Regimen Monograph

A - Regimen Name

OSIM Regimen

Osimertinib

Disease Site
Lung
Non-Small Cell

Intent
Adjuvant

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 adjuvant treatment in patients with completely resected epidermal growth factor receptor (EGFR) mutation-positive NSCLC

Supplementary Public Funding
osimertinib
Exceptional Access Program (osimertinib - For adjuvant therapy after tumour resection in patients with stage IB-IIIA (AJCC 7th edition, or equivalent) NSCLC whose tumours have EGFR exon 19 deletions or exon 21 (L858 R) substitution mutations) (EAP Website)

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B - Drug Regimen

osimertinib	80 mg	PO	Daily

Start within 10 weeks of complete surgical resection if adjuvant chemotherapy was not used OR within 26 weeks of surgical resection if adjuvant chemotherapy was administered.

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C - Cycle Frequency

CONTINUOUS TREATMENT

Until disease progression or unacceptable toxicity, up to a maximum of 3 years

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D - Premedication and Supportive Measures

Antiemetic Regimen: Minimal – No routine prophylaxis; PRN recommended

- 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.

Other Supportive Care:

- Regular application of moisturizers to skin and nails, practice of good hand hygiene, and keeping hands dry help prevent and control skin and nail adverse effects.

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E - Dose Modifications

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

A validated test is required to identify EGFR mutation-positive status prior to treatment.

Electrolyte abnormalities should be corrected prior to treatment.

Dosage with toxicity

Dose Level	Osimertinib Dose (mg/day)
0	80
-1	40
-2	Discontinue

Toxicity	Dose Modification
ILD/pneumonitis	Hold and investigate. Discontinue permanently if confirmed.
Asymptomatic LVEF < 50% and absolute decrease of 10% from baseline	Hold for up to 4 weeks. If recovery to baseline, restart. If no recovery to baseline, discontinue permanently.
QTc interval > 500 msec on at least 2 separate ECGs	Hold until QTc interval is < 481 msec or recovery to baseline if baseline is ≥ 481 msec. Then restart at 1 dose level ↓.
QTc interval prolonged with signs/symptoms of serious arrhythmia (e.g. Torsade de pointes, polymorphic VT) OR Symptomatic congestive heart failure	Discontinue permanently.
Signs & symptoms suggestive of keratitis	Refer promptly to an ophthalmology specialist. For ≥ grade 3 toxicity, also refer to action below.
Signs and symptoms suggestive of aplastic anemia	Hold if suspected; discontinue if confirmed.
Signs and symptoms of Stevens-Johnson syndrome, Toxic epidermal necrolysis	Hold if suspected; discontinue if confirmed.

Signs and symptoms of erythema multiforme	Hold if suspected; consider discontinuing if confirmed. (Discontinue for erythema multiforme major.)
Other ≥ grade 3 toxicity	Hold for up to 3 weeks. If recovery to ≤ grade 2, restart at the same dose or at 1 dose level ↓. If no recovery, discontinue permanently.

Hepatic Impairment

Hepatic Impairment	Osimertinib Dose
Mild (total bilirubin ≤ ULN and AST > ULN OR total bilirubin 1-1.5 x ULN and any AST) or Moderate (total bilirubin 1.5 to 3 x ULN and any AST)	No dosage adjustment required.
Severe	No data; use with caution.

Renal Impairment

Renal Impairment (Creatinine Clearance)	Osimertinib Dose
Mild to moderate (30 to <60 mL/min)	No dosage adjustment required.
Severe (15 to < 30 mL/min)	No dosage adjustment required. Use with caution.
End-stage renal disease (<15 mL/min) or dialysis	No data.

Dosage in the Elderly

No dosage adjustment is required.

No overall differences in efficacy or predicted steady state exposure of osimertinib were observed between patients ≥ 65 years of age and younger patients.

Patients ≥ 65 years of age experienced more ≥ Grade 3 adverse reactions compared to younger patients and had more reported adverse reactions that led to drug dose interruptions or reductions.

Dosage based on ethnicity

No dosage adjustment required due to ethnicity.

In clinical trials, the incidence of ILD was higher in Japanese patients compared to other Asian and non-Asian patients.

