CERITINIB (Zykadia)

INDICATION (ICD10) C34

Check the most recent Blueteq eligibility criteria before prescribing. Blueteq registration required. (www.england.nhs.uk/publication/national-cancer-drugs-fund-list/) (CER1) (CER2)

1. Ceritinib monotherapy for anaplastic lymphoma kinase-positive rearrangement advanced stage IIIB or IV non-small-cell lung cancer previously treated with crizotinib (The only TKI treatment that the patient has progressed on is 1st line crizotinib or 2nd line crizotinib after 1st line chemotherapy and that the patient has not been treated with either 1st line alectinib or 1st line ceritinib). Either has no brain metastases or, if the patient has brain metastases, the patient is symptomatically stable prior to starting ceritinib. PS 0, 1 or 2. (TA395)
2. Ceritinib monotherapy for anaplastic lymphoma kinase-positive rearrangement locally advanced or metastatic non-small cell lung cancer previously untreated with an ALK inhibitor. Treatment-naïve to 1st line cytotoxic chemotherapy-containing systemic treatment for this locally advanced or metastatic NSCLC indication (the only previous cytotoxic treatment allowed for patients to be treated with 1st line ceritinib is adjuvant or neoadjuvant chemotherapy or chemotherapy given concurrently with radiotherapy). Either has no known brain metastases or if the patient has brain metastases, the patient is symptomatically stable prior to starting ceritinib. PS 0, 1 or 2. (TA500)

REGIMEN

CERITINIB 450mg orally daily continuously

CYCLE FREQUENCY AND NUMBER OF CYCLES

Until disease progression. A formal medical review as to whether treatment with ceritinib should continue or not will be scheduled to occur at least by the end of the first 8 weeks of treatment.

ADMINISTRATION

Available as 150mg tablets
Swallow whole with food.
Grapefruit and grapefruit juice and Seville oranges should be avoided while on ceritinib

ANTI-EMETICS

Moderate risk

CONCURRENT MEDICATION REQUIRED

Ceritinib	Diarrhoea – Loperamide may be required

EXTRAVASATION AND TYPE OF LINE / FILTERS

Not applicable

INVESTIGATIONS

Blood results required before SACT administration
FBC, U&E every cycle
LFTs every 2 weeks for 3 cycles then every cycle
Neutrophils x 10^9/L ≥1.5
Platelets x 10^9/L ≥100
Creatinine every cycle
ECG baseline
Baseline weight

MAIN TOXICITES AND ADVERSE REACTIONS

Ceritinib	Increased LFTs Diarrhoea QT prolongation

INTERACTIONS WHICH MAY REQUIRE DOSE MODIFICATIONS
(not exhaustive list check SPC/BNF/Stockleys)

Ceritinib	Strong CYP3A inducers and inhbitorsm- use of these drugs are cautioned with the use of ceritinib eg ketoconazole, ritonavir, itraconazole, voriconazole and posaconazole. QT prolongation use with caution in patients who have or may develop prolongation of the QT interval eg patients taking anti-arrhythmics, domperidone, droperidol, clarithromycin, amiodarone, haloperidol and methadone. Avoid grapefruit and Seville oranges

DOSE MODIFICATIONS
Non-haematological
Ceritinib

Any patient with a grade 3 or 4 toxicity not controlled by optimum supportive care will require a dose reduction as below.

Level	Ceritinib dose
Starting dose	450mg daily
First dose reduction	300mg daily
Second dose reduction	150mg daily

Management of adverse events may require dose reduction, temporary interruption or discontinuation of treatment. Ceritinib treatment should be permanently discontinued if patients are unable to tolerate the 150mg daily dose.

Cardiac

QTc >500msec on at least 2 separate ECGs	Withhold ceritinib until recovery to baseline or to a QTc ≤480msec. Correct electrolyte abnormalities, then reinitiate with dose reduced by 150mg
QTc >500msec or >60msec change from baseline and torsade de pointes or polymorphic ventricular tachycardia or signs/symptoms of serious arrhythmia	Permanently discontinue ceritinib.
Bradycardia pulse less than 60 beats per minute (bpm) (symptomatic, may be severe and medically significant, medical intervention indicated)	Withhold ceritinib until recovery to grade ≤1 bradycardia or to a heart rate of 60bpm or above. Evaluate concomitant medicines known to cause bradycardia and/or anti-hypertensives. If a contributing medicine is identified and adjusted reinitiate ceritinib at the previous dose upon recovery to asymptomatic bradycardia or to a heart rate of 60bpm or above. If no contributing concomitant medicinal product is identified, or if contributing concomitant medicinal products are not discontinued or dose modified, reinitiate ceritinib with dose reduced by 150mg upon recovery to asymptomatic bradycardia or to a heart rate of 60bpm or above.
Bradycardia pulse less than 60 beats per minute (bpm) (life-threatening consequences, urgent intervention indicated)	Permanently discontinue ceritinib if no contributing concomitant medicine is identified. If a contributing concomitant medicinal product is identified and discontinued, or its dose is adjusted, reinitiate ceritinib with dose reduced by 150mg upon recovery to asymptomatic bradycardia or to a heart rate of 60bpm or above, with frequent monitoring. Discontinue permanently in the event of recurrence.

Hyperglycaemia

Persistent hyperglycaemia greater than 250mg/dL despite optimal anti-hyperglycaemic therapy	Withhold ceritinib until hyperglycaemia is adequately controlled, then reinitiate ceritinib with dose reduced by 150mg. If adequate glucose control cannot be achieved with optimal medical management, permanently discontinue ceritinib.

Other

Lipase or amylase elevation grade ≥3	Withhold ceritinib until lipase or amylase returns to grade ≤1, then reinitiate with dose reduced by 150mg.
Any grade treatment-related pneumonitis	Permanently discontinue ceritinib.
Severe (grade 3) or intolerable nausea, vomiting or diarrhoea despite optimal anti-emetic or anti-diarrhoeal therapy	Withhold ceritinib until improved. Then reinitiate ceritinib with dose reduced by 150mg.

Hepatic impairment

Ceritinib

ALT or AST elevation >5xULN with total bilirubin ≤2xULN	Withhold ceritinib until recovery to baseline or ≤3xULN, then reinitiate with dose reduced by one decrement.
ALT or AST elevation >3xULN with concurrent total bilirubin elevation >2xULN	Permanently discontinue ceritinib

REFERENCES

1. Cho, B et al; J Thorac Oncol 2017; 12 (9): 1357–1367 (ASCEND-8)