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

AFAT Regimen

Afatinib

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

First-line monotherapy for patients with advanced or metastatic EGFR-positive NSCLC. Not funded for patients with disease progression on prior EGFR TKI therapy, or maintenance therapy for NSCLC (see EAP criteria for details).

Safety and efficacy have not been established in patients with EGFR mutations other than exon 19-deletions (DEL19) and the exon 21 L858R point mutation.

Supplementary Public Funding

AFAtinib
Exceptional Access Program (AFAtinib - For first-line monotherapy in patients with advanced or metastatic non-small cell lung cancer (NSCLC), according to specific criteria) (EAP Website)

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B - Drug Regimen

AFAtinib	40 mg	PO	Daily

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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:

- Patients must be adequately educated about the management of diarrhea and provided with loperamide when starting afatinib.
- Since sunlight can exacerbate skin rash reactions, patients should be advised to avoid the sun or use adequate sun protection.
- Also refer to CCO Antiemetic Recommendations.
- **Screen for hepatitis B virus in all cancer patients starting systemic treatment.** Refer to the hepatitis B virus screening and management guideline.

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E - Dose Modifications

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

EGFR mutation-positive status must be confirmed by a validated test before treatment in patients with adenocarcinoma of the lung.

Dosage with toxicity

Dose Level	Afatinib Dose (mg/day)
0	40
-1	30
-2	20
-3	Discontinue

Do not re-escalate previously reduced doses.

Refer to G - Interactions section for dosing recommendations when co-administered with P-gp inhibitors or inducers.

Table A: Dose Modifications for Toxicity Other than Diarrhea

Toxicity Grade	Action*
Grade 1 or 2	Maintain same dose
Prolonged (≥ 7 days) or intolerable grade 2 (including rash, nausea, vomiting and renal impairment) despite adequate symptomatic management** Or Grade 3 or 4**	Hold until ≤ grade 1 then restart at ↓ 1 dose level For skin reactions, consider referral to a specialist.
Keratitis	Hold and refer to ophthalmologist; consider discontinuation
Interstitial Lung Disease	Hold; investigate and treat patient appropriately. Discontinue if confirmed.

LVEF below institution's lower limit of normal Or Cardiac signs and symptoms	Hold and refer to cardiologist; consider discontinuation
Severe hepatic impairment during treatment	Discontinue
Gastrointestinal perforation	
Bullous, blistering or exfoliating skin conditions, as well as suspected toxic epidermal necrolysis or Stevens-Johnson syndrome	

*Permanently discontinue afatinib for any toxicity not recovered to ≤ grade 1 within 14 days or if cannot tolerate 20 mg/day.

**Consider holding afatinib for worsening hepatic function; discontinue if severe hepatic impairment.

Table B: Management of Diarrhea

Patients should have an adequate supply of loperamide readily available at the start of and during treatment.

Diarrhea Grade	Action
Any	Take 4mg (2 tablets) of loperamide immediately, followed by 2mg (1 tablet) with every loose bowel movement up to maximum daily dose of 20mg (10 tablets). Continue until resolved for ≥ 12 hours. Give oral hydration (1.5L/m^2/day plus equivalent of actual fluid loss) and electrolytes especially for ≥ grade 2. Hospitalize for IV fluids if patients becomes dehydrated. Avoid lactose containing products.
Grade 1 or Grade 2 < 48 hrs	Maintain same afatinib dose.
Grade 2 lasting ≥ 48 hours despite adequate anti-diarrheal treatment or Grade 3	Hold afatinib until grade ≤ 1 then restart at ↓ 1 dose level. Discontinue if not recovered to ≤ grade 1 within 14 days.
Grade 4	Discontinue

Hepatic Impairment

Similar exposure was observed in single-dose study in normal hepatic function versus mild/moderate hepatic impairment.

Hepatic Impairment	Afatinib Starting Dose / Action
Mild (Child Pugh A)	No dose adjustment required. Monitor closely for toxicity.
Moderate (Child Pugh B)	
Severe (Child Pugh C)	Do not treat

Renal Impairment

Higher exposure of afatinib was observed in renal impairment, which may increase the risk of developing adverse events. Monitor patients closely for toxicities.

CrCl (mL/min)	Afatinib Starting Dose
≥ 60	No adjustment required
30-59	No adjustment required; monitor for adverse reactions
15-29	30 mg daily
< 15 or on dialysis	Do not treat (not studied)

Dosage in the Elderly

No dose adjustment required. Elderly patients are more likely to experience severe adverse events, especially diarrhea. Monitor these patients closely for toxicities.

Dosage based on gender:

Higher exposure was observed in female patients as well as patients with lower body weight, which may increase the risk of developing adverse events. Monitor closely for toxicities.

