Non-Hodgkin lymphoma idelalisib

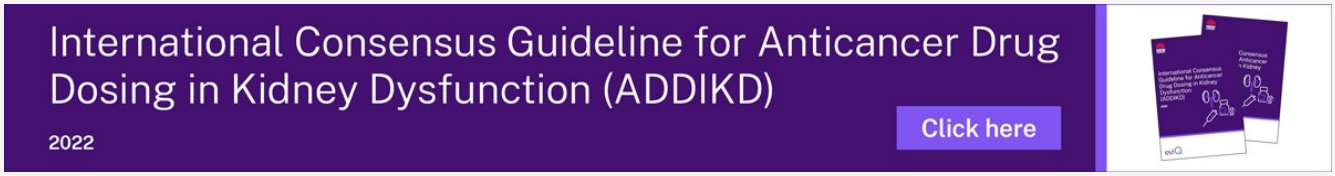
ID: 3411 v.1 **Endorsed**

⚠ Infection and pneumonitis risk:
Idelalisib can cause serious infections and/or fatal pneumonitis. See 'Pneumocystis jirovecii pneumonia (PJP) prophylaxis' and 'CMV monitoring' in the Clinical information section below for more information.

Patients with lymphoma should be considered for inclusion into clinical trials. Link to ALLG website, ANZCTR website and Lymphoma Australia website.

This protocol is based on limited evidence; refer to the evidence section of this protocol for more information.

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.



Treatment schedule - Overview

Drug	Dose	Route
Idelalisib	150 mg TWICE a day	PO

Continuous until disease progression or unacceptable toxicity

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Drug status: **Idelalisib:** (PBS authority)

Idelalisib is available as **100 mg** and **150 mg** tablets

Cost: ~ $4,790 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		
Idelalisib	150 mg (PO)	TWICE a day with or without food

Continuous until disease progression or unacceptable toxicity

Indications and patient population

- Follicular lymphoma, as monotherapy where disease is refractory to at least 2 prior systemic therapies including both rituximab and an alkylating agent

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. 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. Read more about preventing anti-cancer therapy induced nausea and vomiting
Pneumonitis	Pneumonitis, including organising pneumonia, some with a fatal outcome have occurred with idelalisib. Treatment may be interrupted in patients presenting with pulmonary symptoms or radiographic appearances. Patient should be assessed for an explanatory etiology, considering infectious causes (e.g. CMV). If pneumonitis is suspected the patient should be treated accordingly. If moderate-severe symptomatic pneumonitis or organising pneumonia is diagnosed, appropriate treatment should be initiated and idelalisib should be permanently discontinued.
Gastrointestinal toxicity	Severe diarrhoea or colitis (grade 3 or higher) and intestinal perforation has been associated with idelalisib treatment in clinical trials. Some fatal outcomes were observed. Severe diarrhoea or colitis can be delayed or occur at any time during treatment. Infectious causes (e.g.Clostridum difficile, CMV) should be excluded when assessing patients with colitis. Interruption of idelalisib and additional treatment (e.g. antidiarrhoeal and anti-inflammatory agents such as enteric budesonide) may be recommended. Assess hydration status for all patients with diarrhoea, especially in those with increased risk for dehydration (eg. pre-existing renal failure). Monitor patients for any new or worsening abdominal pain, chills, fever, nausea or vomiting and advise them to promptly report symptoms. Discontinue idelalisib permanently in patients who experience intestinal perforation.
Hepatotoxicity	Hepatotoxicity has been observed with this treatment. Onset of hepatic dysfunction typically occurs within 3 months of starting treatment. Monitor for abnormal liver function tests (LFTs), jaundice and tiredness. Refer to blood tests and dose modification sections for specific recommendations.
Skin toxicity	Severe or life-threatening (grade ≥ 3) cutaneous reactions have been reported in patients treated with idelalisib. Fatal cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have occurred when patients were treated with idelalisib administered concomitantly with other medications associated with SJS-TEN. Idelalisib may be interrupted or discontinued.
Lymphocytosis	A transient increase in lymphocyte counts has been observed with idelalisib therapy. Lymphocytosis associated with idelalisib should not be considered progressive disease in the absence of other clinical findings.
Progressive multifocal leukoencephalopathy	Progressive multifocal leukoencephalopathy (PML) has been reported in one idelalisib study in a CLL patient, who had received rituximab previously. In any patient receiving idelalisib who reports the new onset of, or changes in pre-existing neurologic signs and symptoms, a diagnosis of PML should be considered. Read more about progressive multifocal leukoencephalopathy and the Therapeutic Goods Administration Medicines Safety update on progressive multifocal leukoencephalopathy from the Australian Government, Department of Health.

