receiving EXKIVITY.

Monitor cardiac function, including assessment of left ventricular ejection fraction at baseline and during treatment. Permanently discontinue EXKIVITY for symptomatic cardiac failure.

Diarrhea

EXKIVITY can cause diarrhea, which can be severe. In the pooled EXKIVITY safety population, diarrhea occurred in 93% of patients, including Grade 3 events in 20% of patients and Grade 4 events in 0.4% of patients. The median time to first onset of diarrhea was 5 days, but diarrhea has occurred within 24 hours after administration of EXKIVITY. In the 48% of patients whose diarrhea resolved, the median time to resolution was 3 days. Prolonged diarrhea may lead to dehydration or electrolyte imbalance, with or without renal impairment. Treat diarrhea promptly.

Advise patients to start an antidiarrheal agent (eg, loperamide) at first evidence of increased frequency of bowel movement or first episode of unformed, loose stool and to increase fluid intake during diarrhea episodes. Monitor electrolytes and instruct patients to increase fluid and electrolyte intake as needed.

Embryo-Fetal Toxicity
Based on findings from animal studies and its mechanism of action, EXKIVITY can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective nonhormonal contraception during treatment with EXKIVITY and for 1 month after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with EXKIVITY and for 1 week after the last dose of EXKIVITY.

ADVERSE REACTIONS

The most common (>20%) adverse reactions are diarrhea, rash, nausea, stomatitis, vomiting, decreased appetite, paronychia, fatigue, dry skin, and musculoskeletal pain. The most common (>2%) Grade 3 or 4 laboratory abnormalities were decreased lymphocytes, increased amylase, increased lipase, decreased potassium, decreased hemoglobin, increased creatinine, and decreased magnesium.

DRUG INTERACTIONS

CYP3A Inhibitors
Coadministration of EXKIVITY with strong or moderate CYP3A inhibitors increased mobocertinib plasma concentrations, which may increase the risk of adverse reactions, including QTc interval prolongation. Avoid concomitant use of strong or moderate CYP3A inhibitors with EXKIVITY. If concomitant use of moderate CYP3A inhibitors cannot be avoided, reduce the EXKIVITY dose and monitor the QTc interval more frequently with ECGs.

CYP3A Inducers
Coadministration of EXKIVITY with strong or moderate CYP3A inducers decreases mobocertinib plasma concentrations, which may reduce EXKIVITY antitumor activity. Avoid concomitant use of strong or moderate CYP3A inducers with EXKIVITY.

CYP3A Substrates
Coadministration of EXKIVITY with CYP3A substrates may decrease plasma concentrations of CYP3A substrates, which may reduce the efficacy of these substrates. Avoid concomitant use of hormonal contraceptives with EXKIVITY. Avoid concomitant use of EXKIVITY with other CYP3A substrates where minimal concentration changes may lead to serious therapeutic failures. If concomitant use is unavoidable, increase the CYP3A substrate dosage in accordance with the approved product Prescribing Information.

Prolonged QTc Interval
EXKIVITY can cause QTc interval prolongation. Coadministration of EXKIVITY with drugs known to prolong the QTc interval may increase the risk of QTc interval prolongation. Avoid concomitant use of other medications known to prolong the QTc interval with EXKIVITY. If concomitant use is unavoidable, monitor the QTc interval more frequently with ECGs.

USE IN SPECIFIC POPULATIONS

Pregnancy
Based on findings from animal studies and its mechanism of action, EXKIVITY can cause fetal harm when administered to a pregnant woman. There are no clinical data available on the use of EXKIVITY in pregnant women.

Females and Males of Reproductive Potential
Verify pregnancy status in females of reproductive potential prior to initiating EXKIVITY. Advise females of reproductive potential to use effective nonhormonal contraception during treatment with EXKIVITY and for at least 1 week following the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with EXKIVITY and for at least 1 week following the final dose.

Lactation
There are no data on the presence of mobocertinib or its metabolites in human milk or their effects on the breastfed child or on milk production. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with EXKIVITY and for 1 week after the last dose.

To report SUSPECTED ADVERSE REACTIONS, contact Takeda Pharmaceuticals U.S.A., Inc. at **1-844-217-6468** or the FDA at **1-800-FDA-1088** or **www.fda.gov/medwatch.**

Please see full Prescribing Information, including Boxed Warning.

To learn more about EXKIVITY, please visit EXKIVITYhcp.com.

You may always reach me by phone or email at the contact information provided below.

Cheers,

Nicole Wits - Field Access Director

nicole.wits@takeda.com or 847.912.7674

NDC, National Drug Code.

References: 1. Exkivity. Prescribing Information. Takeda Pharmaceuticals U.S.A., Inc.; 2021. Accessed September 15, 2021. https://takeda.info/Exkivity-Prescribing-Information **2.** Jordan EJ et al. *Cancer Discov.* 2017;7(6):596-609.

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