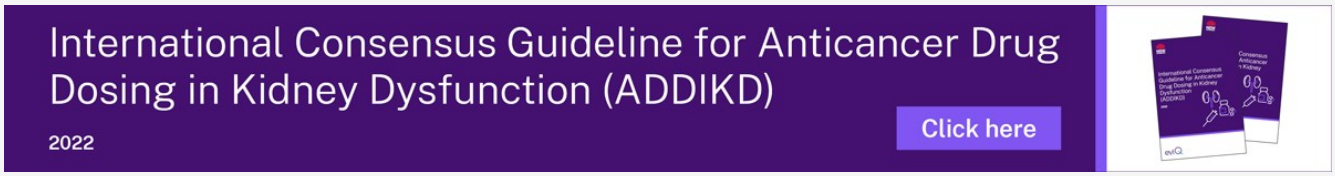
# Non small cell lung cancer locally advanced or metastatic osimertinib

**ID: 1996** v.2 **Endorsed**

Check for clinical trials in this patient group. Link to Australian Clinical Trials website

Link to Clinical practice guidelines for the treatment of lung cancer

The anticancer drug(s) in this protocol may have been included in the ADDIKD guideline. Dose recommendations in kidney dysfunction have yet to be updated to align with the ADDIKD guideline. Recommendations will be updated once the individual protocol has been evaluated by the reference committee. For further information refer to the ADDIKD guideline. To assist with calculations, use the eviQ Estimated Glomerular Filtration Rate (eGFR) calculator.




**Related pages:**

- Non small cell lung cancer metastatic aFATinib
- Non small cell lung cancer metastatic erlotinib SUPERSEDED
- Non small cell lung cancer metastatic gefitinib SUPERSEDED

## Treatment schedule - Overview

| Drug | Dose | Route |
|---|---|---|
| Osimertinib | 80 mg ONCE a day | PO |

**Continuous until disease progression or unacceptable toxicity**

**Drug status:** Osimertinib is PBS authority

Osimertinib is available as **40 mg** and **80 mg** tablets

**Cost:** ~ $7,440 per month

## Treatment schedule - Detail

*The supportive therapies (e.g. antiemetics, premedications, etc.), infusion times, diluents, volumes and routes of administration, if included, are listed as defaults. They may vary between institutions and can be substituted to reflect individual institutional policy.*

*Antiemetics if included in the treatment schedule are based upon recommendations from national and international guidelines. These are **defaults only** and may be substituted to reflect individual institutional policy. Select here for recommended doses of alternative antiemetics.*

| Continuous treatment | | |
|---|---|---|
| Osimertinib | 80 mg (PO) | ONCE a day at the same time, with or without food |

**Continuous until disease progression or unacceptable toxicity**

## Indications and patient population

**Indications:**

- First line palliative treatment of locally advanced or metastatic non small cell lung cancer (NSCLC) with activating epidermal growth factor receptor mutations.
- Second line treatment of locally advanced or metastatic T790M mutation positive (confirmed), NSCLC after progression on first generation EGFR TKI.

**Caution:**

- Not suitable for patients with curable stage III NSCLC.

## Clinical information

| | |
|---|---|
| **Caution with oral anti-cancer drugs** | Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs.<br>Read more about the COSA guidelines and oral anti-cancer therapy |
| **Emetogenicity minimal or low** | No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen.<br>Read more about preventing anti-cancer therapy induced nausea and vomiting |
| **Cardiac toxicity** | Tyrosine kinase inhibitors have been associated with cardiac complications of varying degrees and severity.<br>Patients, especially those with pre-existing cardiovascular disease, should have a baseline cardiac assessment including an electrocardiogram (ECG) and biochemistry and be closely monitored; consider an echocardiogram (ECHO) as clinically indicated.<br>Cardiac assessment should then be repeated as clinically indicated or when starting new medication which affects the QT interval.<br>Read more about cardiac toxicity associated with anti-cancer drugs |
| **Prolongation of QT interval** | This treatment may prolong the QT interval and increase the risk of cardiac arrhythmia. Use with caution in patients with a congenital long QT syndrome, patients treated with a high cumulative dose of anthracycline therapy, patients taking medications that may prolong the QT interval and those with electrolyte disturbances. Risk factors (e.g. electrolyte abnormalities) should be corrected, where possible, prior to commencement of treatment and the concurrent use of drugs that may prolong the QT interval should be avoided. Baseline and periodic monitoring of electrocardiogram (ECG) and electrolytes (potassium, magnesium, calcium) should be considered in patients at high risk of QT prolongation.<br>Read more about drugs that may prolong QTc interval at crediblemeds.org (registration required). |
| **Acneiform rash** | EGFR targeted therapies are commonly associated with acneiform rash. The rash may peak in the first 2 to 4 weeks.<br>Ensure advice on skin care (i.e. moisturisers) and sunscreen is provided. Prophylactic or early therapy with a tetracycline antibiotic (e.g. doxycycline) and 1% hydrocortisone cream to affected areas may be considered. Patients developing skin rash should be monitored for infectious sequelae, dose reductions and/or delay or cessation of treatment may be required.<br>Read more about acneiform rash associated with EGFR inhibitors |
| **Diarrhoea** | Antidiarrhoeals (e.g. loperamide) are usually prescribed with this treatment.<br>Read more about treatment induced diarrhoea |
| **Pulmonary toxicity** | Interstitial lung disease (ILD) has been reported in patients treated with EGFR inhibitors.<br>Read more about pulmonary toxicity associated with anti-cancer drugs. |
| **Blood tests** | FBC, EUC, eGFR, LFTs, calcium, magnesium and phosphate at baseline. Repeat monthly during treatment, or as clinically indicated |

| | |
|---|---|
| **Hepatitis B screening and prophylaxis** | Routine screening for HBsAg and anti-HBc is NOT usually recommended for patients receiving this treatment.<br>Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy |
| **Vaccinations** | Live vaccines should be used with caution in cancer patients. For cancer patients who are not receiving immunosuppressive therapy, there is currently no data as to the safety of giving live vaccines.<br>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook<br>Read more about COVID-19 vaccines and cancer. |
| **Fertility, pregnancy and lactation** | Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients.<br>Read more about the effect of cancer treatment on fertility |

## Dose modifications

*Evidence for dose modifications is limited, and the recommendations made on eviQ are intended as a guide only. They are generally conservative with an emphasis on safety. Any dose modification should be based on clinical judgement, and the individual patient's situation including but not limited to treatment intent (curative vs palliative), the anti-cancer regimen (single versus combination therapy versus chemotherapy versus immunotherapy), biology of the cancer (site, size, mutations, metastases), other treatment related side effects, additional co-morbidities, performance status and patient preferences.Suggested dose modifications are based on clinical trial findings, product information, published guidelines and reference committee consensus . The dose reduction applies to each individual dose and not to the total number of days or duration of treatment cycle unless stated otherwise. Non-haematological gradings are based on Common Terminology Criteria for Adverse Events (CTCAE) unless otherwise specified. Renal and hepatic dose modifications have been standardised where possible. For more information see dosing considerations & disclaimer .*