CMV monitoring	All patients should have cytomegalovirus (CMV) status assessed before starting idelalisib. Monitor closely for laboratory and clinical evidence of CMV infection. If patient is CMV positive or has evidence of a history or CMV infection at baseline, at least monthly clinical and laboratory monitoring for CMV infection is recommended. Use of idelalisib may need to be interrupted or stopped. For patients with **asymptomatic CMV viraemia**, monitor for evidence of high or rising viral load and if confirmed, consider interrupting idelalisib and commence antiviral therapy to prevent invasive disease. For patients with **symptomatic CMV viraemia,** initiate antiviral therapy and consider interrupting idelalisib until CMV disease has resolved. Pre-emptive CMV therapy should be considered if benefits of resuming idelalisib outweigh the risks. Patients with fever and/or other signs of infection should be evaluated promptly and treated accordingly.
Tumour lysis risk	Assess patient for risk of developing tumour lysis syndrome. Read more about prevention and management of tumour lysis syndrome.
Pneumocystis jirovecii pneumonia (PJP) prophylaxis	PJP prophylaxis is recommended in all patients during idelalisib treatment e.g. trimethoprim/sulfamethoxazole 160/800 mg PO one tablet twice daily, twice weekly (e.g. on Mondays and Thursdays) OR one tablet three times weekly (e.g. on Mondays, Wednesdays and Fridays). Post-treatment prophylaxis should continue for 2 to 6 months after the discontinuation of idelalisib and be based on clinical judgement, taking into account the patient's risk factors (e.g. concomitant corticosteroid treatment and prolonged neutropenia). Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients
Antiviral prophylaxis	Antiviral prophylaxis is recommended. Read more about antiviral prophylaxis drugs and doses
Growth factor support	G-CSF (short or long-acting) is available on the PBS for chemotherapy induced neutropenia depending on clinical indication and/or febrile neutropenia risk. Access the PBS website
Blood tests	FBC, EUC, eGFR, LFTs, and LDH at baseline then every 2 weeks for the first 12 weeks, every 4 weeks between weeks 12 and 24, every 6 weeks between weeks 24 and 48, and then every 12 weeks or as clinically indicated.
Hepatitis B screening and prophylaxis	Routine screening for HBsAg and anti-HBc is recommended prior to initiation of treatment. Prophylaxis should be determined according to individual institutional policy. Read more about hepatitis B screening and prophylaxis in cancer patients requiring cytotoxic and/or immunosuppressive therapy
Vaccinations	Live vaccines are contraindicated in cancer patients receiving immunosuppressive therapy and/or who have poorly controlled malignant disease. Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook. 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. 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).

Haematological toxicity	
ANC x 10^9/L	
0.5 to less than 1.0	No dose reduction required. Monitor ANC at least weekly and consider adding G-CSF.
less than 0.5	Delay treatment until recovery. Monitor ANC at least weekly until ANC ≥ 0.5, then resume idelalisib at 100 mg TWICE a day. Consider adding G-CSF.
Platelets x 10^9/L	
25 to less than 50	No dose reduction required. Monitor platelet counts at least weekly.
less than 25	Delay treatment until recovery. Monitor platelet count at least weekly. May resume idelalisib at 100 mg TWICE a day when platelets ≥ 25.

Renal impairment
No dose adjustments are necessary.

Hepatic impairment	
Hepatic dysfunction (ALT/AST)	
> 3-5 x ULN	No dose reduction required. Monitor as least weekly until ≤ 1 x ULN.
> 5-20 x ULN	Delay treatment and monitor at least weekly until ≤ 1 x ULN, then resume idelalisib at 100 mg TWICE a day. If no recurrence, the dose can be re-escalated to 150 mg TWICE a day at the discretion of the treating clinician. If there is recurrence, delay treatment until return to grade 1 or below. Consider resuming idelalisib at the discretion of the treating clinician.
> 20 x ULN	Discontinue idelalisib permanently.
Bilirubin	
> 1.5-3 x ULN	No dose reduction required. Monitor as least weekly until ≤ 1 x ULN.
> 3-10 x ULN	Delay treatment and monitor at least weekly until ≤ 1 x ULN, then resume idelalisib at 100 mg TWICE a day.
> 10 x ULN	Discontinue idelalisib permanently.

Diarrhoea	
Grade 2	No dose reduction required. Monitor as least weekly until recovery.
Grade 3	Delay treatment and monitor at least weekly until recovery, then resume idelalisib at 100 mg TWICE a day. If no recurrence, the dose can be re-escalated to 150 mg TWICE a day at the discretion of the treating clinician.
Grade 4	Discontinue idelalisib permanently.

