Brand and Other Names:BIOMOB

INN: Mobocertinib (Rx)

Dosing & Uses

ADULT

Dosage Forms & Strengths

Capsule
- 40mg

Non-Small Cell Lung Cancer

Indicated for locally advanced or metastatic non–small cell lung cancer (NSCLC) in adults with epidermal growth factor receptor (EGFR) exon 20 insertion mutations and whose disease has progressed on or after platinum-based chemotherapy HIV-1 infection in adults

160 mg PO qDay

Continue until disease progression or unacceptable toxicityHIV-1 Pre-exposure

Dosage Modifications

Dose reductions for adverse reactions
- First dose reduction: 120 mg PO qDay
- Second dose reduction: 80 mg PO qDay

QT (QTc) prolongations and torsades de pointes
- Grade 2 (QTc interval 481-500 msec)
  First occurrence: Withhold until Grade ⩽1 or baseline; upon recovery, resume at same dose
  Recurrence: Withhold until Grade ⩽1 or baseline; upon recovery, resume at next lower dose or permanently discontinue
- Grade 3 (QTc interval ⩾501 msec or QTc interval increases >60 msec from baseline)
- First occurrence: Withhold until Grade ⩽1 or baseline; upon recovery, resume at next lower dose or permanently discontinue
- Recurrence: Permanently discontinue
- Grade 4 (torsades de pointes; polymorphic ventricular tachycardia; signs/symptoms of serious arrhythmia): Permanently discontinue

Interstitial lung disease (ILD)/pneumonitis
- Any grade: Withhold if ILD/pneumonitis is suspected
- Permanently discontinue if ILD/pneumonitis confirmed

Decreased ejection fraction (EF) or heart failure (HF)
- Grade 2 decreased EF
- Withhold until Grade ⩽1 or baseline
- If recovered to baseline within 2 weeks, resume at same dose or next lower dose
- If not recovered to baseline within 2 weeks, permanently discontinue
- Grade 2 HF or Grade ⩾3 EF: Permanently discontinue

Diarrhea
- Intolerable or recurrent Grade 2 or Grade 3: Withhold until Grade ⩽1 or baseline; resume at same dose or next lower dose
- Grade 4
- First occurrence: Withhold until Grade ⩽1 or baseline; resume at next lower dose
- Recurrence: Permanently discontinue

Other adverse reactions
- Intolerable or recurrent Grade 2 or Grade 3: Withhold until Grade ⩽1 or baseline; resume at same dose or next lower dose
- Grade 4
- First occurrence: Withhold until Grade ⩽1 or baseline; resume at the next lower dose if recovery occurs within 2 weeks
- Permanently discontinue if no recovery occurs within 2 weeks
- Recurrence: Permanently discontinue

Coadministration of moderate or strong CYP3A4 inhibitors
- Avoid coadministration
- If use of moderate CYP3A4 inhibitor unavoidable, reduce mobocertinib dose by ~50% (eg, 160 to 80mg, 120 to 60 mg, or 80 to 40 mg); closely monitor QTc interval
- Once moderate CYP3A4 inhibitor has been discontinued for 3-5 half-lives, resume at dose taken before initiating moderate CYP3A4 inhibitor

Renal impairment
- Mild-to-moderate (eGFR 30-89 mL/min/1.73 m2): No dosage adjustment necessary
- Severe (eGFR <30 mL/min/1.73 m2): No recommended dosage established

Hepatic impairment
- Mild-to-moderate (total bilirubin [TB] <3x ULN and any AST): No dosage adjustment necessary
- Severe (TB >3x ULN and any AST): No recommended dosage established

Dosing Considerations

Verify pregnancy status in females of reproductive potential

Patient selection
- Select patients based on presence of EGFR exon 20 insertion mutations

