NOVARTIS

ZYKADIA® (ceritinib)
150 mg Hard Capsules

Basic Succinct Statement (BSS)

CODE: BSS RD 26 NOV 18; APPR 1 JUL 20

ZYKADIA®

Important note: Before prescribing, consult full prescribing information.

Presentation: Hard gelatin capsules containing 150 mg ceritinib.

Indications: ZYKADIA® as monotherapy is indicated for the first-line treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC). ZYKADIA® as monotherapy is indicated for the treatment of adult patients with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer (NSCLC) previously treated with crizotinib.

Dosage and administration:

Adults: The recommended dose of ZYKADIA® is 450 mg orally once daily with food until disease progression or unacceptable toxicity. ♦Temporary dose interruption and/or dose reduction of ZYKADIA® therapy may be required based on individual safety and tolerability. ♦Zykadia should be discontinued in patients unable to tolerate 150 mg taken once daily with food.

Children (below the age of 18 years): The safety and efficacy of ZYKADIA® have not been established in pediatric patients.

Special patient populations: ♦Reduce the dose by approximately one-third, rounded to the nearest multiple of the 150mg dosage strength in patients with severe hepatic impairment. No dose adjustment is recommended for patients with mild or moderate hepatic impairment

Contraindications: None.

Warnings and precautions: ♦**Hepatotoxicity:** Monitor with liver laboratory tests including ALT, aspartate aminotransferase (AST), and total bilirubin once a month and as clinically indicated, with more frequent testing in patients who develop transaminase elevations. Based on the severity of the adverse drug reaction, withhold ZYKADIA® with resumption at a reduced dose, or permanently discontinue. ♦**Interstitial lung disease (ILD) / Pneumonitis:** Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis. Exclude other potential causes of ILD/pneumonitis, and permanently discontinue ZYKADIA® in patients diagnosed with treatment-related ILD/pneumonitis. ♦**QT interval prolongation:** When possible, avoid use of ZYKADIA® in patients with congenital long QT syndrome. Conduct periodic monitoring with electrocardiograms (ECGs) and electrolytes in patients with congestive heart failure, bradyarrhythmias, electrolyte abnormalities or those who are taking medications that are known to prolong the QTc interval. Withhold ZYKADIA® in patients who develop QTc interval greater than 500 msec on at least 2 separate ECGs until the QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then resume ZYKADIA® at the next lower dosage. Permanently discontinue ZYKADIA® in patients who develop QTc interval prolongation in combination with Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia. ♦**Bradycardia:** Avoid using ZYKADIA® in combination with other agents known to cause bradycardia (e.g., beta-blockers,

non-dihydropyridine calcium channel blockers, clonidine, and digoxin) to the extent possible. Monitor heart rate and blood pressure regularly. In cases of symptomatic bradycardia that is not life-threatening, withhold ZYKADIA® until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, evaluate the use of concomitant medications, and adjust the dose of ZYKADIA® if necessary. Permanently discontinue ZYKADIA® for life-threatening bradycardia if no contributing concomitant medication is identified; however, if associated with concomitant medication known to cause bradycardia or hypotension, withhold ZYKADIA® until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, and if concomitant medication can be adjusted or discontinued, reinitiate ZYKADIA® by reducing dose by 150 mg upon recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, with frequent monitoring. ♦ **Gastrointestinal adverse reactions:** Monitor and manage patients using standards of care, including anti-diarrheals, anti-emetics, or fluid replacement, as indicated. If vomiting occurs during the course of treatment, the patient should not take an additional dose, but should continue with the next scheduled dose. Based on the severity of the adverse drug reaction, withhold ZYKADIA® with resumption at a reduced dose. ♦**Hyperglycemia:** Monitor fasting serum glucose prior to the start of ZYKADIA® treatment and periodically thereafter as clinically indicated. Initiate or optimize anti-hyperglycemic medications as indicated. ♦**Pancreatitis**: Monitor lipase and amylase prior to the start of ZYKADIA® treatment and periodically thereafter as clinically indicated. Based on the severity of the laboratory abnormalities, withhold ZYKADIA® with resumption at a reduced dose. ♦**Embryo-fetal Toxicity:** ZYKADIA® may cause fetal harm when administered to a pregnant woman. Advice females of reproductive potential to use effective contraception during treatment with ZYKADIA® and for 6 months following completion of therapy.

Adverse reactions: ♦ Gastrointestinal adverse reactions, hepatotoxicity, interstitial lung disease/pneumonitis, QT interval prolongation, hyperglycaemia, bradycardia, pancreatitis.

Interactions:

♦**Strong CYP3A inhibitors:** Avoid concurrent use of strong CYP3A inhibitors. If concomitant use of strong CYP3A inhibitors is unavoidable, reduce the Zykadia dose by approximately one-third, rounded to the nearest multiple of the 150 mg dosage strength. After discontinuation of a strong CYP3A inhibitor, resume the Zykadia dose that was taken prior to initiating the strong CYP3A inhibitor. ♦**Strong CYP3A and P-gp inducers:** Avoid concomitant use of strong CYP3A inducers. ♦**CYP3A and CYP2C9 substrates:** Avoid co-administration of Zykadia with sensitive CYP3A substrates, and CYP2C9 substrates for which minimal concentration changes may lead to serious toxicities. If unavoidable, consider dose reduction for co-administered medicines that are CYP3A or CYP2C9 substrates. Increase international normalized ratio (INR) monitoring frequency if warfarin co-administration is unavoidable. ♦**Drug-food/drink interactions:** Zykadia should be taken with food. Patients should be instructed to avoid grapefruit or grapefruit juice as they may inhibit CYP3A in the gut wall and increase the bioavailability of ceritinib.