Rash	
Grade 1 or 2	No dose reduction required. Monitor until resolved.
Grade 3 or 4	Delay treatment until recovery to ≤ grade 1 and resume idelalisib at 100 mg TWICE a day at the discretion of the treating clinician. If no recurrence, the dose can be re-escalated to 150 mg TWICE a day at the discretion of the treating clinician. If SJS or TEN is suspected interrupt idelalisib immediately. Permanently discontinue idelalisib if there is a severe cutaneous reaction.

CMV infection	
Patients with positive baseline CMV serology	Monitor patients with CMV viraemia (positive polymerase (PCR) or antigen test). Consider delaying idelalisib until the infection has resolved. Provide treatment according to established clinical guidelines.
Patients with CMV viraemia without associated clinical signs of CMV infections	Careful monitoring is recommended.
If the benefits of resuming idelalisib outweigh the risks, consider pre-emptive CMV therapy.	

Pneumonitis	
Symptomatic pneumonitis (any grade)	Discontinue idelalisib. However, if re-treatment is appropriate once pneumonitis has resolved, consider resuming idelalisib at 100 mg TWICE a day, at the discretion of the treating physician.
Organising pneumonia	Permanently discontinue idelalisib

Pneumocystis jirovecii pneumonia (PJP)
Delay treatment for suspected PCP infection of any grade; permanently discontinue idelalisib if PJP infection is confirmed.

Intestinal perforation
Permanently discontinue idelalisib.

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*

Idelalisib		
	Interaction	**Clinical management**
CYP3A inhibitors (e.g. amiodarone, aprepitant, azole-antifungals, ritonavir, lapatinib, nilotinib, sorafenib, macrolides, ciclosporin, grapefruit juice etc.)	Increased toxicity of idelalisib possible due to reduced clearance	Avoid combination or monitor for idelalisib toxicity
CYP3A inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St John's wort, dexamethasone etc.)	Reduced efficacy of idelalisib possible due to increased clearance	Avoid combination or monitor for decreased clinical response to idelalisib
CYP3A substrates (e.g. atorvastatin, benzodiazepines, calcineurin inhibitors, clarithromycin, dihydroergotamine, simvastatin, etc.)	Increased toxicity of these drugs possible due to inhibition of CYP3A by idelalisib resulting in reduced clearance	Avoid combination or monitor for increased toxicity of the interacting drugs.

General		
	Interaction	**Clinical management**
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. 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. If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia). For more information link to TGA Medicines Safety Update.
Vaccines	Diminished response to vaccines and increased risk of infection with live vaccines.	Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy. 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

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

Any toxicity grade 2 or greater may require delay of treatment and review by medical officer before commencing treatment.

- weigh patient on each visit

This is a continuous oral treatment

Treatment - Time out

Idelalisib

- administer orally TWICE a day
- to be swallowed whole with a glass of water; do not break, crush or chew
- may be taken with or without food

Note: if a dose is missed and it is less than 6 hours late, it should be taken as soon as the patient remembers. If it is more than 6 hours late, the patient should not take the missed dose.

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

Discharge information

Idelalisib tablets

- Idelalisib tablets with written instructions on how to take them.

Antiemetics

- Antiemetics as prescribed.

Antidiarrhoeals

- Antidiarrhoeals as prescribed.

Growth factor support

- Arrangements for administration if prescribed.

Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. tumour lysis prophylaxis, PJP prophylaxis, antifungals, antivirals.

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
Headache	

Early (onset days to weeks)	
Neutropenia	Abnormally low levels of neutrophils in the blood. This increases the risk of infection. Any fever or suspicion of infection should be investigated immediately and managed aggressively. Read more about immediate management of neutropenic fever
Thrombocytopenia	A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding. Read more about thrombocytopenia
Abdominal pain	Dull ache, cramping or sharp pains are common with some anti-cancer drugs. These are caused by either increased or decreased gastrointestinal motility and can be associated with diarrhoea or constipation.
Anorexia	Loss of appetite accompanied by decreased food intake. Read more about anorexia
Fatigue	Read more about fatigue
Skin rash	Anti-cancer drugs can cause a number of changes in the skin with maculo-papular rash the most common type of drug-induced skin reaction. Read more about skin rash
Constipation	
Gastrointestinal perforation	A rupture of the wall of the stomach, small intestine or large bowel. Symptoms include acute abdominal pain, tenderness and signs of sepsis.
Arthralgia and myalgia	Generalised joint pain or and/or stiffness and muscle aches, often worse upon waking or after long periods of inactivity. Can improve with movement. May be mild or severe, intermittent or constant and accompanied by inflammation. Read more about arthralgia and myalgia
Respiratory tract infection	
Dizziness	Feeling faint or lightheaded, weak or unsteady. Advise patients to stand up slowly from sitting down or lying down positions and increase fluid intake if dehydrated.
Dyspnoea	
Hepatotoxicity	Anti-cancer drugs administered either alone or in combination with other drugs and/or radiation may cause direct or indirect hepatotoxicity. Hepatic dysfunction can alter the metabolism of some drugs resulting in systemic toxicity.
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Electrolyte imbalance	Hypokalaemia, hypercalcaemia, hyponatraemia and hyperuricaemia may occur with idelalisib.
Hyperlipidaemia and hypercholesterolaemia	Abnormally elevated levels of lipids and cholesterol in the blood.
Hypoalbuminaemia	Abnormally low levels of albumin in the blood.

