Regimen Monograph

Regimen Name | Drug Regimen | Cycle Frequency | Premedication and Supportive Measures | Dose Modifications | Adverse Effects | Interactions | Drug Administration and Special Precautions | Recommended Clinical Monitoring | Administrative Information | References | Other Notes | Disclaimer

A - Regimen Name

DACO Regimen

Dacomitinib

Disease Site
Lung
Non-Small Cell

Intent
Palliative

Regimen Category
Evidence-Informed :

Regimen is considered appropriate as part of the standard care of patients; meaningfully improves outcomes (survival, quality of life), tolerability or costs compared to alternatives (recommended by the Disease Site Team and national consensus body e.g. pan-Canadian Oncology Drug Review, pCODR). Recommendation is based on an appropriately conducted phase III clinical trial relevant to the Canadian context OR (where phase III trials are not feasible) an appropriately sized phase II trial. Regimens where one or more drugs are not approved by Health Canada for any indication will be identified under Rationale and Use.

Rationale and Uses
For first-line treatment in patients with EGFR-mutation-positive non-small-cell lung cancer

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B - Drug Regimen

dacomitinib	45 mg	PO	Daily

(This drug is not currently publicly funded for this regimen and intent)

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

Other Supportive Care:

- Use of sunscreen and protective clothing is advised for patients who are exposed to the sun.
- Prophylactic treatment with doxycycline and a low-potency corticosteroid (e.g., alclometasone, hydrocortisone) may be beneficial in reducing the impact of dermatologic adverse events (Lacouture et al 2010, Lacouture et al 2016).
- Start proactive management of diarrhea at the first sign of diarrhea, especially within the first 2 weeks of starting treatment, including adequate hydration combined with antidiarrheal medications; continue until bowel movements have stopped for 12 hours.

Also refer to CCO Antiemetic Recommendations.

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E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated.

Use only in patients with EGFR exon 19 deletion or exon 21 L858R substitution mutations confirmed using a validated test.

Dosage with toxicity

Dose Level	Dacomitinib Dose (mg/day)
0	45
-1	30
-2	15
-3	Discontinue

Toxicity	Grade	Action
Diarrhea	Grade 1	Continue dose. Treat with anti-diarrheal medications (e.g., loperamide) and oral fluids.
	Grade 2	Continue dose. Treat with anti-diarrheal medications (e.g., loperamide) and oral fluids. If not improved to Grade ≤ 1 within 24 hours, hold dose. Then resume at same dose.* If recurs, hold dose. Then consider 1 dose level ↓.*
	Grade ≥ 3	Hold dose. Treat with anti-diarrheal medications (e.g., loperamide), oral / IV fluids, and / or electrolytes. Resume at 1 dose level ↓.*
Skin-related adverse reactions	Grade 1 or 2	Continue dose. Treat as clinically indicated (e.g. antibiotics, topical steroids, and/or emollients). If Grade 2 rash persists, hold dose. Then resume at the same dose level or at 1 dose level ↓.*

	Grade ≥ 3	Hold dose. Treat as clinically indicated (e.g. broad spectrum oral or intravenous antibiotics and topical steroids). Resume at 1 dose level ↓.*
Keratitis	Grade 2, 3 or 4	Hold dose. Refer patient to ophthalmologist. Resume at 1 dose level ↓.*
Other toxicity	Intolerable Grade 2	Hold dose. Resume at 1 dose level ↓.*
	Grade ≥ 3	Hold dose. Resume at 1 dose level ↓.*
Interstitial Lung Disease (ILD)/Pneumonitis	Any	Hold dose if suspected. Discontinue if confirmed.

*Do not restart treatment until toxicity resolved to Grade ≤ 1; for other Grade ≥ 3 toxicity, treatment may be restarted if toxicity resolved to Grade ≤ 2.

Hepatic Impairment

No starting dose adjustments required when administering dacomitinib to patients with mild, moderate or severe hepatic impairment (Child-Pugh class A, B or C).

Renal Impairment

Renal Impairment	Dacomitinib Starting Dose
Mild or Moderate (CrCl ≥ 30 mL/min)	No dose adjustment required.
Severe (CrCl < 30 mL/min)	No data available.

Dosage in the Elderly

No starting dose adjustment required in patients ≥ 65 years of age. Patients ≥ 65 years experienced more serious adverse events (AEs), more Grade 3 AEs, and more permanent treatment

discontinuations due to AEs compared to patients < 65 years. Higher incidences of decreased appetite, rash, mucosal inflammation and asthenia were observed in patients ≥ 65 years of age compared to younger patients.

Dosage based on gender

Gender has no effect on the steady state clearance of dacomitinib based on population pharmacokinetic analyses.

In clinical trials, female patients experienced more Grade 3 AEs, dose reductions, dose interruptions, and treatment discontinuation. The following adverse events were reported at a greater frequency by female patients than male patients: weight decreased, conjunctivitis and alopecia.

Dosage based on ethnicity

There was no clinically relevant difference between Asian and non-Asian ethnicity in the steady state clearance of dacomitinib based on population pharmacokinetic analyses.

In clinical trials, non-Asians experienced more serious adverse events. Non-Asian patients reported more frequently the following AEs: rash, dry skin, dyspnea, mucosal inflammation, asthenia, and skin fissures. The following AEs were experienced more frequently in Asian patients: diarrhea, dermatitis acneiform, decreased appetite, stomatitis, paronychia, weight decreased, upper respiratory tract infection, AST increased, ALT increased and mouth ulceration.

