Zanubrutinib

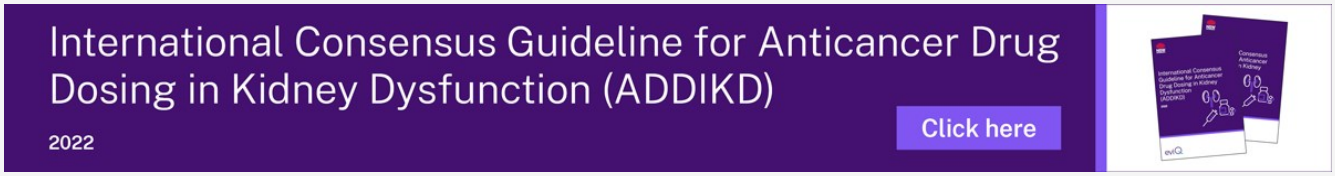
ID: 4081 v.2 **Endorsed**

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

Some indications in this protocol are based on limited evidence; please refer to the individual evidence sections for more information.

This protocol does not have a calculator.

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
Zanubrutinib	160 mg TWICE a day *	PO

*Can be given as 320 mg ONCE daily, at the discretion of the treating clinician.

Continuous until disease progression or unacceptable toxicity

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Drug status: **Zanubrutinib:** (PBS Authority)

Zanubrutinib is available as **80 mg** capsules

Cost: ~ $7,440 per cycle

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		
Zanubrutinib	160 mg (PO)	TWICE a day , approximately 12 hours apart.* Can be taken with or without food. Swallow capsules whole with a glass of water.

*Can be given as 320 mg ONCE daily, at the discretion of the treating clinician.

Continuous until disease progression or unacceptable toxicity

Indications and patient population - Mantle cell lymphoma

- Mantle cell lymphoma in patients who have received at least one prior therapy.

Indications and patient population - Waldenstrom macroglobulinaemia

- Waldenstrom macroglobulinaemia following at least one prior therapy.
- Previously untreated Waldenstrom macroglobulinaemia in patients unsuitable for chemoimmunotherapy.

Indications and patient population - Chronic lymphocytic leukaemia/Small lymphocytic lymphoma

- Monotherapy for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL), including patients with deletion 17p and/or TP53 mutation

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
Cardiac toxicity	Zanubrutinib has been associated with atrial fibrillation and flutter, particularly in patients with cardiac risk factors, hypertension and acute infections. Patients should be monitored for signs and symptoms of atrial fibrillation and atrial flutter and managed as appropriate. Patients who develop arrhythmic symptoms or new onset of dyspnoea should be evaluated clinically, and if indicated, an electrocardiogram (ECG) should be performed. Read more about cardiac toxicity associated with anti-cancer drugs
Haemorrhage	Haemorrhagic events have been reported, both with and without thrombocytopenia. These include minor haemorrhagic events (i.e. contusion, epistaxis, petechiae) and major haemorrhagic events (i.e. gastrointestinal bleeding, intracranial haemorrhage, haematuria). Zanubrutinib may increase the risk of haemorrhage in patients receiving antiplatelet or anticoagulant therapies. Patients should be monitored for signs of bleeding. Consider the benefit-risk of withholding zanubrutinib at least 3 to 7 days pre and post-surgery depending on the risk of bleeding and type of surgery.
Infection risk	Fatal and non-fatal infections (including bacterial, viral or fungal) have occurred in patients treated with zanubrutinib monotherapy. The most common grade 3 or higher infection was pneumonia. Infections due to hepatitis B virus (HBV) or herpes zoster virus reactivation have also occurred. Consider prophylaxis according to standard of care in patients who are at increased risk for infections. Monitor for signs and symptoms of infection and treat appropriately.
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 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). 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
Antifungal prophylaxis	Consider antifungal prophylaxis for at-risk patients. Clinical vigilance and early intervention is recommended in patients with an increased risk of fungal infections. Read more about antifungal prophylaxis drugs and doses.
Blood tests	FBC, EUC, eGFR and LFTs at baseline and repeat monthly during treatment 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