PEDIATRIC

Safety and efficacy not established

Adverse Effects

>10%

All grades
- Diarrhea (92%)
- Rash (78%)
- Decreased red blood cells (59%)
- Increased creatinine (52%)
- Decreased lymphocytes (52%)
- Stomatitis (46%)
- Increased amylase (40%)
- Vomiting (40%)
- Decreased appetite (39%)
- Paronychia (39%)
- Nausea (37%)
- Increased lipase (35%)
- Musculoskeletal pain (34%)
- Dry skin (32%)
- Fatigue (29%)
- Decreased potassium (29%)
- Decreased platelets (26%)
- Decreased leukocytes (25%)
- Increased alkaline phosphatase (25%)
- Pruritus (24%)
- Cough (24%)
- Decreased albumin (23%)
- Decreased magnesium (23%)
- Increased ALT (22%)
- Decreased weight (21%)
- Increased AST (21%)
- Decreased sodium (20%)
- Alopecia (19%)
- Abdominal pain (18%)
- Upper respiratory tract infection (16%)
- Gastroesophageal reflux disease (15%)
- Dyspnea (15%)
- Rhinorrhea (13%)
- Dyspepsia (11%)
- Ocular toxicity (11%)

Grade 3 or 4
- Diarrhea (22%)
- Decreased lymphocytes (15%)
- Increased amylase (13%)

1-10%

All grades
- QTc prolongation (10%)
- Hypertension (10%)
- Headache (10%)

Grade 3 or 4
- Increased lipase (10%)
- Decreased potassium (5.3%)
- Nausea (4.4%)
- Stomatitis (4.4%)
- Hypertension (4.4%)
- Dyspnea (4.4%)
- QTc prolongation (3.5%)
- Fatigue (3.5%)
- Decreased red blood cells (3.5%)
- Decreased magnesium (2.7%)
- Increased ALT (2.7%)
- Increased creatinine (2.7%)
- Vomiting (2.6%)
- Musculoskeletal pain (2.6%)
- Abdominal pain (1.8%)
- Rash (1.8%)
- Increased alkaline phosphatase (1.8%)
- Decreased albumin (1.8%)
- Increased AST (1.8%)

<1%

Grade 3 or 4
- Decreased appetite (0.9%)
- Paronychia (0.9%)
- Pruritus (0.9%)
- Decreased platelets (0.9%)
- Decreased sodium (0.9%)

Interactions

Contraindicated

Mavacamten

Warnings

Black Box Warnings

QTc prolongation and torsades de pointes
- Life-threatening heart rate–corrected QTc prolongation, including torsades de pointes, may occur
- Monitor QTc and electrolytes periodically during treatment
- Increase monitoring frequency in patients with risk factors for QTc prolongation (eg, congenital long QT syndrome, heart disease, electrolyte abnormalities)
- Avoid coadministration with drugs that may further prolong the QTc interval (eg, drugs known to prolong QTc interval, strong or moderate CYP3A inhibitors)
- Withhold, reduce dose, or permanently discontinue treatment based on the severity of QTc prolongation

Contraindications

None

Cautions

ILD/pneumonitis, which can be fatal, reported; monitor for new or worsening pulmonary symptoms indicative of ILD/pneumonitis

Cardiac toxicity (including decreased EF, cardiomyopathy, and congestive HF) resulting in HF, may occur; monitor cardiac function (eg, assessment of left ventricular EF at baseline and during treatment)

May cause fetal harm

QTc prolongation and torsades de pointes
- Life-threatening QTc prolongation, including torsades de pointes, reported
- Assess QTc and electrolytes at baseline and correct abnormalities in sodium, potassium, calcium, and magnesium before initiating therapy

Diarrhea
- Severe diarrhea reported
- Median time to first onset of diarrhea was 5 days; diarrhea occurred within 24 hr after administration
- 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 sign of diarrhea or increased bowel movement frequency and to increase fluid and electrolyte intake
- Monitor electrolytes

Drug interaction overview
- CYP3A4 substrate
- Moderate CYP3A4 inducer
- Inhibitor of breast cancer resistance protein (BCRP); clinical significance of changes in pharmacokinetics of sulfasalazine (a BCRP substrate) when coadministered with multiple doses of mobocertinib is unknown
- Strong or moderate CYP3A4 inhibitors
- Avoid coadministration
- If use of moderate CYP3A4 inhibitors is unavoidable, reduce mobocertinib dose and monitor QTc interval more frequently
- Strong or moderate CYP3A4 inhibitors may increase mobocertinib plasma concentrations and toxicities, including QTc interval
- Strong or moderate CYP3A4 inducers
- Avoid coadministration
- Strong or moderate CYP3A4 inducers may decrease mobocertinib plasma concentrations and antitumor activity

