▸ **Uncommon** Pancreatitis

SIDE-EFFECTS, FURTHER INFORMATION **Gastro-intestinal effects** Manufacturer advises monitor for signs of gastro-intestinal toxicity and consider dose reduction or discontinuation of treatment.

Interstitial lung disease Manufacturer advises monitor patients who exhibit pulmonary symptoms and consider dose reduction or discontinuation of treatment.

● CONCEPTION AND CONTRACEPTION Manufacturer recommends effective contraception in women of childbearing potential during treatment and for up to 3 months after discontinuation of treatment.

● PREGNANCY Manufacturer advises avoid unless essential—no information available. See also *Pregnancy and reproductive function* in Cytotoxic drugs p. 938.

● BREAST FEEDING Manufacturer advises avoid—no information available.

● HEPATIC IMPAIRMENT Manufacturer advises caution in severe impairment (limited information available).
Dose adjustments Manufacturer advises reduce dose by approx. 33% in severe impairment (round to the nearest multiple of the 150 mg dosage strength).

● RENAL IMPAIRMENT Manufacturer advises caution in severe impairment—no information available.

● MONITORING REQUIREMENTS

▸ Manufacturer advises monitor fasting plasma-glucose concentration, amylase and lipase levels before treatment initiation and periodically thereafter as clinically indicated.

▸ Manufacturer advises measure baseline liver function, then monitor every 2 weeks for the first three months of treatment and monthly thereafter; if transaminases are elevated, more frequent monitoring should be performed as clinically indicated.

▸ Manufacturer advises monitor for pulmonary symptoms indicative of interstitial lung disease and pneumonitis—discontinue treatment if diagnosis confirmed; also monitor heart rate and blood pressure regularly.

● DIRECTIONS FOR ADMINISTRATION Manufacturer advises *Zykadia*® capsules should be taken with food at the same time each day—consult product literature for dosing information if patients are unable to take capsules with food.

● PATIENT AND CARER ADVICE Patients and carers should be counselled on the administration of capsules.
Missed doses If a dose is more than 12 hours late, the missed dose should not be taken and the next dose should be taken at the normal time.
Driving and skilled tasks Manufacturer advises patients and their carers should be counselled on the effects on driving and skilled tasks—increased risk of fatigue and vision disorders.

● NATIONAL FUNDING/ACCESS DECISIONS

NICE decisions

▸ **Ceritinib for previously treated anaplastic lymphoma kinase-positive non-small cell lung cancer (June 2016)** NICE TA395
Ceritinib (*Zykadia*®) is recommended, within its marketing authorisation, as an option for treating advanced anaplastic lymphoma kinase-positive non-small cell lung cancer in adults previously treated with crizotinib; only if the manufacturer provides the discount agreed in the patient access scheme.
www.nice.org.uk/guidance/ta395

▸ **Ceritinib for untreated ALK-positive non-small cell lung cancer (January 2018)** NICE TA500
Ceritinib (*Zykadia*®) is recommended, within its marketing authorisation, as an option for untreated anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer in adults, only if the manufacturer provides it with the discount agreed in the patient access scheme.
www.nice.org.uk/guidance/ta500

Scottish Medicines Consortium (SMC) decisions
SMC No. 1097/15
The *Scottish Medicines Consortium* has advised (December 2015) that ceritinib (*Zykadia*®) is accepted for use within NHS Scotland for the treatment of adults with anaplastic lymphoma kinase (ALK)-positive advanced non-small cell lung cancer previously treated with crizotinib. This advice is contingent upon the continuing availability of the patient access scheme in NHS Scotland or a list price that is equivalent or lower.

● MEDICINAL FORMS There can be variation in the licensing of different medicines containing the same drug.

Capsule
CAUTIONARY AND ADVISORY LABELS 21, 25
EXCIPIENTS: May contain Gelatin, propylene glycol
▸ **Zykadia** (Novartis Pharmaceuticals UK Ltd) ▼
Ceritinib 150 mg Zykadia 150mg capsules | 150 capsule PoM £4,923.45

Cobimetinib

11-Feb-2019

● DRUG ACTION Cobimetinib is a mitogen-activated protein kinase (MAPK) inhibitor.

● INDICATIONS AND DOSE

Treatment of BRAF V600 mutation-positive unresectable or metastatic melanoma (in combination with vemurafenib) (specialist use only)
▸ BY MOUTH
▸ Adult: 60 mg once daily for 21 days; subsequent cycles repeated after a 7-day interval, for dose adjustment due to side-effects—consult product literature

IMPORTANT SAFETY INFORMATION
RISKS OF INCORRECT DOSING OF ORAL ANTI-CANCER MEDICINES
See Cytotoxic drugs p. 938.

● CAUTIONS Left ventricular dysfunction · risk factors for bleeding

● INTERACTIONS → Appendix 1: cobimetinib

● SIDE-EFFECTS

▸ **Common or very common** Anaemia · basal cell carcinoma · chills · dehydration · diarrhoea · electrolyte imbalance · fever · haemorrhage · hyperglycaemia · hypertension · nausea · photosensitivity reaction · pneumonitis · serous retinopathy · skin reactions · vision disorders · vomiting

▸ **Uncommon** Rhabdomyolysis

● CONCEPTION AND CONTRACEPTION Manufacturer advises use of two effective contraceptive methods during treatment and for at least 3 months after stopping treatment.

● PREGNANCY Manufacturer advises avoid unless essential—toxicity in *animal* studies. See also *Pregnancy and reproductive function* in Cytotoxic drugs p. 938.

● BREAST FEEDING Manufacturer advises avoid—no information available.

● HEPATIC IMPAIRMENT Manufacturer advises caution.

● RENAL IMPAIRMENT Manufacturer advises caution in severe impairment—limited information available.

● MONITORING REQUIREMENTS

▸ Creatine kinase elevation Manufacturer advises baseline creatine kinase and creatinine levels should be measured before starting treatment, and then at monthly intervals during treatment or as clinically indicated—consult product literature if elevated.