Haematological toxicity	
ANC x 10^9/L	
Less than 1.0 with infection or fever OR Less than 0.5 lasting longer than 10 consecutive days	Delay treatment until recovery and recommence zanubrutinib as below: 1st occurrence: No dose reduction 2nd occurrence: Reduce zanubrutinib to 160 mg ONCE daily or 80 mg TWICE daily* 3rd occurrence: Reduce zanubrutinib to 80 mg ONCE daily 4th occurrence: Cease treatment
* Consider the use of daily G-CSF prophylaxis, which can be reduced in frequency as response allows, in preference to dose reductions.[1]	
Platelets x 10^9/L	
25 to 50 with bleeding OR Less than 25 lasting longer than 10 consecutive days	Delay treatment until recovery and recommence zanubrutinib as below: 1st occurrence: No dose reduction 2nd occurrence: Reduce zanubrutinib to 160 mg ONCE daily or 80 mg TWICE daily 3rd occurrence: Reduce zanubrutinib to 80 mg ONCE daily 4th occurrence: Cease treatment

Renal impairment	
Creatinine clearance (mL/min)	
Greater than 30	No dose adjustments necessary
Less than 30	Monitor for adverse reactions

Hepatic impairment	
Hepatic dysfunction	
Dose modifications are not needed in patients with mild or moderate hepatic impairment.	
Severe (Child-Pugh class C)	Recommended dose is 80 mg TWICE daily **Note:** The safety of zanubrutinib has not been evaluated in patients with severe hepatic impairment. Monitor patients closely for adverse reactions

Non-Haematological toxicity	
Greater than or equal to grade 3	Delay treatment until recovery and recommence zanubrutinib as below: 1st occurrence: No dose reduction 2nd occurrence: Reduce zanubrutinib to 160 mg ONCE daily or 80 mg TWICE daily 3rd occurrence: Reduce zanubrutinib to 80 mg ONCE daily 4th occurrence: Cease treatment
Intracranial haemorrhage (any grade)	Discontinue zanubrutinib

Concomitant use with CYP3A4 inhibitor	
Moderate CYP3A4 inhibitor	Reduce zanubrutinib dose to 80 mg TWICE daily for the duration of inhibitor use **Modify dose for adverse events**
Strong CYP3A4 inhibitor	Reduce zanubrutinib dose to 80 mg ONCE daily for the duration of inhibitor use **Interrupt dose for adverse events**

Note: *After discontinuation of a CYP3A4 inhibitor, resume previous dose of zanubrutinib.*

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*

Zanubrutinib		
	Interaction	**Clinical management**
Strong CYP3A4 inhibitors (e.g. posaconazole, voriconazole, clarithromycin, ritonavir etc.) **Moderate CYP3A4 inhibitors (e.g. ciprofloxacin, diltiazem, erythromycin, fluconazole, verapamil, grapefruit juice, Seville oranges etc.)**	Potentially increased zanubrutinib toxicity due to increased plasma concentrations.	Reduce dose to 80 mg once daily if co-administered with a strong CYP3A inhibitor. Reduce dose to 80 mg twice daily if co-administered with a moderate CYP3A inhibitor. Monitor patients closely for zanubrutinib toxicities; further dose adjustments may be required. If CYP3A4 inhibitor is discontinued, resume previous dose of zanubrutinib.
Moderate or strong CYP3A4 inducers (e.g. carbamazepine, phenytoin, rifampin, St John's Wort etc.)	Potentially reduced efficacy of zanubrutinib due to decreased plasma concentrations.	Avoid co-administration with strong CYP3A4 inducers if possible. Use moderate CYP3A4 inducers with caution. Monitor patients closely for decreased zanubrutinib efficacy.

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

This is a continuous oral treatment

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

Treatment - Time out

Zanubrutinib

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

Note: if a dose is not taken at the scheduled time, it can be taken as soon as possible on the same day, with a return to the normal schedule the following day. Treating clinicians may prescribe a ONCE daily dose.

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

Discharge information

Zanubrutinib capsules

- Zanubrutinib capsules with written instructions on how to take them.