The dose recommendations in kidney dysfunction (i.e.renal impairment) displayed may not reflect those in the ADDIKD guideline and have been included for historical reference only. Recommendations will be updated once the individual protocol has been evaluated by the reference committee, with this version of the protocol then being archived. Clinicians are expected to refer to the ADDIKD guideline prior to prescribing in kidney dysfunction.
**International Consensus Guideline for Anticancer Drug Dosing in Kidney Dysfunction (ADDIKD)**.

| **Renal impairment** | |
|---|---|
| **Creatinine clearance (mL/min)** | |
| 15 to 50 | No dose modifications necessary |
| less than 15 | No dose modification information available |

| **Hepatic impairment** | |
|---|---|
| **Hepatic dysfunction** | |
| Mild/Moderate | No dose modifications necessary |
| Severe | Osimertinib not recommended |

| **Diarrhoea** | |
|---|---|
| Grade 1 or Grade 2 | Treat diarrhoea. No dose modifications necessary |

| | |
|---|---|
| Grade 3 or Grade 4 | Treat diarrhoea. Delay treatment until toxicity has resolved to Grade 0-2 and consider restarting osimertinib as follows:<br>If resolved to grade 0-2 within 3 weeks: consider restarting osimertinib at the same dose (80 mg) or a lower dose (40 mg)<br>If NOT resolved to grade 0-2 within 3 weeks: permanently discontinue osimertinib |

| **Pulmonary** | |
|---|---|
| Interstitial lung disease/ Pneumonitis | PI recommends permanent discontinuation of treatment. Reintroduction may be considered at the discretion of the treating clinician. |

| **QTc prolongation** | |
|---|---|
| QTc greater than or equal to 500 msec on at least 2 separate ECGs | Withhold treatment until QTc interval is less than 481 msec or recovery to baseline if baseline QTc is greater than or equal to 481 msec, then restart at a reduced dose (40 mg) |
| QTc prolongation with signs/symptoms of serious arrhythmia | Permanently discontinue treatment |

| **Rash acneiform** | |
|---|---|
| Grade 1 or Grade 2 | Institute supportive measures for symptomatic relief. No dose modifications necessary |
| Grade 3 or Grade 4 (e.g. Stevens-Johnson syndrome) | Institute supportive measures for symptomatic relief, delay treatment until toxicity has resolved to Grade 0-2 and consider restarting osimertinib as follows:<br>If resolved to grade 0-2 within 3 weeks : consider restarting osimertinib at the same dose (80 mg) or a lower dose (40 mg)<br>If NOT resolved to grade 0-2 within 3 weeks : permanently discontinue osimertinib |

Link to more information on Acneiform rash associated with EGFR inhibitors

| **All other adverse effects** | |
|---|---|
| Grade 1 or Grade 2 | Treat symptoms. No dose modifications necessary |
| Grade 3 or Grade 4 | Treat symptoms. Delay treatment until toxicity has resolved to Grade 0-2 and consider restarting osimertinib as follows:<br>If resolved to grade 0-2 within 3 weeks: consider restarting osimertinib at the same dose (80 mg) or a lower dose (40 mg)<br>If NOT resolved to grade 0-2 within 3 weeks: permanently discontinue osimertinib |

## Interactions

*Drug interactions in eviQ protocols are under review and being updated to align with current literature. Further site-wide updates and changes will occur in due course.* ***References & Disclaimer***

*The drug interactions shown below are not an exhaustive list. For a more comprehensive list and for detailed information on specific drug interactions and clinical management, please refer to the specific drug product information and the following key resources:*

- *MIMS - interactions tab (includes link to a CYP-450 table) (login required)*
- *Australian Medicines Handbook (AMH) – interactions tab (login required)*
- *Micromedex Drug Interactions (login required)*
- *Cancer Drug Interactions*
- *Cytochrome P450 Drug Interactions*

| Osimertinib | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **BCRP/ABCG2 substrates (e.g. glecaprevir and pibrentasvir, pazopanib, rosuvastatin, sulfasalazine, topotecan)** | Increased serum concentration of BCRP/ABCG2 substrates | Avoid combination or monitor closely for exposure related toxicities e.g. symptoms of myopathy or rhabdomyolysis when used in combination with rosuvastatin |
| **Strong CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort etc.)** | Reduced efficacy of osimertinib due to increased clearance/ decreased serum concentration | Avoid combination or consider osimertinib dose increase (with careful monitoring) to 160 mg daily. The osimertinib dose should be decreased to 80 mg daily 3 weeks after the strong CYP3A4 inducer is discontinued |
| **Drugs that may prolong the QTc interval (e.g. azole antifungals, tricyclic antidepressants, antiarrhythmics etc.)** | Additive effect with osimertinib; may lead to torsades de pointes and cardiac arrest | Avoid combination or minimise additional risk factors (e.g. correct electrolyte imbalances) and monitor ECG for signs of cardiac arrhythmia |

| General | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Warfarin** | Anti-cancer drugs may alter the anticoagulant effect of warfarin. | Monitor INR regularly and adjust warfarin dosage as appropriate; consider alternative anticoagulant. |
| **Direct oral anticoagulants (DOACs) e.g. apixaban, rivaroxaban, dabigatran** | Interaction with both CYP3A4 and P-gp inhibitors /inducers.<br><br>DOAC and anti-cancer drug levels may both be altered, possibly leading to loss of efficacy or toxicity (i.e. increased bleeding). | Apixaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors. If treating VTE, avoid use with strong CYP3A4 and P-gp inducers.<br><br>Rivaroxaban: avoid concurrent use with strong CYP3A4 and P-gp inhibitors.<br><br>Dabigatran: avoid combination with strong P-gp inducers and inhibitors.<br><br>If concurrent use is unavoidable, monitor closely for efficacy/toxicity of both drugs. |
| **Digoxin** | Anti-cancer drugs can damage the lining of the intestine; affecting the absorption of digoxin. | Monitor digoxin serum levels; adjust digoxin dosage as appropriate. |
| **Antiepileptics** | Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity. | Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy. |
| **Antiplatelet agents and NSAIDs** | Increased risk of bleeding due to treatment related thrombocytopenia. | Avoid or minimise combination.<br>If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding. |
| **Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)** | Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.) | Avoid combination.<br>If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia).<br>For more information link to TGA Medicines Safety Update |
| **Vaccines** | Diminished response to vaccines and increased risk of infection with live vaccines. | Live vaccines should be used with caution in cancer patients. For cancer patients who are not receiving immunosuppressive therapy, there is currently no data as to the safety of giving live vaccines.<br>For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook |

## Administration

*eviQ provides safe and effective instructions on how to administer cancer treatments. However, eviQ does not provide every treatment delivery option, and is unable to provide a comprehensive list of cancer treatment agents and their required IV line giving set/filter. There may be*

*alternative methods of treatment administration, and alternative supportive treatments that are also appropriate. Please refer to the individual product information monographs via the TGA website for further information.*

## Administration

**This is a continuous oral treatment**

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each treatment.

