## 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
Monotherapy for treatment of EGFR tyrosine kinase inhibitor naive patients with metastatic (including cytologically proven pleural effusion) adenocarcinoma of the lung with activating EGFR mutations(s). Not funded for patients with disease progression on prior EGFR TKI therapy (see EAP funding 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.

Monotherapy for the treatment of patients with locally advanced or metastatic non-small cell lung cancer of squamous histology who progressed after platinum-based chemotherapy (not currently publicly funded for this indication).
Supplementary Public Funding

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

# B - Drug Regimen

<table>
<thead>
<tr>
<th>AFAtinib</th>
<th>40 mg</th>
<th>PO</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Outpatient prescription in 20, 30 or 40 mg tablets)</td>
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<td></td>
</tr>
</tbody>
</table>

# C - Cycle Frequency

**CONTINUOUS TREATMENT**

Until disease progression or unacceptable toxicity.

# D - Premedication and Supportive Measures

**Antiemetic Regimen:** Minimal

**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.

# E - Dose Modifications

Doses should be modified according to the protocol by which the patient is being treated. The following recommendations have been adapted from clinical trials or product monographs and could...
be considered.

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

**Dosage with toxicity**

Dose levels: 40 mg, 30 mg, 20 mg
Do not re-escalate previously reduced doses.

**Table A: Dose Modifications for Toxicity Other than Diarrhea**

<table>
<thead>
<tr>
<th>Toxicity Grade</th>
<th>Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 or 2 related organ</td>
<td>Maintain same dose</td>
</tr>
<tr>
<td>Prolonged (≥ 7 days) or intolerable grade 2 related organ/non-hematologic despite adequate symptomatic management Or Grade 2 creatinine ↑</td>
<td>Hold until ≤ grade 1 then ↓ 1 dose level</td>
</tr>
<tr>
<td>Grade 3 or 4 related organ/ non-hematologic</td>
<td>Hold until ≤ grade 1 then ↓ 1 dose level</td>
</tr>
<tr>
<td>Keratitis</td>
<td>Hold and refer to ophthalmologist; consider discontinuation</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>Hold; investigate and treat patient appropriately. Discontinue if confirmed.</td>
</tr>
<tr>
<td>LVEF below institution’s lower limit of normal Or Cardiac signs and symptoms</td>
<td>Hold and refer to cardiologist; consider discontinuation</td>
</tr>
<tr>
<td>Severe hepatic impairment during treatment, Bullous, blistering, exfoliating or other severe skin reactions</td>
<td>Discontinue</td>
</tr>
<tr>
<td>Any toxicity not recovered to ≤ grade 1 within 14 days of afatinib hold</td>
<td>Discontinue</td>
</tr>
</tbody>
</table>

**Table B: Management of Diarrhea**

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

<table>
<thead>
<tr>
<th>Diarrhea grade</th>
<th>Action</th>
</tr>
</thead>
</table>
| Any grade diarrhea              | 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/m²/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.

<table>
<thead>
<tr>
<th>Grade 1 or Grade 2 &lt; 48 hrs</th>
<th>Maintain same afatinib dose.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 2 lasting ≥ 48 hours despite adequate anti-diarrheal treatment or Grade 3</td>
<td>Hold afatinib until grade ≤ 1 then ↓ 1 dose level. Discontinue if not recovered to ≤ grade 1 within 14 days</td>
</tr>
<tr>
<td>Grade 4 or Grade 2-3 ≥ 14 days despite adequate hydration and afatinib discontinuation</td>
<td>Discontinue</td>
</tr>
</tbody>
</table>

**Hepatic Impairment**

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

<table>
<thead>
<tr>
<th>Hepatic Impairment</th>
<th>Starting Dose / Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild (Child Pugh A)</td>
<td>No dose adjustment recommended.</td>
</tr>
<tr>
<td></td>
<td>Monitor closely for toxicity.</td>
</tr>
<tr>
<td>Moderate (Child Pugh B)</td>
<td></td>
</tr>
<tr>
<td>Severe (Child Pugh C)</td>
<td>Do not treat</td>
</tr>
</tbody>
</table>