Antiemetics

- Antiemetics as 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)	
Headache	
Nausea and vomiting	Read more about prevention of treatment induced nausea and vomiting

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
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
Atrial fibrillation	
Cardiotoxicity	Cardiotoxicity may manifest as asymptomatic reduction in left ventricular ejection fraction (LVEF), arrhythmia, cardiomyopathy, hypertension, cardiac ischaemia and congestive heart failure (CHF). The risk of cardiotoxicity is increased by a number of factors, particularly a history of heart disease and electrolyte imbalances. Read more about cardiotoxicity associated with anti-cancer drugs
Constipation	
Diarrhoea	Read more about treatment induced diarrhoea
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	
Fatigue	Read more about fatigue
Fever	
Fluid retention and oedema	An excess amount of fluid around the cells, tissues or serous cavities of the body, leading to swelling.
Haemorrhage	
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.
Hypertension	High blood pressure is commonly associated with many anti-cancer drugs. Pre-existing hypertension should be controlled prior to initiation of drugs capable of causing hypertension.
Metabolism and electrolyte imbalance	Hypocalcaemia, hypophosphataemia, hyperkalaemia or hypokalaemia, and hyperglycaemia may occur with zanubrutinib.
Respiratory tract infection	
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

Late (onset weeks to months)	
Anaemia	Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood. Read more about anaemia

Evidence - Mantle cell lymphoma

The expert reference committee supported publication of the protocol based on the information summarised below. The committee was most strongly influenced by the outcome of the phase I/II study of zanubrutinib in B-cell malignancies, which

included a cohort of patients with relapsed or refractory (RR) mantle cell lymphoma (MCL).

Source	Study & Year Published	Supports Use	Is the dose and regimen consistent with the protocol?	Comments
Phase I/II trial	Tam et al. 2021[2]	Yes	**Yes**	-
Phase II trial	Song et al. 2020[3]	Yes	**Yes**	-
Guidelines	**Date published/revised**	**Supports Use**	**Is the dose and regimen consistent with the protocol**	**Comments**
NCCN	2020[4]	Yes	**Yes**	-
BCCA	N/A	N/A	N/A	-
CCO	Oct 2021	Yes	**Yes**	Guideline for relapsed/refractory mantle cell lymphoma

Efficacy

The efficacy and safety of zanubrutinib monotherapy in RR MCL were evaluated in the BGB-3111-AU-003[2] and BGB-3111-206[3] trials, as well as in the pooled analysis of the patient-level data across these two trials.[5] 37 patients were enrolled in the BGB-3111-AU-003 trial with a median follow-up of 18.8 months and 86 patients were enrolled in the BGB-3111-206 trial with a median follow-up of 18.4 months. A subsequent pooled analysis of patient-level data from the two trials included 112 patients with a median follow-up of > 24 months.[5]

In the BGB-3111-AU-003 trial, 91% of patients had an objective response (OR) with a median time to achieving a response of 2.8 months (range 1.9-9.8 months). A total of 31% of patients achieved a complete response (CR) with a median time to CR of 5.5 months (range 1.9-11.1 months). Response to zanubrutinib was independent of baseline characteristics, including disease bulk, blastoid variant, MCL international prognostic index (MIPI), and the number of lines of previous treatment. The median progression-free survival (PFS) was 21.1 months and the overall survival (OS) rate at 12 months was 83%.[2]

In the BGB-3111-206 trial, 84% of patients had an OR with a median time to response of 2.7 months. The overall response rate (ORR) in patients with TP53 mutated disease (27.8% of the study cohort) was comparable to those with wild-type disease, however, the median duration of response (DOR) and PFS were shorter at 14.5 vs. 19.5 months and 14.7 vs. 22.1 months, respectively. A total of 68.6% of patients achieved CR with a median time to CR of 2.9 months. The estimated median PFS was 22.1 months with an OS rate of 84.1% at 12 months in all patients treated in this trial.[3]

In the pooled analysis of these two trials, the ORR was 84.8%, and the complete response rate was 62.5%. The median DOR was 24.9 months with a PFS of 25.8 months and OS of 38.2 months.[5]

Toxicity

A summary of the toxicities associated with this protocol are included in the table below. The most clinically significant toxicities for this treatment are infections, anaemia and bleeding.