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F - Adverse Effects

Refer to dacomitinib drug monograph(s) for additional details of adverse effects.

Very common (≥ 50%)	Common (25-49%)	Less common (10-24%)	Uncommon (< 10%), but may be severe or life-threatening
• Diarrhea (may be severe) • Rash, pruritus, dry skin (may be	• Abnormal electrolyte(s) • Anorexia, weight loss	• ↑ LFTs (may be severe) • Conjunctivitis (may be severe)	• Pneumonitis

severe) • Mucositis (generally mild) • Nail disorder (may be severe)		• Alopecia • Cough, dyspnea • Nausea, vomiting (generally mild) • Hand-foot syndrome (HFS) (may be severe) • Fatigue • Musculoskeletal pain • Insomnia	

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G - Interactions

Refer to dacomitinib drug monograph(s) for additional details.

- Avoid concomitant use of proton pump inhibitors due to risk of reduced efficacy of dacomitinib. Antacids may be used, if required. If needed, administer dacomitinib at least 2 hours before or 10 hours after H2-blockers.
- Avoid concomitant use of CYP2D6 substrates with narrow therapeutic indices due to serious or life-threatening toxicities.
- Use alternatives for drugs with active metabolites formed by CYP2D6.

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H - Drug Administration and Special Precautions

Refer to dacomitinib drug monograph(s) for additional details.

Administration

- Administer dacomitinib with or without food, under consistent conditions (i.e. always on an empty stomach or always after the same type of meal).
- Tablets should be swallowed whole. Do not chew or crush the tablets.
- If a dose is missed, the dose should be skipped and the next dose should be taken at the next scheduled time.
- If the patient vomits after taking the dose, they should not take an extra dose. The next dose should be taken on the next day at the usual time.
- Store at room temperature (15 to 30ºC) in the original package.

Contraindications

- Patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container

Warning/Precautions

- Patients experiencing fatigue should exercise caution when driving or operating machinery.
- The safety of dacomitinib in patients with cardiac impairment or with a history or presence of brain or meningeal metastases is not known.
- Tablets contain lactose; carefully consider use in patients with hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption.

Pregnancy/Lactation

- Dacomitinib is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least **2 months** after the last dose.
- Breastfeeding is not recommended during treatment and for at least **2 months** after the last dose.
- Fertility effects are unknown.

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I - Recommended Clinical Monitoring

Treating physicians may decide to monitor more or less frequently for individual patients but should always consider recommendations from the product monograph.

Recommended Clinical Monitoring

- Electrolytes, including potassium, calcium and magnesium, especially in patients at risk of dehydration; Baseline and as clinically indicated
- Liver function tests; Baseline and as clinically indicated
- Renal function tests, especially in patients at risk of dehydration; Baseline and as clinically indicated
- Clinical toxicity assessment for GI (including dehydration), skin/nail, ocular, and respiratory effects (including pneumonitis); As clinically indicated

- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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K - References

Dacomitinib drug monograph, Ontario Health (Cancer Care Ontario).

Lacouture ME, Keefe DM, Sonis S, et al. A phase II study (ARCHER 1042) to evaluate prophylactic treatment of dacomitinib-induced dermatologic and gastrointestinal adverse events in advanced non-small-cell lung cancer. Ann Oncol. 2016;27(9):1712–1718.

Lacouture, ME, Mitchell EP, Piperdi B et al. Skin toxicity evaluation protocol with panitumumab (STEPP), a phase II, open-label, randomized trial evaluating the impact of a pre-emptive skin treatment regimen on skin toxicities and quality of life in patients with metastatic colorectal cancer. J Clin Oncol 2010; 28: 1351-7.

Wu YL, Cheng Y, Zhou X, 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 Oncol 2017;18:1454-66.

PEBC Advice Documents or Guidelines

- Therapy for Stage IV Non-Small-Cell Lung Cancer With Driver Alterations: ASCO and OH(CCO) Joint Guideline Update

June 2022 Updated dose modifications (hepatic impairment) and interactions sections

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M - Disclaimer

Regimen Abstracts

A Regimen Abstract is an abbreviated version of a Regimen Monograph and contains only top level information on usage, dosing, schedule, cycle length and special notes (if available). It is intended for healthcare providers and is to be used for informational purposes only. It is not intended to constitute or be a substitute for medical advice, and all uses of the Regimen Abstract are subject to clinical judgment. Such information is provided on an "as-is" basis, without any representation, warranty, or condition, whether express, or implied, statutory or otherwise, as to the information's quality, accuracy, currency, completeness, or reliability, and Cancer Care Ontario disclaims all liability for the use of this information, and for any claims, actions, demands or suits that arise from such use.

Information in regimen abstracts is accurate to the extent of the ST-QBP regimen master listings, and has not undergone the full review process of a regimen monograph. Full regimen monographs will be published for each ST-QBP regimen as they are developed.

Regimen Monographs

Refer to the New Drug Funding Program or Ontario Public Drug Programs websites for the most up-to-date public funding information.

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Some Formulary documents, such as the medication information sheets, regimen information sheets and symptom management information (for patients), are intended for patients. Patients should always consult with their healthcare provider if they have questions regarding any information set out in the Formulary documents.

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