Any toxicity grade 2 or greater may require dose reduction, delay or omission of treatment and review by medical officer before recommencing treatment.

### Treatment - Time out

#### Osimertinib

- administer orally ONCE a  day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food
- if difficulty is experienced swallowing the tablet advise patient to:
  - drop the tablet in 50 mL of plain drinking water. No other liquids should be used
  - stir until the tablet is dispersed
  - drink the liquid straight away
  - rinse the empty glass with half a glass of water and drink it.
- via a nasogastric tube:
  - follow the same process as above but use 15 mL for initial dispersion and 15 mL for rinse
  - administer all within 30 minutes of adding the tablets to the water
  - flush the nasogastric tube as per manufacturers instructions.

**Note**: missed doses should not be taken if it is less than 12 hours until the next dose. If a dose is forgotten or vomited, it should not be replaced.

**Continue safe handling precautions (reproductive risk only) for 7 days after completion of drug(s).**

## Discharge

#### Osimertinib tablets

Osimertinib tablets with written instructions on how to take them

#### Antidiarrhoeals

- Antidiarrhoeals as prescribed.

#### Patient information

- Ensure patient receives patient information sheet.

# Side effects

*The side effects listed below are not a complete list of all possible side effects for this treatment. Side effects are categorised into the approximate onset of presentation and should only be used as a guide.*

| Immediate (onset hours to days) | |
|---|---|
| **Nausea and vomiting** | Read more about prevention of treatment induced nausea and vomiting |

| Early (onset days to weeks) | |
|---|---|
| **Acneiform rash** | A skin rash, characterised by papules and pustules affecting the face and upper body. This is commonly associated with small molecule EGFR inhibitors and some monoclonal antibodies (e.g. cetuximab, panitumumab).<br>Read more about acneiform rash associated with EGFR inhibitors |
| **Anorexia** | Loss of appetite accompanied by decreased food intake.<br>Read more about anorexia |
| **Diarrhoea** | Read more about treatment induced diarrhoea |
| **Fatigue** | Read more about fatigue |
| **Ocular changes** | Symptoms may include eye pain, blurred vision, blepharitis, uveitis, optic neuritis, tear duct stenosis, conjunctivitis, hyperlacrimation, watery or dry eyes and photophobia. |
| **Oral mucositis** | Erythematous and ulcerative lesions of the gastrointestinal tract (GIT). It commonly develops following chemotherapy, radiation therapy to the head, neck or oesophagus, and high dose chemotherapy followed by a blood and marrow transplant (BMT).<br>Read more about oral mucositis |
| **QT prolongation** | This treatment can cause QTc interval prolongation. QTc prolongation can lead to ventricular arrhythmias that may be fatal. |

| Late (onset weeks to months) | |
|---|---|
| **Abnormal hair growth** | Hair may become fine, brittle and curly. Eyelashes and eyebrows may grow more quickly and become unusually long. |
| **Pulmonary toxicity** | Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation.<br>Read more about pulmonary toxicity associated with anti-cancer drugs |
| **Paronychia** | An inflammatory reaction involving the folds of the skin surrounding the fingernail.<br>Read about nail toxicities |

## Evidence

### First-line setting

**FLAURA trial**[1]

The evidence supporting the use of osimertinib in the first line setting is provided by results from a double-blind, phase III trial (FLAURA trial), randomising patients with locally advanced or metastatic EGFR mutant (exon 19 deletion or L858R) non small cell lung cancer, who had not previously received first-line treatment with gefitinib or erlotinib.

Between December 2014 and March 2016, a total of 994 patients were screened, 556 were randomly assigned to trial treatment in a 1:1 ratio to receive osimertinib 80 mg once daily (279 patients) or a standard EGFR-TKI (277 patients receiving gefitinib 250 mg once daily or erlotinib 150 mg once daily).

The primary end point was investigator-assessed progression-free survival.

A number of patients continued treatment beyond RECIST-defined progression (67% in osimertinib group and 70% in the EGFR-TKI group). 55 out of 129 RECIST-defined progressed patients in the EGFR-TKI group received osimertinib as a second-line treatment.

### Second-line setting

**AURA3 trial**[2]

The evidence supporting the use of osimertinib in the second line setting is provided by results from an open-label, phase III trial (AURA3 trial), randomising patients with locally advanced or metastatic non small cell lung cancer, with T790M mutation who had disease progression after first line EGFR-TKI therapy.

Between August 2014 and September 2015, 419 patients were randomly assigned to trial treatment in a 2:1 ratio to receive

osimertinib at a dose of 80 mg once daily (279 patients) or intravenous pemetrexed at 500 mg/m$^2$ of BSA plus either carboplatin (AUC5) or cisplatin (75 mg/m$^2$) every 3 weeks for up to 6 cycles (140 patients); maintenance pemetrexed was also allowed.

The primary end point was investigator-assessed progression-free survival.

82 out of 136 RECIST-defined progressed patients in the platinum-pemetrexed group received osimertinib as a third line treatment.

## Efficacy

### First-line setting

**FLAURA trial**[1]

At time of data cut-off and interim analysis, the median duration of follow up was 15.0 months for progression-free survival and 9.7 months for survival for all patients. Median duration of total treatment exposure was 16.2 months for patients receiving osimertinib, and 11.5 months for those receiving standard EGFR-TKI. Results of the trial found the median progression-free survival was significantly longer with osimertinib than with standard EGFR-TKIs (18.9 months vs. 10.2 months; hazard ratio for disease progression or death, 0.46; 95% confidence interval [CI], 0.37 to 0.57; P<0.001). The objective response rate was similar in the two groups: 80% with osimertinib and 76% with standard EGFR-TKIs (odds ratio, 1.27; 95% CI, 0.85 to 1.90; P = 0.24). The median duration of response was 17.2 months (95% CI, 13.8 to 22.0) with osimertinib versus 8.5 months (95% CI, 7.3 to 9.8) with standard EGFR-TKIs.