Adverse events - mantle cell lymphoma[2]

Table 3. Any-grade treatment-emergent AEs in ≥15% of patients, grade ≥3 AEs in >2 patients, and all AEs of interest in the safety population (N = 32)

AE*	Any-grade AEs	Grade ≥ 3 AEs
Patients with 1 AE	31 (96.9)	19 (59.5)
Diarrhea	14 (43.8)	1 (3.1)
Contusion	12 (37.5)	0
Constipation	10 (31.3)	0
Upper respiratory tract infections	10 (31.3)	0
Fatigue	8 (25.0)	1 (3.1)
Dyspnea	8 (25.0)	0
Peripheral edema	7 (21.9)	2 (6.3)
Back pain	7 (21.9)	1 (3.1)
Rash	7 (21.9)	0
Arthralgia	6 (18.8)	0
Cough	6 (18.8)	0
Muscle spasms	5 (15.6)	0
Pruritis	5 (15.6)	0
Localized infection	5 (15.6)	0
Urinary tract infection	5 (15.6)	0
Pneumonia	4 (12.5)	3 (9.4)
Myalgia	3 (9.4)	3 (9.4)
AEs of interest		
Bleeding	18 (56.3)	3 (9.4)
Major hemorrhage*	3 (9.4)	3 (9.4)
Atrial fibrillation/flutter	2 (6.3) grades 2 and 3	1 (3.1)
Hypertension	2 (6.3)	1 (3.1)
Second primary malignancies	6 (18.8)	1 (3.1)
Skin cancers	5 (15.6)	1 (3.1)
Infections	22 (68.8)	6 (18.8)
Opportunistic infections	3 (9.4)	2 (6.3)
Tumor lysis syndrome	2 (6.3)	2 (6.3)
Anemia	4 (12.5)	4 (12.5)
Neutropenia†	4 (12.5)	3 (9.4)
Thrombocytopenia‡	4 (12.5)	2 (6.3)

All data are n (%).
*Defined as any serious or grade ≥3 bleed at any site or central nervous system bleed of any grade.
†Includes the MedDRA preferred terms neutropenia, neutrophil count decreased, and febrile neutropenia.
‡Includes the MedDRA preferred terms of thrombocytopenia and platelet count decreased.

Evidence - Waldenstrom macrogloublinaemia

Zanubrutinib is an oral inhibitor of Bruton's tyrosine kinase (BTK), with higher BTK occupancy and less off-target toxicity than ibrutinib.

The primary evidence for the use of zanubrutinib in relapsed/refractory (RR) Waldenstrom macroglobulinemia (WM) or patients with previously untreated WM who are unsuitable for standard immunochemotherapy comes from a phase III randomised control trial (ASPEN). In this study, a total of 201 patients, including 164 with RR disease and 37 treatment-naive (TN) patients not suitable for standard therapy with MYD88 L265P mutation, were randomised to either ibrutinib or zanubrutinib (cohort 1) between January 2017 and July 2018. The median age was 70 years, 18 - 19% were TN and only a small proportion of patients were $CXCR4^{WHIM}$ mutated (8% in ibrutinib arm, 11% in zanubrutinib arm). The primary endpoint was the proportion of patients achieving a very good partial response (VGPR) – essentially a ≥90% reduction in IgM level or complete response (CR). The secondary endpoints included major response rate (MRR), duration of response (DOR), progression-free survival (PFS) and safety. The median follow-up period was 19.4 months.[6]

