Basic Succinct Statement

SPEXIB®

Important note: Before prescribing, consult full prescribing information.

Presentation: Hard gelatin capsules containing 150 mg ceritinib.

Indications:

Ceritinib 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).

Ceritinib is indicated for the treatment of patients with anaplastic lymphoma kinase (ALK) positive metastatic non small cell lung cancer (NSCLC) who have progressed on or are intolerant to crizotinib.

Dosage and administration:

Adults: Recommended dose is 450 mg taken orally once daily with food at the same time each day. Maximum recommended dose is 450 mg taken orally once daily with food. ♦Temporary dose interruption and/or dose reduction of ceritnib therapy may be required based on individual safety and tolerability. ♦Ceritinib 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 ceritinib have not been established in pediatric patients.

Special populations: ♦Renal impairment: Mild to moderate: No dose adjustment. Severe: Caution should be used. ♦Hepatic impairment: Severe: Dose should be reduced by approximately one-third, rounded to the nearest multiple of the 150 mg dosage strength. Mild to moderate: No dose adjustment.

Contraindications: None.

Warnings and precautions:

♦**Hepatotoxicity:** Liver laboratory tests should be monitored prior to the start of treatment and monthly thereafter. In patients who develop transaminase elevations, more frequent monitoring of liver transaminases and total bilirubin should be done as clinically indicated. ♦**Interstitial lung disease (ILD) / Pneumonitis:** Patients should be monitored for pulmonary symptoms indicative of ILD/pneumonitis. Other potential causes of ILD/pneumonitis should be excluded, and ceritinib should be permanently discontinued in patients diagnosed with any-grade treatment-related ILD/pneumonitis. ♦**QT interval prolongation:** Ceritinib should be avoided in patients with congenital long QT syndrome. Periodic monitoring of both electrocardiograms (ECGs) and electrolytes (e.g., potassium) is recommended in patients with congestive heart failure, bradyarrhythmias, or electrolyte abnormalities and in patients who are taking medications that are known to prolong the QT interval. In case of vomiting, diarrhea, dehydration, or impaired renal function, correct electrolytes as clinically indicated. Ceritinib should be permanently discontinued in patients who develop QTc greater than 500 msec or greater than 60 msec change from baseline and Torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia. Ceritinib should be withheld in patients who develop QTc greater than 500 msec on at least 2 separate ECGs until recovery to baseline or a QTc less than 481 msec, then ceritinib should be reinitiated by reducing dose by 150 mg.

♦**Bradycardia:** Use of ceritinib should be avoided 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. Heart rate and blood pressure should be monitored regularly. In cases of symptomatic bradycardia that is not life-threatening, ceritinib should be withheld 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 ceritnib if necessary. Ceritinib should be permanently discontinued for life-threatening bradycardia if no contributing concomitant medication is identified; however, if associated with concomitant medication known to cause bradycardia or hypotension, ceritinib should be withheld until recovery to asymptomatic bradycardia or to a heart rate of 60 bpm or above, and if concomitant medication can be adjusted or discontinued, ceritinib should be reinitiated 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:** Patients should be monitored and managed using standards of care, including anti-diarrheals, anti-emetics, or fluid replacement, as indicated. Dose interruption and dose reduction may be employed as necessary. If vomiting occurs during the course of treatment, the patient should not take an additional dose, but should continue with the next scheduled dose. ♦**Hyperglycemia:** Fasting serum glucose should be monitored prior to the start of ceritnib treatment and periodically thereafter as clinically indicated. Anti-hyperglycemic medications should be initiated or optimized as indicated. ♦**Elevations of lipase and/or amylase:** Lipase and amylase should be monitored prior to the start of ceritinib treatment and periodically thereafter as clinically indicated.

Pregnancy, lactation, females and males of reproductive potential:

Pregnancy: Should not be given to pregnant women unless the potential benefit outweighs the potential risk to the fetus.

Lactation: A decision should be made whether to discontinue breast-feeding or discontinue ceritinib taking into account the importance of ceritinib to the mother.

Females and males of reproductive potential: Females of reproductive potential to be advised to use effective contraception (methods that result in less than 1% pregnancy rates) while on treatment and for up to 3 months after discontinuation.

Infertility: The potential for ceritinib to cause infertility in male and female patients is unknown.

Adverse drug reactions:

Very common (≥10%): Liver laboratory test abnormalities, diarrhoea, fatigue, abdominal pain, nausea, decreased appetite, vomiting, weight decreased, constipation, blood creatinine increased, rash, anaemia, and oesophageal disorder.

Common (≥1 to <10%): Electrocardiogram QT prolonged, hyperglycaemia, amylase increased, vision disorder, pericarditis, hypophosphataemia, lipase increased, bradycardia, abnormal liver function tests, pneumonitis, renal failure, hepatotoxicity, and renal impairment.

Uncommon (≥0.1 to <1%): Pancreatitis.

Interactions: ♦Strong CYP3A inhibitors: Concurrent use of strong CYP3A inhibitors should be avoided. If concomitant use of strong CYP3A inhibitors is unavoidable, including but not limited to, ritonavir, saquinavir, telithromycin, ketoconazole, itraconazole, voriconazole,

posaconazole, and nefazodone, the dose of ceritinib should be reduced by approximately one-third, rounded to the nearest multiple of the 150 mg dosage strength. After discontinuation of a strong CYP3A inhibitor, ceritinib should be resumed at the dose that was taken prior to initiating the strong CYP3A inhibitor. ♦**P-gp inhibitors:** Caution should be exercised with concomitant use of P-gp inhibitors and carefully monitor adverse drug reactions. ♦**Strong CYP3A and P-gp inducers:** Concomitant use of strong CYP3A inducers should avoided, including but not limited to, carbamazepine, phenobarbital, phenytoin, rifabutin, rifampin, and St. John's Wort (*Hypericum perforatum*). Caution should be exercised with concomitant use of P-gp inducers. ♦**CYP3A and CYP2C9 substrates:** Co-administration of ceritinib with substrates primarily metabolized by CYP3A or CYP2C9, CYP3A substrates known to have narrow therapeutic indices (e.g., ciclosporin, dihydroergotamine, ergotamine, fentanyl, pimozide, quinidine, tacrolimus, alfentanil and sirolimus), and CYP2C9 substrates known to have narrow therapeutic indices (e.g., phenytoin and warfarin) should be avoided. If unavoidable, consider dose reduction for co-administered medicines that are CYP3A or CYP2C9 substrates with narrow therapeutic indices. International normalized ratio (INR) monitoring frequency should be increased if warfarin co-administration is unavoidable. ♦**CYP2A6 and CYP2E1 substrates:** Caution should be exercised with concomitant use of CYP2A6 and CYP2E1 substrates and carefully monitor adverse drug reactions. ♦**Drug-food/drink interactions:** Ceritnib 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.

Packs: Pack of 3 x 50 hard capsules.

Note: Before prescribing, consult full prescribing information available from Novartis Healthcare Private Limited, Inspire BKC, Part of 7th Floor, Bandra Kurla Complex, Bandra (East), Mumbai – 400 051, Maharashtra, India, Tel:.+ 022 5024 3000

For the use of only oncologist.

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