- Sensitive CYP3A4 substrates
- Avoid coadministration with hormonal contraceptives OR other CYP3A4 substrates where minimal concentration changes may lead to serious therapeutic failures
- If use is unavoidable, increase CYP3A4 substrate dosage in accordance with its prescribing information
- Mobocertinib may decrease plasma concentrations of CYP3A4 substrates
- Drugs that prolong QTc interval
- Avoid coadministration
- If coadministration unavoidable, reduce mobocertinib dose and monitor QTc interval more frequently

Pregnancy

Based on findings from animal studies and its mechanism of action, may cause fetal harm when administered to pregnant females

No data are available on use in pregnant females

Verify pregnancy status in females of reproductive potential

Contraception
- Females of reproductive potential: Use effective nonhormonal contraception during treatment and for 1 month after last dose; mobocertinib may render hormonal contraceptives ineffective
- Males with female partners of reproductive potential: Use effective contraception during treatment and for 1 week after the last dose

Infertility
- Based on animal studies, fertility in males and females of reproductive potential may be impaired

Animal data
- Oral administration to pregnant rats during organogenesis resulted in embryolethality and maternal toxicity at plasma exposures approximately 1.7x the human exposure based on AUC at the 160-mg once-daily clinical dose
- Advise pregnant females of potential risk to a fetus

Lactation

There are no data on presence of mobocertinib or its metabolites in human milk, its effects on breastfed children, or its effects on milk production

Advise women not to breastfeed during treatment and for 1 week after last dose

Pregnancy Categories

A: Generally acceptable. Controlled studies in pregnant women show no evidence of fetal risk.

B: May be acceptable. Either animal studies show no risk but human studies not available or animal studies showed minor risks and human studies done and showed no risk.

C: Use with caution if benefits outweigh risks. Animal studies show risk and human studies not available or neither animal nor human studies done.

D: Use in LIFE-THREATENING emergencies when no safer drug available. Positive evidence of human fetal risk.

X: Do not use in pregnancy. Risks involved outweigh potential benefits. Safer alternatives exist.

NA: Information not available.

Pharmacology

Mechanism of Action

Kinase inhibitor of EGFR; irreversibly binds to and inhibits EGFR exon 20 insertion mutations at lower concentrations than wild-type (WT) EGFR

In cultured cell models, mobocertinib inhibited cell proliferation driven by different EGFR exon 20 insertion mutation variants

In animal tumor implantation models, mobocertinib exhibited antitumor activity against xenografts with the EGFR exon 20 insertions NPH or ASV

Absorption

Peak plasma time: 4 hr

Absolute bioavailability: 37%

Distribution

Plasma bound: 99.3%

Vd (steady-state): 3509 L

Plasma-to-blood ratio
- Mobocertinib: 0.76
- AP32960: 1.2
- AP32914: 0.71

Metabolism

Primarily metabolized by CYP3A4

Active metabolites: AP32960 and AP32914 are equipotent to mobocertinib and account for 36% and 4% of the combined molar AUC, respectively

Elimination

Half-life (steady-state)
- Mobocertinib: 18 hr
- AP32960: 24 hr
- AP32914: 18 hr

Clearance (steady-state)
- Mobocertinib: 138 L/hr
- AP32960: 149 L/hr
- AP32914: 159 L/hr

Excretion

Mobocertinib: Feces (76% [6% unchanged]); urine (4% [1% unchanged])
AP32960: Feces (12%); urine (1%)
AP32914: Below detection limit in both urine and feces

Administration

Oral Administration

Take with or without food at same time each day

Swallow capsules whole; do not open, chew, or dissolve contents

Missed or vomited dose
- Missed dose >6 hr: Skip dose and take next dose the following day at its regularly scheduled time
- Vomited dose: Do not take an additional dose; take next dose as prescribed the following day

Storage

Store at 20-25ºC (68-77ºF); excursions permitted to 15-30ºC (59-86ºF)

BIOMOB

Manufactured by
Biospring
Healing beyond boundaries