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F - Adverse Effects

Refer to afatinib 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 severe) • Mucositis (may be severe) • Paronychia (may be severe)	• Anorexia, weight loss • Nausea, vomiting	• Epistaxis • Insomnia • Cough • Infection (may be severe) • Headache • Musculoskeletal pain • Constipation • Alopecia • ↑ LFTs (may be severe) • Abnormal electrolytes (↓ K) • Dizziness • Conjunctivitis (may be severe) • Rhinorrhea	• Cardiotoxicity • Venous thromboembolism • Hand-foot syndrome • Stevens-Johnson syndrome • Toxic epidermal necrolysis • GI perforation • Pancreatitis • Renal failure • Pneumonitis

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G - Interactions

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

- Avoid concomitant use with strong P-glycoprotein (P-gp) inhibitors as they may increase afatinib exposure. If concomitant use is unavoidable, monitor for toxicity. Consider reducing afatinib dose if combination is not tolerated.*
- Avoid concomitant use with strong P-gp inducers as they may decrease afatinib exposure. May consider afatinib dose adjustment for patients requiring chronic therapy with a P-gp inducer.**

*The US Prescribing Information suggests reducing afatinib dose by 10mg and monitoring for toxicity.

**The US Prescribing Information suggests increasing afatinib dose by 10 mg, as tolerated, when used with chronic concomitant P-gp inducer therapy. Then, reducing afatinib back to the original dose 2 to 3 days after discontinuing the P-gp inducer.

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H - Drug Administration and Special Precautions

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

Administration:

- Tablets should be swallowed whole with a glass of water and not crushed or chewed.
- Afatinib should be taken on an empty stomach, at least 1 hour before or 3 hours after eating.
- If a dose is missed, afatinib should be taken as soon as it is remembered. If there are less than 8 hours until the next scheduled dose, patients should skip the missed dose and take the next one as scheduled.
- If vomiting occurs after taking the dose, patients should not take a replacement tablet. The next dose should be taken at its scheduled time.
- Patients should have an adequate supply of loperamide readily available at the start of, and throughout therapy.
- Stored at 15 - 30^{O}C;
- Blister card should be stored in the original package away from moisture and light;
- Only one pouch should be opened at a time. All the tablets in a blister card should be consumed, before opening a new one.

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components.

Warnings/Precautions:

- Afatinib is not recommended for patients with:
  - Significant or recent gastrointestinal disorders with diarrhea as a major symptom (e.g. Crohn's disease, malabsorption or any other relevant disorder).
  - A history of interstitial lung disease
  - Severe hepatic or renal impairment
  - With hereditary galactose intolerance, severe lactase deficiency or glucose-galactose malabsorption as afatinib tablets contains lactose.
- Use with caution in patients with:
  - Abnormal LVEF or those with significant cardiac history as afatinib has not been studied in these patient populations.
  - A history of keratitis, ulcerative keratitis, severe dry eye or those who use contact lenses.
- Blurred vision and keratitis have been observed; caution is required when driving or operating machinery.

Pregnancy/Lactation:

- This regimen is not recommended for use in pregnancy. Adequate contraception should be used by patients and their partners while on treatment and after the last treatment dose. Recommended methods and duration of contraception may differ depending on the treatment. Refer to the drug monograph(s) for more information.
- Breastfeeding is not recommended during this treatment and after the last treatment dose. Refer to the drug monograph(s) for recommendations after the last treatment dose (if available).
- Fertility effects: Probable

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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.

Refer to the hepatitis B virus screening and management guideline for monitoring during and after treatment.

Recommended Clinical Monitoring

- Liver function tests; baseline and at each visit, more frequently in patients with hepatic impairment
- Renal function tests and electrolytes; baseline and at each visit (especially in patients at high risk of dehydration)
- LVEF for patients with cardiac risk factors or conditions that can affect LVEF; baseline and as clinically indicated
- Clinical toxicity assessment of skin and nails, diarrhea, mucositis and other GI, respiratory, ophthalmic, cardiac effects and hypersensitivity/immune reactions; at each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

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J - Administrative Information

Outpatient prescription for home administration

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K - References

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

Sequist LV, Yang JC, Yamamoto N, et al. Phase III study of afatinib or cisplatin plus pemetrexed in patients with metastatic lung adenocarcinoma with EGFR mutations. J Clin Oncol 2013;31(27):3327-34. 3.

Soria JC, Felip E, Cobo M, et al.; LUX-Lung 8 Investigators. Afatinib versus erlotinib as second-line treatment of patients with advanced squamous cell carcinoma of the lung (LUX-Lung 8): an open-label randomised controlled phase 3 trial. Lancet Oncol. 2015 Aug;16(8):897-907.

Yang JC, Shih JY, Su WC, et al. Afatinib for patients with lung adenocarcinoma and epidermal growth factor receptor mutations (LUX-Lung 2): a phase 2 trial. Lancet Oncol 2012;13(5):539-48.

PEBC Advice Documents or Guidelines

- Use of the EGFR Inhibitors Gefitinib, Erlotinib, Afatinib, Dacomitinib or Icotinib in the Treatment of NSCLC
- Systemic Treatment for Patients with Advanced Non-Small Cell Lung Cancer
- Therapy for Stage IV Non-Small-Cell Lung Cancer With Driver Alterations: ASCO and OH(CCO) Joint Guideline Update

April 2024 Updated pregnancy/breastfeeding section

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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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