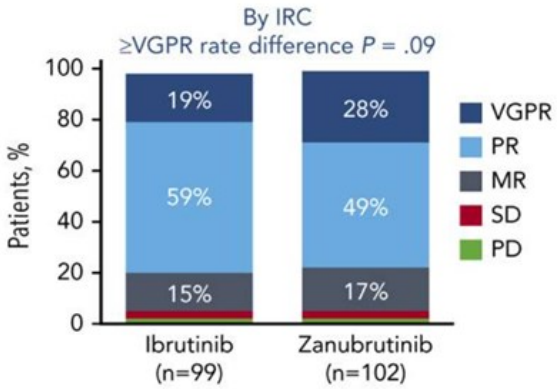
The efficacy and safety of zanubrutinib in MYD88 wildtype ($MYD88^{WT}$) WM was reported in a sub-study of the phase III ASPEN trial.[7] In this study (cohort 2), 28 patients with WM (23 with RR disease and 5 TN patients) received zanubrutinib, of which 26 had $MYD88^{WT}$, and 2 did not have sufficient material for genetic analysis. The median age of patients in cohort 2 overall was 72 years, and the median follow-up was 17.9 months. This was an exploratory study with no pre-specified primary efficacy endpoint. Endpoints included in the analysis included the proportion of patients who achieved CR, VGPR, overall response rate (ORR), MRR, PFS, overall survival (OS) and adverse events (AEs).

The safety and efficacy of long-term zanubrutinib in patients with RR and TN WM treated on a phase I/II trial (BGB3111-AU003) has also been reported.[1] A total of 77 patients (11 with $MYD88^{WT}$) were included with a median follow-up of 37 months and 23 months in RR and TN patients respectively. The endpoints assessed included patients achieving VGPR or CR, ORR, PFS, DOR, OS and changes in markers of disease burden.

Efficacy

The frequency of WM patients with $MYD88^{L265P}$ mutations achieving VGPR, as determined by an independent review committee, was numerically but not significantly higher in patients treated with zanubrutinib compared to ibrutinib on the phase III ASPEN study (28% vs 19% respectively, p = 0.09). No patient achieved CR. Investigator-assessed rates of VGPR were 28% and 17% in the zanubrutinib and ibrutinib arms, respectively (p = 0.04). It should be noted that the PFS outcome for patients treated with chemoimmunotherapy is similar between patients achieving VGPR and CR. The proportion of patients achieving VGPR in intermediate or high-risk groups based on the international prognostic scoring system (IPSS) were similar.

Best overall responses seen in the ASPEN trial[6]



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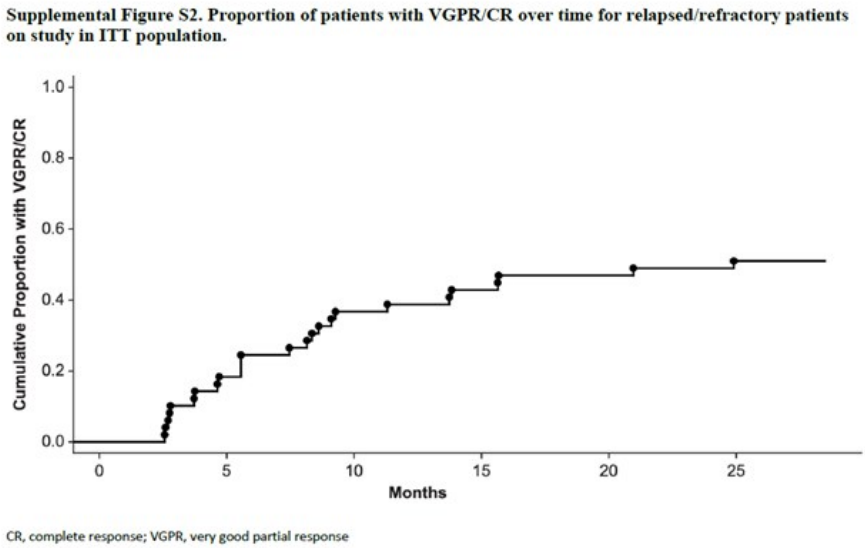
The proportion of $MYD88^{L265P}$ patients achieving MRR (at least a partial response with ≥ 50% reduction in IgM) was similar in those treated with zanubrutinib or ibrutinib (78% vs 80% in RR patients, 74% vs 67% in TN patients). The median time to major response for both arms was 2.8 months. The MRR was also comparable between $CXCR4^{WHIM}$ and $CXCR^{WT}$ patient subgroups with both zanubrutinib and ibrutinib. In the long-term follow-up of patients treated on the phase I/II BGB-311-AU003 study, the proportion of patients achieving VGPR/CR increased over time, with 21% of patients at six months compared to 49% of patients at 24 months, with evidence of a plateau at approximately 20 months.