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F - Adverse Effects

Refer to osimertinib 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 • Rash, dry skin (may rarely be severe)	• Nail disorder • Mucositis	• Anorexia • Cough, dyspnea • Nausea, vomiting • Fatigue • Constipation • Musculoskeletal pain • Headache	• QT interval prolonged • Cardiotoxicity • Venous thromboembolism • Eye disorders • Pneumonitis • Bronchiolitis obliterans organizing pneumonia • Myelosuppression • Stevens-Johnson syndrome • Toxic epidermal necrolysis • Erythema multiforme • Cutaneous vasculitis • Creatinine increased • ↑ LFTs

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G - Interactions

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

- Avoid co-administration with strong CYP3A4 inducers as reduced osimertinib concentration and/or efficacy is possible. If coadministration is unavoidable, closely monitor therapy and increase osimertinib dose to 160mg daily during concurrent use. Continue this dose for 3 weeks after discontinuation of the strong CYP3A4 inducer. Then, resume osimertinib dose at 80mg daily.
- Monitor closely when co-administered with BCRP or P-gp substrates with narrow therapeutic indices, due to increased risk of substrate toxicity.
- Avoid drugs that may prolong the QT interval and those that may disrupt electrolyte levels given increased risk of QT prolongation.

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H - Drug Administration and Special Precautions

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

Administration

- Osimertinib may be taken orally with or without food at the same time each day.
- The tablet should be swallowed whole with water and not crushed, split or chewed.
- If a dose is missed, it may be taken within 12 hours. If there are less than 12 hours until the next dose, the missed dose should be skipped and the next dose should be taken at the scheduled time.
- If the patient has difficulty swallowing, the tablet may be dispersed in 50 ml of non-carbonated water (room temperature) and swallowed immediately. An additional 50 ml of water should be added to capture drug residue and immediately swallowed. No other liquids should be added.
- For nasogastric administration, the tablet may be dispersed in 15 mL of noncarbonated water; using an additional 15 mL of water for residue rinses. The 30 mL of liquid should be administered within 30 minutes via the nasogastric tube and flush appropriately as per the nasogastric tube manufacturer's instructions.
- Store tablets at room temperature (15-30^{o}C).

Contraindications

- Patients who are hypersensitive to this drug or to ingredients in the formulation or component in the container

Other Warnings/Precautions

- Not recommended in patients with congenital long QT syndrome or those taking other medications know to prolong QTc
- Patients at risk for prolonged QTc such as those with cardiac disease, history of arrhythmias, electrolyte disturbances or conditions leading to electrolyte disturbances, bradycardia, acute neurological events, diabetes mellitus and autonomic neuropathy should be monitored closely and electrolyte abnormalities corrected prior to treatment.
- Patients with abnormal LVEF, significant cardiac history, significant rhythm and conduction abnormalities, or resting QTc > 470 msec were excluded from clinical trials.
- Exercise caution in patients with cardiac risk factors and those with conditions that can affect LVEF.
- Patients with a history of ILD/pneumonitis, evidence of clinically active ILD or those with radiation pneumonitis requiring steroids were excluded from clinical trials.
- Ocular events have been reported. Contact lens use is risk factor for ocular toxicity, including keratitis. Caution should be used when driving or operating machinery in patients who experience visual disturbances.

Pregnancy and 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: Documented in animals

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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

- CBC; Baseline, at each visit, and as clinically indicated
- Liver function tests; Baseline, at each visit, and as clinically indicated
- Renal function tests; Baseline and at each visit; more frequent in patients with severe renal impairment
- Electrolytes (calcium, potassium and magnesium), especially in patients at risk of electrolyte abnormalities; Baseline, at each visit, and as clinically indicated
- ECG; Baseline and as clinically indicated
- LVEF in patients with cardiac risk factors or those who develop cardiac signs/symptoms during treatment; Baseline, during treatment*, and as clinically indicated
- Clinical toxicity assessment for GI, skin and respiratory effects, signs and symptoms of CHF, thromboembolism and ocular effects; At each visit
- Grade toxicity using the current NCI-CTCAE (Common Terminology Criteria for Adverse Events) version

*LVEF was monitored every 12 weeks while on treatment in some clinical trials

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J - Administrative Information

Outpatient prescription for home administration

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K - References

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

Wu YL, Tsuboi M, He J, et al. Osimertinib in resected EGFR-mutated non-small-cell lung cancer. N Engl J Med 2020 Oct 29;383(18):1711-23.

December 2023 Modified Dose modifications, Adverse effects, Interactions, and Special precautions 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.

The information set out in the drug monographs, regimen monographs, appendices and symptom management information (for health professionals) contained in the Drug Formulary (the "Formulary") is intended for healthcare providers and is to be used for informational purposes only. The information is not intended to cover all possible uses, directions, precautions, drug interactions or adverse effects of a particular drug, nor should it be construed to indicate that use of a particular drug is safe, appropriate or effective for a given condition. The information in the Formulary is not intended to constitute or be a substitute for medical advice and should not be relied upon in any such regard. All uses of the Formulary are subject to clinical judgment and actual prescribing patterns may not follow the information provided in the Formulary.

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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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