In the FLAURA trial after a median follow up of 43 months, the median OS was 38.6 months (95% CI, 34.5 to 41.8) in the osimertinib group and 31.8 months (95% CI, 26.6 to 36.0) (hazard ratio for death 0.80; 95.05% CI, 0.64 to 1.00; P=0.046) in the standard EGFR-TKI group.[3]

Health related quality of life reported improvements were statistically significant favouring the osimertinib group for emotional and social functioning. Cognitive functioning remained stable with osimertinib but deteriorated with erlotinib/gefitinib. Reported odds of improvement and time to deterioration of symptoms was similar in both groups.[4]

**Kaplan-Meier Estimates for Progression Free Survival According to Treatment Group**[1]

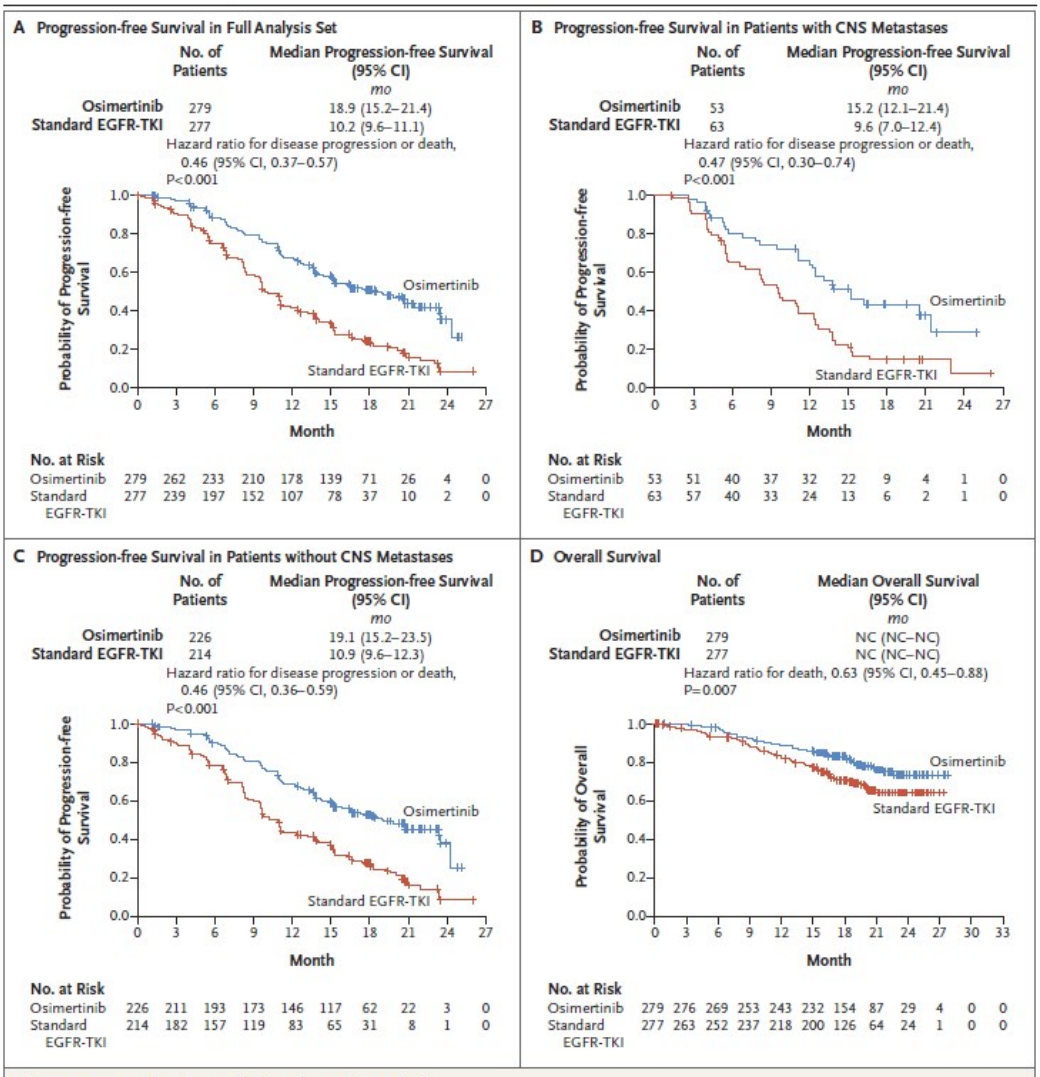
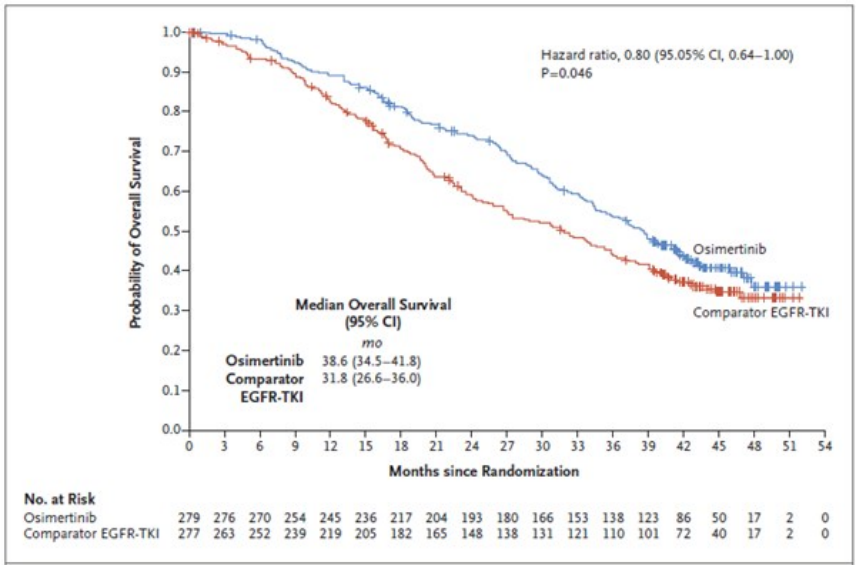



**Figure 1. Progression-free Survival and Overall Survival.**

Shown are Kaplan–Meier estimates of the duration of progression-free survival in the full analysis set as assessed by investigators (Panel A), in patients with known or treated central nervous system (CNS) metastases at trial entry (Panel B), and in patients without known or treated CNS metastases at trial entry (Panel C). Also shown are Kaplan–Meier estimates of overall survival (Panel D). Censored data are indicated by tick marks. For the analysis of progression-free survival, data for patients who had not had a progression event or had not died at the time of the analysis were censored at the time of their last assessment (according to Response Evaluation Criteria in Solid Tumors) that could be evaluated. For the analysis of overall survival, data for any patients who were not known to have died at the time of the analysis were censored at the last recorded date that the patient was known to be alive. CI denotes confidence interval, EGFR-TKI epidermal growth factor receptor tyrosine kinase inhibitor, and NC could not be calculated.