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia
Diarrhoea	Read more about treatment induced diarrhoea
Pulmonary toxicity	Pulmonary toxicity may include damage to the lungs, airways, pleura and pulmonary circulation. Read more about pulmonary toxicity associated with anti-cancer drugs

Evidence

Between April 2011 and October 2012, 41 sites in USA and Europe conducted an open labelled single arm phase 2 multicentre study to assess the efficacy of idelalisib as a single agent. This study recruited 125 patients with relapsed or refractory indolent non-Hodgkin Lymphoma (iNHL), and treated them with idelalisib 150 mg twice daily until disease progressed, unacceptable toxicity or death.[1]

Disease characteristics at study entry

Diagnosis	Number of Patients (%)
Follicular Lymphoma	72 (57.6)
Grade: Grade 1	21 (29.2)
Grade 2	39 (54.2)
Grade 3a	12 (16.7)
FLIPI: Low (≤ 1)	15 (20.8)
Intermediate (2)	18 (25.0)
High (≥ 3)	39 (54.2)
Small Lymphocytic Lymphoma	28 (22.4)
Lymphoplasmacytic Lymphoma/Waldenström macroglobulinemia	10 (8.0)
Marginal Zone Lymphoma	15 (12.0)

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All patients had at least 2 prior systemic therapies, however the median number of prior treatments were 4. All patients had either primary refractory disease, or relapsed within 6 months of rituximab and alkylating chemotherapy.[1]

The primary end point was the overall rate of response (ORR); secondary end points included the duration of response, progression free survival and safety.[1]

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase II trials	Gopal et al. 2014[1]	**Yes**	Yes	
Phase II trials	Salles et al. 2017[2]	**Yes**	Yes	-
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol?**	**Comments**
NCCN	B-Cell Lymphomas 2019 V.4.2019	**Yes**	Yes	-
BCCA	Revised December 2018	**Yes**	Yes	-
CCO	June 2019	**Yes**	Yes	-

Efficacy

The ORR of for all iNHL was 57%, with a complete remission (CR) rate of 6%. The ORR by subtype were similar however it was noted that numbers were small for some categories. Specifically the ORR by subtype were: FL 54%, SLL 61%, MZL 47%, LPL/WM 80%.[1]

The median time to response was 1.9 months, median duration of response 12.5 months and median progression free survival (PFS) was 11 months.[1]

The median duration of treatment was 6.6 months, with a range of 0.6 to 23.9 months. Progressive disease accounted for 33% of all discontinuations, while adverse events 20% of discontinuation.[1]

In a post hoc sub group study analysing only the follicular lymphoma cohort from the phase 2 study, the authors described a median duration of treatment by idelalisib of 8.2 months, during which 59% of all patients experienced a greater than 50% decrease in disease related sum of the product of diameters (SPD). ORR in this sub-analysis was 55.6% with a 13% CR rate. The median time to first response was 2.6 months and the median duration of response was 10.8 months.[2]