Proportion of patients achieving VGPR or CR on treatment with zanubrutinib[6]



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Patients with MYD88^{WT} disease treated in cohort 2 of the ASPEN study, demonstrated an overall MRR of 50% and OS of 81%. The median DOR was not reached in patients who had a response on study.

27% of patients achieved VGPR, and no patient achieved CR, which is similar to the proportion of MYD88^{L265P} patients treated with zanubrutinib in cohort 1 of the ASPEN study. Relapsed refractory patients with MYD88^{WT} WM had a MRR of 29% when treated with single-agent rituximab[8], and a VGPR rate of 33% when treated with combination rituximab and ibrutinib in the INNOVATE study.[9]

The median PFS was not reached for either the ibrutinib or zanubrutinib arms in MYD88^{L265P} WM patients treated in the ASPEN study, at a median follow-up of 19 months.[6] The estimated OS rates at 18 months were 97% and 93%, for ibrutinib and zanubrutinib, respectively. In patients with MYD88^{WT} disease, the median PFS was not reached at a median follow-up of 18 months and the estimated OS rate at 18 months was 88%. In the long-term follow-up of MYD88^{L26P} and MYD88^{WT} patients treated on the phase I/II BGB3111-AU003 study, the median PFS was not reached after a median follow-up of 37 months and 23 months for RR and TN patients, respectively.

Toxicity

The incidence of one or more serious adverse events was comparable between zanubrutinib and ibrutinib in the ASPEN study.[6] Infections of grade 3 or higher were similar between both treatments, although the incidence of pneumonia was higher in ibrutinib-treated patients. Bleeding at all grades occurred more frequently in ibrutinib-treated patients. Atrial fibrillation was approximately 10 times more frequent in ibrutinib-treated patients. Neutropenia was significantly more common in zanubrutinib-treated patients, with a higher proportion of patients receiving granulocyte-colony stimulating factor. Dose reduction due to adverse events was more common for ibrutinib-treated patients.

Adverse events - Waldenstrom macroglobulinaemia[6]

Table 3. Treatment-emergent AEs

Event term, n (%)	Ibrutinib (n = 98)		Zanubrutinib (n = 101)	
	All grade	Grade ≥3	All grade	Grade ≥3
Nonhematologic AEs				
Diarrhea*	31 (32)	1 (1)	21 (21)	3 (3)
Upper respiratory tract infection	28 (29)	1 (1)	24 (24)	0
Contusion*	23 (24)	0	13 (13)	0
Muscle spasms*	23 (24)	1 (1)	10 (10)	0
Epistaxis	19 (19)	0	13 (13)	0
Peripheral edema*	19 (19)	0	9 (9)	0
Cough	17 (17)	0	13 (13)	0
Rash	16 (16)	0	13 (13)	0
Hypertension	16 (16)	11 (11)	11 (11)	6 (6)
Arthralgia	16 (16)	0	13 (13)	3 (3)
Fatigue	15 (15)	1 (1)	19 (19)	1 (1)
Atrial fibrillation/flutter*	15 (15)	4 (4)	2 (2)	0
Nausea	13 (13)	1 (1)	15 (15)	0
Vomiting	13 (13)	1 (1)	9 (9)	0
Pyrexia	12 (12)	2 (2)	13 (13)	2 (2)
Pneumonia*	12 (12)	7 (7)	2 (2)	1 (1)
Headache	11 (11)	1 (1)	15 (15)	1 (1)
Urinary tract infection	10 (10)	2 (2)	10 (10)	0
Hematuria	10 (10)	2 (2)	7 (7)	0
Dizziness	9 (9)	0	13 (13)	0
Constipation	7 (7)	0	16 (16)	0
Nasopharyngitis	7 (7)	0	11 (11)	0
Extremity pain	7 (7)	0	11 (11)	1 (1)
Back pain	6 (6)	0	14 (14)	4 (4)
Dyspnea	6 (6)	0	14 (14)	0
Hematologic AEs				
Neutropenia*	13 (13)	8 (8)†	29 (29)	19 (20)†
Febrile neutropenia	0	0	4 (4)	4 (4)
Thrombocytopenia	10 (10)	3 (3)	10 (10)	6 (6)
Anemia	10 (10)	5 (5)	12 (12)	5 (5)