## Kaplan-Meier Estimates for Overall Survival[3]

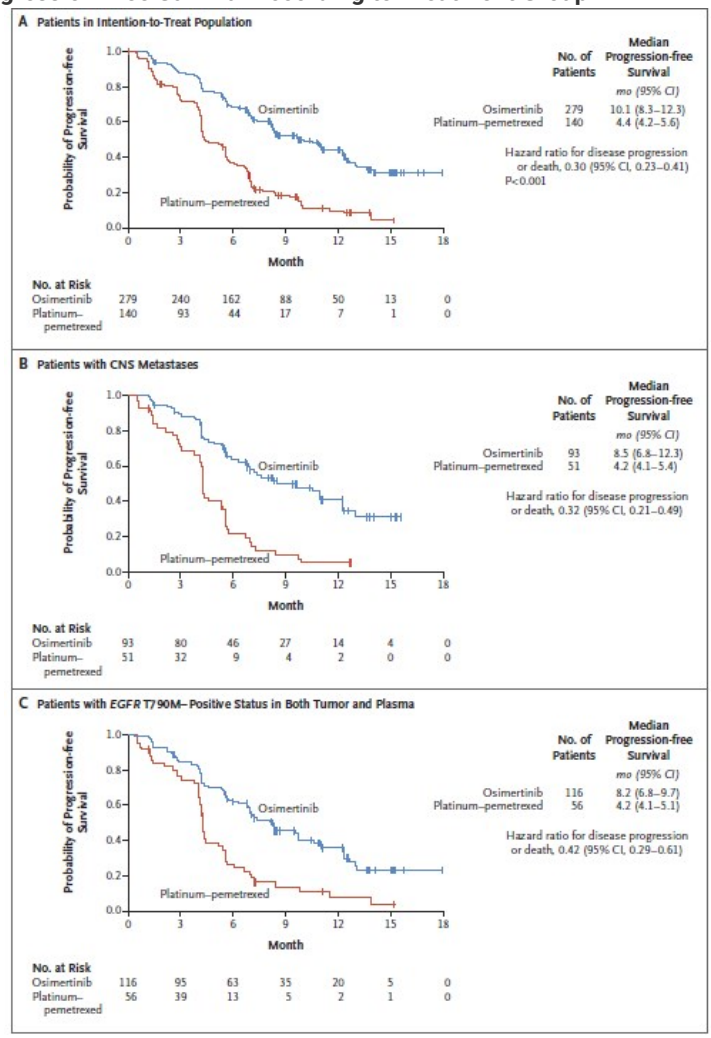


### Second-line setting

**AURA3 trial**[2]

At the time of data cutoff, and interim analysis, the median follow-up for all patients was 8.3 months, and the median duration of treatment was 8.6 months in the osimertinib group and 4.8 months in the platinum-pemetrexed group. The median duration of progression-free survival was significantly longer with osimertinib than with platinum therapy plus pemetrexed (10.1 months vs. 4.4 months; hazard ratio; 0.30; 95% confidence interval [CI], 0.23 to 0.41; P<0.001). The objective response rate was significantly better with osimertinib (71%; 95% CI, 65 to 76) than with platinum therapy plus pemetrexed (31%; 95% CI, 24 to 40) (odds ratio for objective response, 5.39; 95% CI, 3.47 to 8.48; P<0.001). Among 144 patients with metastases to the central nervous system (CNS), the median duration of progression-free survival was longer among patients receiving osimertinib than among those receiving platinum therapy plus pemetrexed (8.5 months vs. 4.2 months; hazard ratio, 0.32; 95% CI, 0.21 to 0.49).

**Kaplan-Meier Estimates for Progression Free Survival According to Treatment Group**[2]

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## Toxicity

### First-line setting

**FLAURA trial**[3]

Adverse events of grade 3 or higher were reported in 42% of patients in the osimertinib group and 47% in the EGFR-TKI group. Rash or acne (59% in the osimertinib group and 79% in the standard EGFR-TKI group), diarrhoea (60% and 58%, respectively), and dry skin (38% and 37% respectively) were the most commonly reported adverse effects (due to any cause). Ejection fraction decrease was reported in 5% in osimertinib group and 2% in the EGFR-TKI group, QT interval changes and interstitial lung disease were reported in a higher percentage of patients in the osimertinib group than in the standard EGFR-TKI group (QT interval changes: 14% and 5%; interstitial lung disease changes: 2% and 1% respectively). There were no fatal cases of torsades des pointes, prolongation of the QT interval, or interstitial lung disease.

**Adverse events**[3]

Table 2. Adverse Events.*

| Adverse Event | Osimertinib (N=279) | | | | Comparator EGFR-TKI (N=277) | | | |
|---|---|---|---|---|---|---|---|---|
| | Any Grade | Grade 1 | Grade 2 | Grade 3 | Any Grade | Grade 1 | Grade 2 | Grade 3 |
| | number of patients (percent) | | | | | | | |
| Diarrhea | 167 (60) | 119 (43) | 41 (15) | 7 (3) | 162 (58) | 118 (43) | 35 (13) | 7 (3) |
| Rash or acne† | 164 (59) | 132 (47) | 29 (10) | 3 (1) | 219 (79) | 111 (40) | 88 (32) | 20 (7) |
| Nail effects† | 108 (39) | 61 (22) | 45 (16) | 2 (1) | 95 (34) | 58 (21) | 35 (13) | 2 (1) |
| Dry skin† | 106 (38) | 89 (32) | 16 (6) | 1 (<1) | 102 (37) | 78 (28) | 21 (8) | 3 (1) |
| Stomatitis | 82 (29) | 66 (24) | 14 (5) | 1 (<1) | 60 (22) | 51 (18) | 8 (3) | 1 (<1) |
| Decreased appetite | 66 (24) | 32 (11) | 27 (10) | 7 (3) | 58 (21) | 29 (10) | 24 (9) | 5 (2) |
| Cough | 60 (22) | 42 (15) | 18 (6) | 0 | 50 (18) | 33 (12) | 17 (6) | 0 |
| Nausea | 55 (20) | 37 (13) | 18 (6) | 0 | 55 (20) | 31 (11) | 23 (8) | 0 |
| Constipation | 51 (18) | 42 (15) | 9 (3) | 0 | 39 (14) | 29 (10) | 10 (4) | 0 |
| Pruritus | 50 (18) | 41 (15) | 8 (3) | 1 (<1) | 44 (16) | 33 (12) | 14 (5) | 0 |
| Renal symptoms‡ | 50 (18) | 32 (11) | 13 (5) | 3 (1) | 32 (12) | 24 (9) | 7 (3) | 1 (<1) |
| Fatigue | 45 (16) | 25 (9) | 17 (6) | 3 (1) | 35 (13) | 23 (8) | 10 (4) | 2 (1) |
| Anemia | 44 (16) | 22 (8) | 15 (5) | 7 (3) | 27 (10) | 19 (7) | 5 (2) | 3 (1) |
| Dyspnea | 42 (15) | 28 (10) | 12 (4) | 2 (1) | 22 (8) | 10 (4) | 9 (3) | 3 (1) |
| Vomiting | 41 (15) | 32 (11) | 9 (3) | 0 | 32 (12) | 24 (9) | 4 (1) | 4 (1) |
| Headache | 39 (14) | 29 (10) | 8 (3) | 2 (1) | 25 (9) | 17 (6) | 8 (3) | 0 |
| Back pain | 36 (13) | 22 (8) | 14 (5) | 0 | 29 (10) | 15 (5) | 14 (5) | 0 |
| Upper respiratory tract infection | 36 (13) | 20 (7) | 16 (6) | 0 | 23 (8) | 12 (4) | 11 (4) | 0 |
| Pyrexia | 32 (11) | 28 (10) | 4 (1) | 0 | 12 (4) | 9 (3) | 2 (1) | 1 (<1) |
| Insomnia | 31 (11) | 23 (8) | 8 (3) | 0 | 21 (8) | 12 (4) | 9 (3) | 0 |
| Nasopharyngitis | 31 (11) | 17 (6) | 14 (5) | 0 | 16 (6) | 11 (4) | 5 (2) | 0 |
| Prolonged QT interval | 28 (10) | 12 (4) | 12 (4) | 4 (1) | 12 (4) | 7 (3) | 3 (1) | 2 (1) |
| Increase in aspartate aminotransferase | 28 (10) | 19 (7) | 7 (3) | 2 (1) | 69 (25) | 39 (14) | 18 (6) | 12 (4) |
| Musculoskeletal pain | 28 (10) | 19 (7) | 9 (3) | 0 | 14 (5) | 8 (3) | 6 (2) | 0 |
| Alopecia | 22 (8) | 18 (6) | 4 (1) | 0 | 35 (13) | 31 (11) | 4 (1) | 0 |
| Increase in alanine aminotransferase | 19 (7) | 11 (4) | 6 (2) | 2 (1) | 74 (27) | 30 (11) | 19 (7) | 21 (8) |