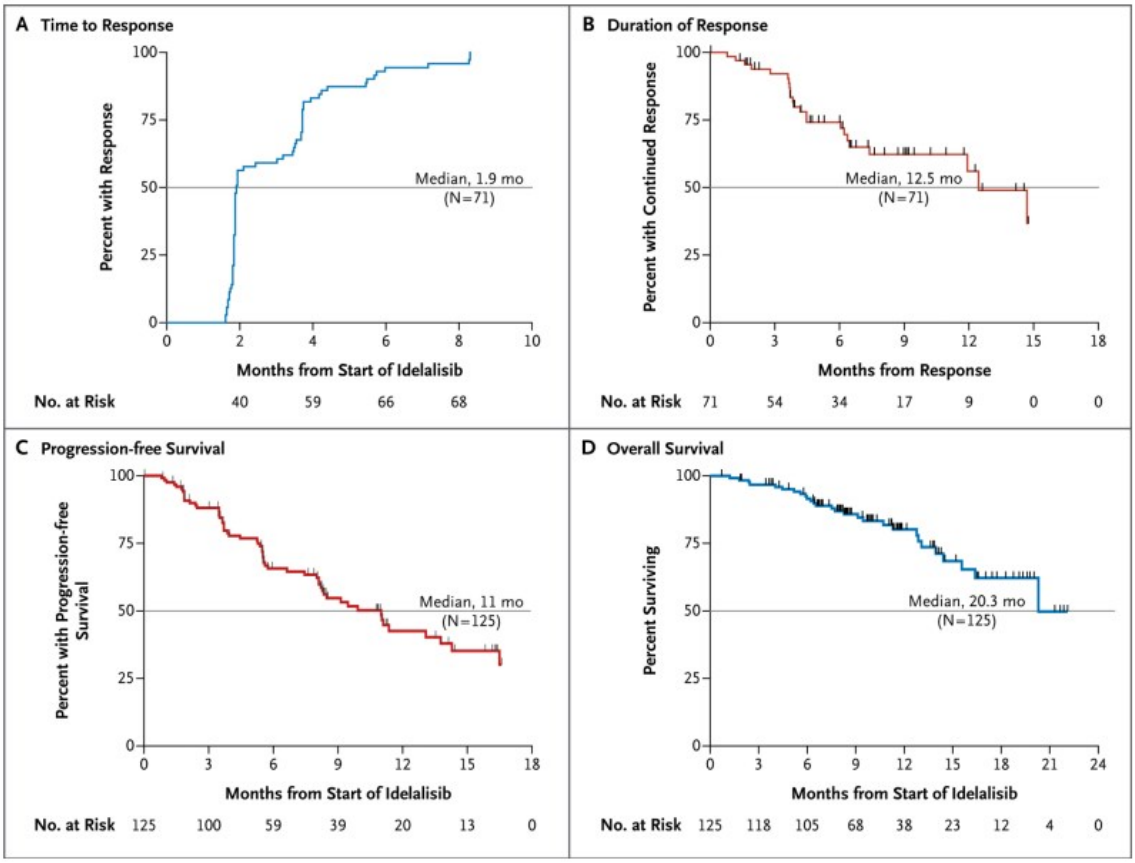

Figure 3. Kaplan–Meier Curves for Secondary End Points
Kaplan–Meier curves are shown for the secondary end points of the time to response (Panel A), the duration of response (Panel B), progression-free survival (Panel C), and overall survival (Panel D) among patients with refractory indolent non-Hodgkin's lymphoma who were treated with idelalisib (intention-to-treat population). The end points were assessed by an independent review committee.

Toxicity

Table 2. Adverse Events during Treatment.*

Event or Abnormality	Grade	
	Any	≥3
	no. (%)	
Adverse event	103 (82)	68 (54)
Diarrhea	54 (43)	16 (13)
Nausea	37 (30)	2 (2)
Fatigue	37 (30)	2 (2)
Cough	36 (29)	0
Pyrexia	35 (28)	2 (2)
Decreased appetite	22 (18)	1 (1)
Dyspnea	22 (18)	4 (3)
Abdominal pain	20 (16)	3 (2)
Vomiting	19 (15)	3 (2)
Upper respiratory tract infection	18 (14)	0
Weight decreased	17 (14)	0
Rash	16 (13)	2 (2)
Asthenia	14 (11)	3 (2)
Night sweats	14 (11)	0
Pneumonia	14 (11)	9 (7)
Peripheral edema	13 (10)	3 (2)
Headache	13 (10)	1 (1)
Hematopoietic laboratory abnormality		
Decreased neutrophils	70 (56)	34 (27)
Decreased hemoglobin	35 (28)	2 (2)
Decreased platelets	32 (26)	8 (6)
Chemical laboratory abnormality		
Increased ALT	59 (47)	16 (13)
Increased AST	44 (35)	10 (8)
Increased alkaline phosphatase	28 (22)	0
Increased bilirubin	13 (10)	0

* Included are adverse events and selected laboratory abnormalities that occurred during treatment in 10% or more of the 125 patients in the study, regardless of whether the event was related to the study drug. Adverse events that occurred during treatment are classified according to the preferred term in the *Medical Dictionary for Regulatory Activities* (MedDRA), version 15.1. Patients who had multiple events within the same preferred-term category were counted once in that category. ALT denotes alanine aminotransferase, and AST aspartate aminotransferase.

