Dacomitinib Monotherapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	Reimbursement Status
Monotherapy, for the first-line treatment of adult patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) with epidermal growth factor receptor (EGFR)-activating mutations	C34	00565a	CDS - 01/11/2019

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patients individual clinical circumstances.

Dacomitinib is administered once daily until disease progression or unacceptable toxicity.

Drug	Dose	Route	Cycle
Dacomitinib	45mg	PO	Continuous
Dacomitinib is available as 15mg, 30mg and 45mg tablets.			
Dacomitinib tablets should be swallowed with water and can be taken with or without food.			
Patients should be encouraged to take their dose at approximately the same time each day.			
In the case of a missed dose or if vomiting occurs, a replacement dose should not be taken. Normal dosing should be resumed at the next scheduled dose.			

ELIGIBILITY:

- Indications as above
- EGFR activating mutation status as demonstrated by a validated test method
- ECOG 0-1
- Adequate renal, hepatic and haematological status

CAUTION:

Use with caution in patients with

- History of, or currently suspected, diffuse non-infectious pneumonitis or interstitial lung disease

EXCLUSIONS:

- Known hypersensitivity to dacomitinib or its excipients

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Medical Oncologist

TESTS:

Baseline tests:

- Assessment of EGFR mutation status by an accurate and valid test
- Baseline staging scans
- FBC, renal, liver and bone profile

Regular tests:

- FBC, renal, liver and bone profile

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Table 1 shows the dose reduction levels recommended for dacomitinib
- Any dose modification should be discussed with a Consultant.

Table 1: Dacomitinib recommended dose reduction levels

Dose level	Dacomitinib
Recommended starting dose	45 mg
First dose reduction	30 mg
Second dose reduction	15 mg

Renal and Hepatic Impairment:

Table 2: Recommended dose modification of dacomitinib in renal and hepatic impairment

Severity	Renal Impairment	Hepatic Impairment
Mild - moderate	No dose adjustment is recommended	No dose adjustment is recommended
Severe	The recommended dose of dacomitinib has not been established for patients with severe renal impairment.	The starting dose of dacomitinib should be adjusted to 30 mg once daily. The dose may be increased to 45 mg once daily based on individual safety and tolerability after at least 4 weeks of treatment.

Management of adverse events:

Table 3: Recommended dose modification of dacomitinib for adverse events

Adverse reactions	Severity*	Dose modification
Interstitial lung disease (ILD/ Pneumonitis)	Any Grade	Withhold during ILD/Pneumonitis diagnostic evaluation. Permanently discontinue if ILD/Pneumonitis is confirmed
Diarrhoea	Grade 1	No dose modification required. Initiate appropriate medical treatment.
	Grade 2	Withhold if not improved to ≤ Grade 1 within 24 hours despite treatment; upon recovery to ≤ Grade 1, resume at the same dose level or consider reduced dose level
	Grade ≥3	Withhold until recovery ≤ Grade 1; then resume at a reduced dose level
Skin reactions	Grade 1	None**
	Grade 2	Withhold if not improved to ≤ Grade 1 within 72 hours despite treatment; upon recovery resume at the same dose level or consider reduced dose level
	Grade ≥3	Withhold until recovery ≤ Grade 1; then resume at a reduced dose level
Other	Grade 1-2	No dose modification required
	Grade ≥3	Withhold until recovery ≤Grade 2; then resume a reduced dose level

* National Cancer Institute Common Terminology Criteria for Adverse Events [NCI CTCAE] version 4

** Refer to local policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL: Minimal to low (**Refer to local policy).**

PREMEDICATIONS: Not required

OTHER SUPPORTIVE CARE:

- Medication may be required for management of diarrhoea **(Refer to local policy).**
- See local skin care policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

This medicinal product is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse reactions.

- **Interstitial Lung Disease (ILD):** Severe and fatal ILD/pneumonitis has been reported in patients treated with dacomitinib. Monitor patients for pulmonary symptoms indicative of ILD/pneumonitis. Withhold treatment and promptly investigate for ILD in patients who present with worsening of respiratory symptoms which may be indicative of ILD (e.g., dyspnea, cough, and fever). Permanently discontinue if ILD is confirmed.

- **Diarrhoea**: Diarrhoea, including severe diarrhoea, has been very commonly reported during treatment with dacomitinib. Proactive management of diarrhoea should start at the first sign of diarrhoea especially within the first 2 weeks of starting dacomitinib, including adequate hydration combined with anti-diarrhoeal medicinal products and continued until loose bowel movements cease for 12 hours. Anti-diarrhoeal medicinal products (e.g. loperamide) should be used and, if necessary, escalated to the highest recommended approved dose. Patients may require dosing interruption and/or dose reduction of therapy with dacomitinib. Patients should maintain adequate oral hydration and patients who become dehydrated may require administration of intravenous fluids and electrolytes.
- **Dermatologic Adverse Reactions:** Rash, erythematous and exfoliative skin reactions have been reported in patients treated with dacomitinib. See local skin care policy for the prevention and treatment of EGFR-inhibitor adverse skin reactions.
  Rash, erythematous and exfoliative skin conditions may occur or worsen in areas exposed to the sun. Advise patients to use protective clothing and sunscreen before exposure to the sun. Patients may require dosing interruption and/or dose reduction of therapy with dacomitinib. (See Table 4 for management).
- **Hepatotoxicity and increased transaminases**: There have been cases of hepatotoxicity reported in patients treated with dacomitinib in clinical studies. Therefore, periodic liver function testing is recommended. In patients who develop severe elevations in transaminases while taking dacomitinib, treatment should be interrupted.

DRUG INTERACTIONS:

- The concomitant use of proton pump inhibitors should be avoided with dacomitinib. Locally-acting antacids or H2 receptor antagonists can be used as an alternative. If using a H2-receptor antagonist, administer dacomitinib at least 6 hours before or 10 hours after taking an H2-receptor antagonist.
- The concomitant use of CYP2D6 substrates with dacomitinib increases the concentration of drugs that are CYP2D6 substrates, which may increase the risk of toxicities of these drugs. Avoid concomitant use with dacomitinib where minimal increases in concentration of the CYP2D6 substrate may lead to serious or life-threatening toxicities.
- Current drug interaction databases should be consulted for more information

REFERENCES:

- Wu Prof et al. Dacomitinib versus gefitinib as first-line treatment for patients with *EGFR* -mutation-positive non-small-cell lung cancer (ARCHER 1050): a randomised, open-label, phase 3 trial. Lancet Oncology, 2017-11-01, 18:11: 1454-1466
- Dacomitinib (Vizimpro®) Summary of Product Characteristics. Accessed June 2021. Available at: https://www.ema.europa.eu/en/documents/product-information/vizimpro-epar-product-information_en.pdf
- NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V3 2021. Available at: https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf

Version	Date	Amendment	Approved By
1	10/07/2019		Prof Maccon Keane
2	31/10/2019	Reimbursement status updated	NCCP
3	23/06/2021	Reviewed. Amended treatment table and dose modification in hepatic impairment.	Prof Maccon Keane

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.