## Second-line setting

### AURA3 trial[2]

Adverse events of grade 3 or higher were reported in 23% of patients in the osimertinib group and 47 % in the platinum–pemetrexed group. Most commonly reported adverse events were diarrhoea (41%), rash (34%), dry skin (23%), and paronychia (22%) in the osimertinib group. Most commonly reported adverse events in the platinum–pemetrexed group were nausea (49%), decreased appetite (36%), constipation (35%), and anaemia (30%). Interstitial lung disease changes were reported in 4% in the osimertinib group (one resulted in a fatal event) and in 1% in the platinum–pemetrexed group. QT interval prolongation was found in 4% in the osimertinib group 1% in the platinum–pemetrexed group.

### Adverse events[2]

**Table 3. Adverse Events.***

| Adverse Event | Osimertinib (N=279) | | Platinum–Pemetrexed (N=136) | |
|---|---|---|---|---|
| | Any Grade | Grade ≥3 | Any Grade | Grade ≥3 |
| | *number (percent)* | | | |
| Diarrhea | 113 (41) | 3 (1) | 15 (11) | 2 (1) |
| Rash† | 94 (34) | 2 (1) | 8 (6) | 0 |
| Dry skin† | 65 (23) | 0 | 6 (4) | 0 |
| Paronychia† | 61 (22) | 0 | 2 (1) | 0 |
| Decreased appetite | 50 (18) | 3 (1) | 49 (36) | 4 (3) |
| Cough | 46 (16) | 0 | 19 (14) | 0 |
| Nausea | 45 (16) | 2 (1) | 67 (49) | 5 (4) |
| Fatigue | 44 (16) | 3 (1) | 38 (28) | 1 (1) |
| Stomatitis | 41 (15) | 0 | 21 (15) | 2 (1) |
| Constipation | 39 (14) | 0 | 47 (35) | 0 |
| Pruritus | 35 (13) | 0 | 6 (4) | 0 |
| Vomiting | 31 (11) | 1 (<1) | 27 (20) | 3 (2) |
| Back pain | 29 (10) | 1 (<1) | 12 (9) | 1 (1) |
| Thrombocytopenia† | 28 (10) | 1 (<1) | 27 (20) | 10 (7) |
| Nasopharyngitis | 28 (10) | 0 | 7 (5) | 0 |
| Headache | 28 (10) | 0 | 15 (11) | 0 |
| Dyspnea | 24 (9) | 3 (1) | 18 (13) | 0 |
| Neutropenia† | 22 (8) | 4 (1) | 31 (23) | 16 (12) |
| Leukopenia† | 22 (8) | 0 | 20 (15) | 5 (4) |
| Anemia† | 21 (8) | 2 (1) | 41 (30) | 16 (12) |
| Asthenia | 20 (7) | 3 (1) | 20 (15) | 6 (4) |
| Pyrexia | 18 (6) | 0 | 14 (10) | 0 |
| Alanine aminotransferase elevation | 18 (6) | 3 (1) | 15 (11) | 1 (1) |
| Aspartate aminotransferase elevation | 14 (5) | 3 (1) | 15 (11) | 1 (1) |
| Malaise | 11 (4) | 0 | 14 (10) | 0 |

* Listed are adverse events that were reported in at least 10% of the patients in any group. Safety analyses included all the patients who received at least one dose of a trial drug (safety analysis set). Included are adverse events with an onset date on or after the date of first dose and up to and including 28 days after the discontinuation of the trial drug or the day before the first administration of crossover treatment. Some patients had more than one adverse event.

† This category represents a grouped term for the event. If a patient had multiple preferred-term level events within a specific grouped term adverse event, then the maximum grade (according to the Common Terminology Criteria for Adverse Events) across those events was counted.



## References


1 Soria, J. C., Y. Ohe, J. Vansteenkiste et al. 2018. "Osimertinib in Untreated EGFR-Mutated Advanced Non-Small-Cell Lung Cancer." N Engl J Med 378 (2): 113-125.

2 Mok, T. S., Y-L. Wu, M-J. Ahn et al. 2017. "Osimertinib or Platinum-Pemetrexed in EGFR T790M-Positive Lung Cancer." N Engl J Med 376(20): 1993-1994.

3 Ramalingam, S. S., J. Vansteenkiste, D. Planchard, et al. 2020. "Overall Survival with Osimertinib in Untreated, EGFR-Mutated Advanced NSCLC." N Engl J Med 382(1):41-50.

4 Leighl, N. B., N. Karaseva, K. Nakagawa, et al. 2020. "Patient-reported outcomes from FLAURA: Osimertinib versus erlotinib or gefitinib in patients with EGFR-mutated advanced non-small-cell lung cancer." Eur J Cancer 125:49-57.