It was noted that Grade 1-2 transaminase derangements all returned to normal without any dose modifications.[1]

Drug discontinuation due to adverse events accounted for 20%. Dose modification were required in 34%, mostly due to transaminase derangement, diarrhoea and neutropenia.[1]

28 deaths were reported (22%), with 11 deaths occurring during active treatment or within 30 days of treatment cessation; these were largely due to progressive disease (27%) and pneumonia (27%). Deaths occurring in the long term follow up were largely secondary to progressive disease. There was no evidence of cumulative toxic effects documented.[1]

In the subgroup analysis,[2, 3] the authors reported that within the a total of 51% of patients experienced serious adverse events, mostly pyrexia (19%), diarrhoea (11%) and pneumonia (11%). CMV infection was reported in one pneumonia event, and two colitis events. No cases of pneumocystis jirovecii pneumonia were reported, and prophylaxis was not mandated in this study. Pneumonitis was reported in 3 patients – resulting in 1 drug interruption, 1 drug discontinuation and 1 death.[2]

References

1 Gopal, A. K., B. S. Kahl, S. de Vos, et al. 2014. "PI3Kdelta inhibition by idelalisib in patients with relapsed indolent lymphoma." N Engl J Med 370(11):1008-1018.

2 Salles, G., S. J. Schuster, S. de Vos, et al. 2017. "Efficacy and safety of idelalisib in patients with relapsed, rituximab- and

alkylating agent-refractory follicular lymphoma: a subgroup analysis of a phase 2 study." Haematologica 102(4):e156-e159.

3 Gopal, A. K., B. S. Kahl, C. R. Flowers, et al. 2017. "Idelalisib is effective in patients with high-risk follicular lymphoma and early relapse after initial chemoimmunotherapy." Blood 129(22):3037-3039.

History

Version 1

Date	Summary of changes
25/05/2018	New Protocol discussed at Haematology Reference Committee meeting.
25/07/2018	Approved and published on eviQ.
13/09/2019	Reviewed by Haematology Reference Committee with no significant changes, review in 5 years.
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.
28/04/2023	Reviewed by Haematology Reference Committee, no significant changes made. Review in 4 years.

First approved: 25 July 2018
Last reviewed: 28 April 2023
Review due: 30 June 2027

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/p/3411
26 Nov 2023

Patient information - Non-Hodgkin lymphoma (NHL) - Idelalisib

Patient's name:

Your treatment

The treatment schedule below explains how the drug for this treatment is given.

Idelalisib		
This treatment is taken continuously. Your doctor will advise you how long to take the tablets.		
Day	**Treatment**	**How it is given**
Continuous	**Idelalisib** (*eye-del-a-LIS ib*)	Take orally TWICE a day with or without food. Swallow the tablet whole, do not break, crush or chew. If you vomit a capsule(s), take your normal dose the next time it is due. Do not take an extra dose. If you forget to take a dose, and it is less than 6 hours late, take it as soon as you remember. If it is more than 6 hours late, skip that dose and take your normal dose the next time it is due. Do not take an extra dose.

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 become unwell.

IMMEDIATELY go to your nearest hospital Emergency Department, or contact your doctor or nurse if you have any of the following at any time:	**Emergency contact details** Ask your doctor or nurse from your treating team who to contact if you have a problem
• a temperature of 38°C or higher • chills, sweats, shivers or shakes • shortness of breath • uncontrolled vomiting or diarrhoea • pain, tingling or discomfort in your chest or arms • you become unwell.	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

Anti-cancer drugs can reduce the number of blood cells in your body. You will need to have regular blood tests to check that your blood cell count has returned to normal. If your blood count is low, your treatment may be delayed until it has returned to normal. Your doctor or nurse will tell you when to have these blood tests.

Other medications given during this treatment

- **Anti-sickness (anti-nausea) medication:** you may be given some anti-sickness medication. Make sure you take this medication as your doctor or nurse tells you, even if you don't feel sick. This can help to prevent the sickness starting.
- **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.
- **Prophylaxis medication:** you may need to take some medications to prevent infection and to help prevent or reduce some of the side effects of the chemotherapy. Your doctor or nurse will tell you how and when to take these medications.
- **G-CSF:** you may be given injection(s) of a drug called G-CSF (also called filgrastim, lipegfilgrastim or pegfilgrastim) under your skin. This helps to boost your white blood cell count. Your white blood cells help to fight infection. Lipegfilgrastim and pegfilgrastim are given once. Filgrastim is given for several days until your white blood cells recover. Your doctor will decide if you need this medication. Follow this link to read more information on how to give this injection.

