Osimertinib

Indication
Treatment of locally advanced or metastatic non-small-cell lung cancer (NSCLC) for patients who test positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) T790M mutation and have had progressed after previous first line treatment with an EGFR-TK inhibitor.

(NICE TA416)

ICD-10 codes
Codes with a prefix C34

Regimen details

Day	Drug	Dose	Route
1-28	Osimertinib	80mg OD	PO

Cycle frequency
Continuously until disease progression or unacceptable toxicity.

Number of cycles
As above

Administration
Osimertinib is available as 40mg and 80mg tablets.

The dose should be taken once daily, at the same time each day, either with or without food. If a dose is missed it should be taken as soon as possible, however if it is less than 12 hours until the next scheduled dose the missed should be omitted.

Tablets should be swallowed whole with water and should not be crushed, split or chewed. If a patient is unable to swallow the tablet, it may be dispersed in 50 mL of non-carbonated water. It should be dropped in the water, without crushing, stirred until dispersed and immediately swallowed. An additional half a glass of water should be added to ensure that no residue remains and then immediately swallowed. No other liquids should be used. If administration via nasogastric tube is required, the same process as above should be followed but using volumes of 15 mL for the initial dispersion and 15 mL for the residue rinse. The resulting 30 mL of liquid should be administered via the nasogastric tube. This should be administered within 30 minutes of the addition of the tablets to water.

Pre-medication
Nil

Emetogenicity
This regimen has low emetic potential (no routine antiemetics required)

Additional supportive medication

Patients should be supplied with loperamide on commencing treatment. They should be advised to use loperamide immediately at the first sign of diarrhoea and continue for persistent diarrhoea until loose movements cease.

Patients should be advised to use a regular moisturiser.

Extravasation

N/A

Investigations – pre first cycle

Investigation	**Validity period** (or as per local practice)
FBC	14 days
U+E (including creatinine)	14 days
LFTs	14 days
Calcium	14 days
Magnesium	14 days
ECG	Baseline

Investigations – pre subsequent cycles

Clinical review is recommended after 2 weeks, and then at a maximum of 4 week intervals until stabilisation of toxicities. Once this is achieved this period may be extended.

Investigation	**Validity period** (or as per local practice)
FBC	Monthly
U+E (including creatinine)	Monthly
LFTs	Monthly
Calcium	Monthly
Magnesium	Monthly
ECG	As clinically indicated

Standard limits for administration to go ahead

If blood results not within range, authorisation to administer **must** be given by prescriber/ consultant

Investigation	**Limit**
Neutrophils	≥ 1.0 x 10^9/L
Platelets	≥ 100 x 10^9/L
Creatinine clearance (CrCl)	≥ 15mL/min
AST/ALT	< ULN
Bilirubin	< ULN

Dose modifications

If a dose reduction is necessary, the dose should be reduced to 40mg OD.

- **Haematological toxicity**

Patients should be monitored for haematological toxicity.

- **Renal impairment**

No dose modifications are required in patients with mild and moderate renal impairment. Limited data are available in patients with severe renal impairment. The safety and efficacy has not been established in patients with CrCl < 15mL/min or on dialysis.

- **Hepatic impairment**

Use with caution and close monitoring in patients with mild hepatic impairment (bilirubin ≤ ULN and AST/ALT 1-1.5 x ULN **or** bilirubin > 1.0 - 1.5 x ULN and any AST/ALT). Safety and efficacy has not been established in patients with moderate or severe hepatic impairment therefore use in patients with moderate or severe hepatic impairment is not recommended.

- **Other toxicities**

Interstitial Lung Disease (ILD) should be considered if a patient develops acute or worsening of respiratory symptoms including cough, dyspnoea and fever. Treatment should be interrupted pending evaluation. If ILD is diagnosed, treatment should be permanently discontinued.

QT prolongation:
Osimertinib should be administered with caution to patients who have a history of or predisposition for QTc prolongation, or who are taking other medicines known to prolong the QT interval (see interactions below). When using osimertinib in these patients, periodic monitoring of ECG and electrolytes is advised:

- If QTc interval > 500 ms (milliseconds) on at least 2 separate ECGs, withhold osimertinib until QTc interval < 481 ms (or recovery to baseline) correct any electrolyte abnormalities and recommence at reduced dose of 40mg OD.
- If QTc interval > 500 ms or > 60 ms change from baseline **and** accompanied by life-threatening signs of serious arrhythmia permanently discontinue osimertinib.

Other grade ≥ 3 reaction, including diarrhoea: Withhold treatment for up to 3 weeks. If resolved to ≤ grade 2, recommence at full dose or reduced dose. If no improvement after 3 weeks permanently discontinue osimertinib.

Adverse effects - for full details consult product literature/ reference texts

- **Serious side effects**

Myelosupression
Interstitial lung disease
QTc prolongation

- **Frequently occurring side effects**

Diarrhoea – may be severe
Rash, pruritis
Stomatitis

- **Other side effects**

Nail disorders

Significant drug interactions – for full details consult product literature/ reference texts

CYP3A4 inducers (e.g. rifampicin, carbamazepine, phenytoin, St. John's Wort) may decrease efficacy of osimertinib. Avoid co-administration. Concomitant use of St. Johns Wort is contraindicated.

CYP3A4 inhibitors (e.g. itraconazole) may increase plasma levels of osimertinib. Closely monitor for adverse reactions.

Breast Cancer Resistance Protein (BCRP) substrates: osimertinib is a competitive inhibitor of BCRP. If taking BCRP substrates, patients should be closely monitored for tolerability.

Additional comments

Osimertinib may cause foetal harm when administered to a pregnant woman.

References

- National Institute for Health and Clinical Excellence. NICE Technology Appraisal Guidance 416 accessed 1 Feb 2017 via www.nice.org.uk
- Summary of Product Characteristics Osimertinib (AstraZeneca) accessed 1 Feb 2017 via www.medicines.org.uk
- Tony S. Mok Osimertinib or Platinum–Pemetrexed in *EGFR* T790M–Positive Lung Cancer December 6, 2016 NEJM

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