## History

### Version 2

| Date | Summary of changes |
|---|---|
| **18/08/2020** | Protocol reviewed electronically by Medical Oncology Reference Committee. Cardiac toxicity added to clinical |

| Date | Summary of changes |
|---|---|
| | information. Evidence updated. Version number changed to V.2. Review 2 years. |
| **11/01/2021** | Drug status updated as now PBS authority for first line and second line. |
| **21/12/2021** | Changed antiemetic clinical information block to minimal or low, to align with new categories. See ID 7 Prevention of anti-cancer therapy induced nausea and vomiting (AINV) v5. |
| **20/05/2022** | Protocol reviewed electronically by Medical Oncology Reference Committee. EGFR TKI cardiac toxicity clinical information updated. Next review in 2 years. |

### Version 1

| Date | Summary of changes |
|---|---|
| **23/11/2018** | Protocol taken to Medical Oncology Reference Committee meeting. |
| **19/12/2018** | Protocol approved and published on eviQ. Review 1 year. |
| **06/02/2019** | Drug status updated to match PBS listing for second line treatment. |



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*09 Aug 2023*

# Patient information - Lung cancer advanced or metastatic - Osimertinib

**Patient's name:**

## Your treatment

It is important to understand that osimertinib is not a traditional chemotherapy drug and has a different way of working. It works by targeting the cancer cells to stop them growing and spreading. The treatment schedule below explains how the drug for this treatment is given.

| **Osimertinib** | | |
|---|---|---|
| This treatment is continuous. Your doctor will advise you how long to take the treatment for. | | |
| **Day** | **Treatment** | **How it is given** |
| Continuous | **Osimertinib** (*oh-si-mer-ti-nib*) | Take orally ONCE a day.<br><br>Swallow the tablet whole with a glass of water at about the same time each day with or without food.<br><br>If you forget to take a tablet, and if it is less than 12 hours late, take it as soon as you remember. If it is more than 12 hours late, skip that dose and take your normal dose the next time it is due. Do not take a double dose for a missed dose or if a dose is vomited |

## When to get help

Anticancer drugs (drugs used to treat cancer) can sometimes cause serious problems. It is important to get medical help immediately if you suddenly become unwell.

**Emergency contact details**

Ask your doctor or nurse from your treating team when you should get help and who to contact if you have a problem

Daytime: .....

Night/weekend: .....

Other instructions: .....

.....

.....

## Other information about your treatment

### Changes to your dose or treatment delays

Sometimes a treatment may be started at a lower dose or the dose needs to be changed during treatment. There may also be times when your treatment is delayed. This can happen if your doctor thinks you are likely to have severe side effects, if you get severe side effects, if your blood counts are affected and causing delays in treatment, or if you are finding it hard to cope with the treatment. This is called a dose reduction, dose change or treatment delay. Your doctor will explain if you need any changes or

delays to your treatment and the reason why.

### Blood tests and monitoring

You will need to have a blood test before you start treatment and regularly throughout your treatment. Your doctor or nurse will tell you when to have these blood tests.

### Other medications given during this treatment

- **Antidiarrhoeals:** you may be given some medication to treat diarrhoea. Your doctor or nurse will tell you how and when to take your antidiarrhoeal medication.
- **Medication for skin rash:** you may be given some medication (which may include a steroid cream, an antibiotic cream and/or oral antibiotics) to prevent or treat skin rash. Your doctor or nurse will tell you how to take or use these medications.

### Instructions for dissolving osimertinib tablets:

- Osimertinib tablets should not be crushed, cut or chewed. For patients with swallowing difficulties osimertinib tablets can be dissolved.
- You (or whoever is dissolving the tablets) should wear disposable gloves and try to minimise touching the tablets.
- Place the osimertinib tablet in quarter a glass of plain drinking water (approximately 50 mL). No other liquids should be used.
- Stir until the tablet dissolves.
- Drink the liquid straight away.
- Rinse the empty glass with half a glass of water and drink it straight away.

## Side effects

Cancer treatments can cause damage to normal cells in your body, which can cause side effects. Everyone gets different side effects, and some people will have more problems than others.

The table below shows some of the side effects you may get with this treatment. You are unlikely to get all of those listed and you may also get some side effects that have not been listed.

Tell your doctor or nurse about any side effects that worry you. Follow the instructions below and those given to you by your doctor or nurse.

| Immediate (onset hours to days) | |
|---|---|
| **Nausea and vomiting** | • You may feel sick (nausea) or be sick (vomit).<br>• Take your anti-sickness medication as directed even if you don't feel sick.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat small meals more frequently.<br>• Try food that does not require much preparation.<br>• Try bland foods like dry biscuits or toast.<br>• Gentle exercise may help with nausea.<br>• Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.** |
| **Early (onset days to weeks)** | |

| | |
|---|---|
| **Skin rash (acneiform rash)** | • You may get an acne-like skin rash.<br>• Your skin may become red and dry.<br>• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.<br>• Do not scratch your skin.<br>• Do not use over-the-counter acne treatments as these can make the rash worse.<br>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.<br>• You may be given medications to prevent the rash.<br>• **Tell your doctor or nurse as soon as possible if you notice any changes to the rash like itching, pain or pus forming** |
| **Appetite loss (anorexia)** | • You may not feel like eating.<br>• Try to avoid drinking fluids at meal times.<br>• Try to eat small meals or snacks regularly throughout the day.<br>• Try to eat food that is high in protein and calories.<br>• If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian. |
| **Diarrhoea** | • You may get bowel motions (stools, poo) that are more frequent or more liquid.<br>• You may also get bloating, cramping or pain.<br>• Take your antidiarrhoeal medication as directed by your doctor.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat and drink small amounts more often.<br>• Avoid spicy foods, dairy products, high fibre foods, and coffee.<br>• Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment.<br>• **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.** |
| **Tiredness and lack of energy (fatigue)** | • You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy.<br>• Do not drive or operate machinery if you are feeling tired.<br>• Nap for short periods (only 1 hour at a time)<br>• Prioritise your tasks to ensure the best use of your energy.<br>• Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted).<br>• Try some gentle exercise daily.<br>• Allow your friends and family to help.<br>• **Tell your doctor or nurse if you get any of the symptoms listed above.** |
| **Eye problems** | • You may get:<br>  ◦ eye pain<br>  ◦ red, sore or swollen eyes<br>  ◦ blurred vision<br>  ◦ watery or gritty eyes<br>  ◦ changes in your eyesight<br>  ◦ sensitivity to sunlight.<br>• Protect your eyes from the weather (sun and wind) by wearing sunglasses, especially if you have lost your eyelashes.<br>• **Tell your doctor or nurse if you get any of the symptoms listed above. Eye drops may help with your symptoms.** |

| | |
|---|---|
| **Mouth pain and soreness (mucositis)** | • You may have:<br>◦ bleeding gums<br>◦ mouth ulcers<br>◦ a white coating on your tongue<br>◦ pain in the mouth or throat<br>◦ difficulty eating or swallowing.<br>• Avoid spicy, acidic or crunchy foods and very hot or cold food and drinks.<br>• Try bland and soft foods.<br>• Brush your teeth gently with a soft toothbrush after each meal and at bedtime. If you normally floss continue to do so.<br>• Rinse your mouth after you eat and brush your teeth, using either:<br>◦ 1/4 teaspoon of salt in 1 cup of warm water, or<br>◦ 1/4 teaspoon of bicarbonate of soda in 1 cup of warm water<br>• Ask your doctor or nurse for eviQ patient information - Mouth problems during cancer treatment.<br>• **Tell your doctor or nurse if you get any of the symptoms listed above.** |
| **Heart changes** | • You may get chest pain, shortness of breath, an abnormal heartbeat or swelling in your arms or legs.<br>• Before, during or after treatment you may be asked to have tests to see how well your heart is working.<br>• You will also have other blood tests to check your electrolyte levels.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department, if you get any of the symptoms listed above.** |