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). • Take your anti-sickness medication as directed even if you don't feel sick. • Drink plenty of fluids (unless you are fluid restricted). • Eat small meals more frequently. • Try food that does not require much preparation. • Try bland foods like dry biscuits or toast. • Gentle exercise may help with nausea. • Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment. • **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.**
Headache	• You can take paracetamol if you have a headache. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get a very bad headache that is not helped by pain medication.**
Early (onset days to weeks)	

Infection risk (neutropenia)	• This treatment lowers the amount of white blood cells in your body. The type of white blood cells that help to fight infection are called neutrophils. Having low level of neutrophils is called neutropenia. If you have neutropenia, you are at greater risk of getting an infection. It also means that your body can't fight infections as well as usual. This is a serious side effect, and can be life threatening. • Wash your hands often. • Keep a thermometer at home and take your temperature regularly, and if you feel unwell. • Do your mouth care regularly. • Inspect your central line site (if you have one) daily for any redness, pus or swelling. • Limit contact with people who are sick. • Learn how to recognise the signs of infection. • Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **a temperature of 38°C or higher** ◦ **chills, shivers, sweats or shakes** ◦ **a sore throat or cough** ◦ **uncontrolled diarrhoea** ◦ **shortness of breath** ◦ **a fast heartbeat** ◦ **become unwell even without a temperature.**
Low platelets (thrombocytopenia)	• This treatment lowers the amount of platelets in your blood. Platelets help your blood to clot. When they are low, you are at an increased risk of bleeding and bruising. • Try not to bruise or cut yourself. • Avoid contact sport or vigorous exercise. • Clear your nose by blowing gently. • Avoid constipation. • Brush your teeth with a soft toothbrush. • Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to. • Tell your doctor or nurse if you have any bruising or bleeding. • **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if you have any uncontrolled bleeding.**
Stomach pain	• You may get: ◦ dull aches ◦ cramping or pain ◦ bloating or flatulence (gas). • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have stomach pain that you are unable to control.**
Appetite loss (anorexia)	• You may not feel like eating. • Try to avoid drinking fluids at meal times. • Try to eat small meals or snacks regularly throughout the day. • Try to eat food that is high in protein and calories. • If you are worried about how much food you can eat, or if you are losing weight, ask to speak to a dietitian.
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. • Do not drive or operate machinery if you are feeling tired. • Nap for short periods (only 1 hour at a time) • Prioritise your tasks to ensure the best use of your energy. • Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted). • Try some gentle exercise daily. • Allow your friends and family to help. • **Tell your doctor or nurse if you get any of the symptoms listed above.**

Skin rash	• You may get a red, bumpy rash and dry, itchy skin. • Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream. • Do not scratch your skin. • Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher. • **Talk to your doctor or nurse about other ways to manage your skin rash.**
Constipation	• You may have bowel motions (stools, poo) that are less frequent, harder, smaller, painful or difficult to pass. • You may also get: ◦ bloating, cramping or pain ◦ a loss of appetite ◦ nausea or vomiting. • Drink plenty of fluids (unless you are fluid restricted). • Eat plenty of fibre-containing foods such as fruit, vegetables and bran. • Take laxatives as directed by your doctor. • Try some gentle exercise daily. • **Tell your doctor or nurse if you have not opened your bowels for more than 3 days.**
Bleeding into stomach or bowel	• This side effect is rare, but can be very serious. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of these signs or symptoms:** ◦ **severe stomach pain** ◦ **swollen and hot skin around your stomach** ◦ **bleeding** ◦ **nausea or vomiting** ◦ **fever or chills** ◦ **a fast heartbeat** ◦ **you feel short of breath.**
Joint and muscle pain and stiffness	• You may get muscle, joint or general body pain and stiffness. • Applying a heat pack to affected areas may help. • Talk to your doctor or nurse about other ways to manage these symptoms. You may need medication to help with any pain.
Chest infection	• You can develop a chest infection whilst receiving this treatment. • **Tell your doctor or nurse as soon as possible if you get any of the following symptoms:** ◦ **shortness of breath** ◦ **difficulty breathing** ◦ **wheezing** ◦ **coughing up mucus**
Dizziness or feeling light-headed	• You may feel dizzy or light-headed. • These symptoms may be caused by your treatment, or other problems like dehydration. • If you are feeling dehydrated, drink plenty of fluids (unless you are fluid restricted) as this can be a cause of dizziness. • If you are feeling dizzy, try lying down until the dizziness passes. • When you want to get up from a sitting or lying down position, get up slowly to let your body adjust to the new position. • Tell your doctor or nurse if you get any of the symptoms listed above.
Shortness of breath	• You may have a cough. • You may feel short of breath. • **Tell your doctor or nurse immediately if you feel you have a cough or feel short of breath.**