**Renal Impairment**

Higher exposure was observed in renal impairment, which may present a higher risk of adverse events. Monitor patients closely for toxicities.
**eGFR* (ml/min)** | **Starting dose / action**
---|---
≥ 30 | no dosage adjustment recommended; monitor closely for toxicity
15 - 29 | 30 mg daily
< 15 or on dialysis | Do not treat (not studied)

*using MDRD formula (per product monograph)

**Dosage in the Elderly**

No dose adjustment recommended. 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 present a higher risk of 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

<table>
<thead>
<tr>
<th>Very common (≥ 50%)</th>
<th>Common (25-49%)</th>
<th>Less common (10-24%)</th>
<th>Uncommon (&lt; 10%), but may be severe or life-threatening</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Diarrhea (may be severe)</td>
<td>• Anorexia, weight loss</td>
<td>• Epistaxis</td>
<td>• Cardiotoxicity</td>
</tr>
<tr>
<td>• Rash (may be severe)</td>
<td>• Nausea, vomiting</td>
<td>• Cough</td>
<td>• Venous thromboembolism</td>
</tr>
<tr>
<td>• Mucositis (may be severe)</td>
<td></td>
<td>• Infection</td>
<td>• Hand-foot syndrome</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Headache</td>
<td>• Pancreatitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Musculoskeletal pain</td>
<td>• Renal failure</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Insomnia</td>
<td></td>
</tr>
</tbody>
</table>
• Paronychia  
  (may be severe)

• Constipation  
  • Alopecia  
  • Increased LFTs (may be severe)  
  • Abnormal electrolytes (hypokalemia)  
  • Dizziness  
  • Conjunctivitis (may be severe)

• Pneumonitis

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**G - Interactions**

Refer to [afatinib](#) drug monograph(s) for additional details

- Smoking and alcohol consumption had no significant effects on afatinib pharmacokinetics, while food significantly decreased drug exposure.
- Avoid strong inducers and inhibitors of P-gp (if possible) as these may significantly affect afatinib exposure. Caution and monitor if must use together.

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**H - Drug Administration and Special Precautions**

Refer to [afatinib](#) drug monograph(s) for additional details

**Administration:**

- Tablets are swallowed whole with a glass of water. Do not crush or chew.
- 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, skip the missed dose and take the next one as scheduled.
- If vomiting occurs after taking the dose, do not give a replacement tablet. Take the next dose at its scheduled time.
- Patients should have an adequate supply of loperamide readily available at the start of, and throughout therapy.
- Store at 15 - 30°C;
Store the blister card in the original package away from moisture and light;
Open only one pouch at a time until all the tablets in the blister card are consumed, before opening a new one.

Contraindications:

- Patients who have a hypersensitivity to this drug or any of its components;
- Patients with hereditary galactose intolerance, Lapp lactase deficiency, or glucose-galactose malabsorption;
- Patients with significant or recent gastrointestinal disorders with diarrhea as a major symptom (e.g. Crohn's disease, malabsorption or any other relevant disorder);
- Patients with a history of Interstitial Lung Disease (ILD);
- Patients with severe hepatic or renal impairment.

Warnings/precautions:

- Use with caution in patients with higher exposure (females, low body weight, renal impairment) and monitor for toxicity;
- Use with caution in patients with abnormal LVEF or those with significant cardiac history;
- Blurred vision and keratitis have been observed; caution is required when driving or operating machinery;
- Use with caution patients with a history of keratitis, ulcerative keratitis, severe drug eye or those who use contact lenses.

Pregnancy & Lactation:

- Afatinib is not recommended for use in pregnancy. Adequate contraception should be used by both sexes during treatment, and for at least 2 weeks after the last dose.
- Breastfeeding is not recommended during treatment and for at least 2 weeks after the last dose.
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**

- Liver function tests; baseline and at each visit
- 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; baseline and as clinically indicated
- Clinical toxicity assessment of diarrhea, skin and nails, mucositis and other GI, respiratory, ophthalmic, 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, Cancer Care Ontario.


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**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

August 2017 updated dosage with renal impairment and adverse effects sections

M - Disclaimer

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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