| **Late (onset weeks to months)** | |
|---|---|
| **Hair changes** | • Your hair may become fine or curly and may break easily.<br>• Your eyelashes and eyebrows may grow more than normal.<br>• Use a gentle shampoo and a soft hairbrush.<br>• Take care with hair products like hairspray, hair dye, bleaches and perms.<br>• Ask your doctor or nurse about the Look Good Feel Better program (www.lgfb.org.au). |
| **Lung problems** | • Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment.<br>• You may get:<br>◦ shortness of breath<br>◦ fever<br>◦ dry cough<br>◦ wheezing<br>◦ fast heartbeat<br>◦ chest pain.<br>• Your doctor will monitor how well your lungs are working during your treatment.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.** |
| **Swelling and pain around the fingernails or toenails (paronychia)** | • The skin around your nails may swell and become painful.<br>• Apply a warm compress or soak your nails for 15 minutes, 3 or 4 times a day, in warm water or a mixture of equal parts vinegar and water.<br>• Keep your nails clean and short.<br>• Avoid things like biting your fingernails, getting a manicure, pedicure or false nails.<br>• Wear gloves when you wash the dishes, work in the garden, or clean the house.<br>• Tell your doctor or nurse if you get any of the symptoms listed above. |

## General advice for patients having cancer treatment

### Blood clot risk

- Cancer and anticancer drugs can increase the risk of a blood clot (thrombosis).
- Tell your doctor if you have a family history of blood clots.
- A blood clot can cause pain, redness, swelling in your arms or legs, shortness of breath or chest pain.
- If you have any of these symptoms go to your nearest hospital Emergency Department.

### Medications and vaccinations

- Before you start treatment, tell your doctor about any medications you are taking, including vitamins or herbal supplements.
- Don't stop or start any medications during treatment without talking to your doctor and pharmacist first.
- Paracetamol is safe to take if you have a headache or other mild aches and pains. It is recommended that you avoid taking aspirin, ibuprofen and other anti-inflammatory type medications for pain while you are having treatment. However, if these medications have been prescribed by your doctor, do not stop taking them without speaking with your doctor.
- Vaccinations such as flu and tetanus vaccines are safe to receive while having treatment. Do not have any live vaccines during your treatment or for 6 months after it finishes. If you are unsure, check with your doctor before you have any vaccinations.
- People you live with should be fully vaccinated, including having live vaccines according to the current vaccination schedule. Extra care needs to be taken with hand washing and careful disposal of soiled nappies for infants who have recently received the rotavirus vaccine.

### Other medical and dental treatment

- If you go to hospital or any other medical appointment (including dental appointments), always tell the person treating you that you are receiving anticancer drugs.
- Before you have any dental treatment, talk to your doctor.

### Diet

- While you are receiving this treatment it is important that you try to maintain a healthy diet.
- Speak to your doctor or nurse about whether drinking alcohol is safe with your treatment.
- If you have any concerns about recent weight loss or weight gain or questions about your diet, ask to speak to a dietitian.

### Fertility

- Some cancer treatments can reduce your fertility. This can make it difficult or impossible to get pregnant or father a child.
- Talk to your doctor or nurse before you start any treatment. Depending on your situation there may be fertility sparing options available to you and/or your partner, discuss these with your doctor or nurse.

### Pregnancy and breastfeeding

- Some cancer treatments can be dangerous to unborn babies. Talk to your doctor or nurse if you think there is any chance that you could be pregnant.
- Do not try to get pregnant or father a child during this treatment. Contraception should be used during treatment and after stopping treatment. Ask your doctor or nurse about what type of contraception you should use.
- If you are planning pregnancy/fatherhood after completing this treatment, talk to your doctor. Some doctors advise waiting between 6 months and 2 years after treatment.
- Do not breastfeed if you are on this treatment, as anti-cancer medications can also pass into breast milk.

### Sex life and sexuality

- The desire to have sex may decrease as a result of this treatment or its side effects.
- Your emotions and the way you feel about yourself may also be affected by this treatment.
- It may help to discuss your concerns with your partner and doctor or nurse.

### Quitting smoking

- It is never too late to quit smoking. Quitting smoking is one of the best things you can do to help your treatment work better.
- There are many effective tools to improve your chances of quitting.
- Talk to your treating team for more information and referral to a smoking cessation support service.

### Staying active

- Research shows that exercise, no matter how small, has many benefits for people during and after cancer treatment.
- Talk to your doctor before starting an exercise program. Your doctor can advise whether you need a modified exercise program.

**For more information about cancer treatment, side effects and side effect management see our Patient and carers section.**

## Where to get more information

### Telephone support

- Call Cancer Council on 13 11 20 for cancer information and support
- Call the Lung Foundation Australia on 1800 654 301

### Lung cancer information

- Lung Foundation Australia – lungfoundation.com.au
- Lungevity – lungevity.org

### General cancer information and support

- Australian Rare Cancer (ARC) Portal – arcportal.org.au/
- Beyondblue – beyondblue.org.au
- Cancer Australia – canceraustralia.gov.au
- Cancer Council Australia – cancer.org.au
- Cancer Voices Australia – cancervoicesaustralia.org
- CanTeen – canteen.org.au
- Carers Australia – carersaustralia.com.au
- Carer Help - carerhelp.com.au
- CHILL Cancer related hair loss - scalpcooling.org
- eviQ Cancer Treatments Online – eviQ.org.au
- LGBTQI+ People and Cancer - cancercouncil.com.au/cancer-information/lgbtqi
- Look Good Feel Better – lgfb.org.au
- Patient Information – patients.cancer.nsw.gov.au
- Radiation Oncology Targeting Cancer – targetingcancer.com.au
- Redkite – redkite.org.au
- Return Unwanted Medicines – returnmed.com.au
- Staying active during cancer treatment – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/staying-active

### Quit smoking information and support

Quitting smoking is helpful even after you have been diagnosed with cancer. The following resources provide useful information and support to help you quit smoking. Talk to your treating team about any other questions you may have.

- Call Quitline on 13 QUIT (13 78 48)
- iCanQuit – iCanQuit.com.au
- Patient Information – patients.cancer.nsw.gov.au/coping-with-cancer/physical-wellbeing/quitting-smoking
- Quitnow – quitnow.gov.au

**Additional notes:**

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