Liver problems	• You may get: ◦ yellowing of your skin or eyes ◦ itchy skin ◦ pain or tenderness in your stomach ◦ nausea and vomiting ◦ loss of appetite • You will have regular blood tests to check how well your liver is working. • **Tell your doctor or nurse as soon as possible if you notice that your urine is a dark colour, the whites of your eyes look yellow, or if you have stomach pain.**
Extra fluid in the body (fluid retention)	• You may gain weight over a short amount of time. • Your hands and feet may become swollen, appear red or feel hot and uncomfortable. • Wear loose clothing and shoes that are not too tight. • Try not to stand up or walk around too much at one time. • If your ankles or legs get swollen, try raising them. • Make sure that any cuts or areas of broken skin are treated as soon as possible. • **Tell your doctor or nurse as soon as possible if you get any of the symptoms listed above or gain 1 to 2 kg in a week.** • **Tell your doctor or nurse immediately or go to the nearest hospital Emergency Department if you become short of breath.**
High blood cholesterol levels	• This treatment may increase your blood cholesterol levels. This is not a side effect you will notice. • Your cholesterol levels will be checked during your treatment.

Late (onset weeks to months)	
Low red blood cells (anaemia)	• You may feel dizzy, light-headed, tired and appear more pale than usual. • Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have any chest pain, trouble breathing, or feel like your heart is racing.**
Diarrhoea	• You may get bowel motions (stools, poo) that are more frequent or more liquid. • You may also get bloating, cramping or pain. • Take your antidiarrhoeal medication as directed by your doctor. • Drink plenty of fluids (unless you are fluid restricted). • Eat and drink small amounts more often. • Avoid spicy foods, dairy products, high fibre foods, and coffee. • Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment. • **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.**
Lung problems	• Lung problems are rare, but can be serious. They may occur throughout treatment or after the completion of treatment. • You may get: ◦ shortness of breath ◦ fever ◦ dry cough ◦ wheezing ◦ fast heartbeat ◦ chest pain. • Your doctor will monitor how well your lungs are working during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have chest pain or become short of breath.**

General advice for people having cancer treatment

Chemotherapy safety

- Learn how to keep you and your family safe while you are having anticancer drugs.
- See our patient information sheet - Chemotherapy safety at home.

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 and food safety

- While you are receiving this treatment, it is important that you try to maintain a healthy diet.
- Grapefruit and grapefruit juice can interact with your medication and should be avoided while you are on this treatment.
- 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.
- There are some foods that may cause infection in high risk individuals and should be avoided. For further information on foods to avoid and food hygiene please ask for a copy of the Listeria and food brochure.

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 Leukaemia Foundation on 1800 620 420 (Mon to Fri 9am – 5pm)
- Call the Lymphoma Nurse Support Line on 1800 953 081 (Mon to Fri 9am - 5pm)
- Call the Myeloma Australia Support Line on 1800 693 566 (Mon to Fri 9am - 5pm)

Haematology, transplant and cellular therapy information

- Arrow bone marrow transplant foundation – arrow.org.au
- Australasian Menopause Society – menopause.org.au
- Chris O'Brien Lifehouse - Total Body Irradiation - mylifehouse.org.au/departments/radiation-oncology/total-body-irradiation/
- Healthy Male Andrology Australia – healthymale.org.au/
- International Myeloma Foundation – myeloma.org
- Leukaemia Foundation – leukaemia.org.au
- Lymphoma Australia – lymphoma.org.au
- Myeloma Australia – myeloma.org.au
- NSW Agency for Clinical Innovation, Blood & Marrow Transplant Network – https://aci.health.nsw.gov.au/networks/bmtct
- NSW Agency for Clinical Innovation - aci.health.nsw.gov.au/projects/immune-effector-cell-service
- NCCN Guidelines for Patients Immunotherapy Side Effects: CAR T-Cell Therapy - nccn.org/patientresources/patient-resources/guidelines-for-patients
- Talk Blood Cancer – cmlsupport.org.uk/organisation-type/social-media-groups

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
- eviQ Cancer Treatments Online – eviQ.org.au
- Food Standards Australia New Zealand: Listeria & Food Safety – foodstandards.gov.au/publications/pages/listeriabrochuretext.aspx
- 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

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https://www.eviq.org.au/pi/3411
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