AEIs, events/100 person-months‡	Ibrutinib		Zanubrutinib	
	All grade	Grade ≥3	All grade	Grade ≥3
Infections Opportunistic infections	8.3 0.1	1.2 0	7.9 0.1	1.1 0.1
Bleeding Major hemorrhage	7.0 0.6	0.5 0.5	4.4 0.3	0.3 0.3
Hypertension	1.2	0.8	0.7	0.3
Atrial fibrillation/flutter	1.0	0.2	0.1	0
Neutropenia	0.9	0.5	2.1	1.3
Thrombocytopenia	0.8	0.2	0.6	0.3
Second primary malignancies Skin cancers	0.7 0.6	0.1 0	0.7 0.5	0.1 0
Anemia	0.6	0.3	0.7	0.3
Tumor lysis syndrome	0	0	0	0

Data are for treatment-emergent AEs in all cohort 1 patients. Listed events were reported in ≥10% of patients (all grade) or for grade ≥3, in ≥5% in either arm. Events are listed in descending order of frequency by all-grade incidence in the ibrutinib arm.
*The difference in all-grade incidence between arms is ≥10%. $P = .05$, $P = .005$, and $P = .02$ for comparisons of all-grade diarrhea, muscle spasms, and peripheral edema, respectively. $P = .0004$ and $P = .02$ for the comparisons of all-grade and grade ≥3 atrial fibrillation, and $P = .002$ and $P = .02$ for all-grade and grade ≥3 pneumonia, respectively. All P values (1-sided, testing ibrutinib > zanubrutinib event rates) were calculated using Barnard's exact test without adjustment for multiplicity.
†Includes the *Medical Dictionary for Regulatory Activities*–preferred term "neutrophil count decreased" in 1 and 4 patients in the ibrutinib and zanubrutinib arms, respectively.
‡$P = .08$, $P = .001$, and $P = .009$ for the comparisons of all-grade bleeding, atrial fibrillation, and neutropenia, respectively. $P = .05$ and $P = .03$ for the comparisons of grade ≥3 atrial fibrillation and neutropenia, respectively. All P values are 2-sided without adjustment for multiplicity.[38]

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Evidence - Chronic lymphocytic leukaemia/Small lymphocytic lymphoma

Zanubrutinib has been studied in chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) in a multi-national, phase III clinical trial (ALPINE) comparing two BTK inhibitors, zanubrutinib and ibrutinib in the relapsed/refractory (RR) setting.[10] In this open-label trial conducted from November 2018 to December 2020, 652 patients were randomised to either ibrutinib (325 patients) or zanubrutinib (327 patients). The groups were stratified in terms of baseline characteristics of age, geographic region, chromosome 17p deletion / TP53 mutation status and refractory status. Groups were also similar in terms of immunoglobulin heavy-chain variable region gene (IGHV) mutational status, bulky disease, amount and type of previous therapies received. The median age was 67 years and the median lines of prior therapy was one line in both groups. The median follow up was 29.6 months.[10]

Another multi-centre open-label phase III study (SEQUOIA) investigated zanubrutinib as frontline therapy in untreated CLL/SLL.[11] A total of 590 patients were randomised to zanubrutinib monotherapy (group A, n=241) or bendamustine-rituximab (group B, n=238), unless they had CLL/SLL with deletion of chromosome 17p13.1 (del(17p)) – these patients were either given zanubrutinib monotherapy (group C, n =111) or zanubrutinib with a ramp-up schedule of venetoclax (group D, n= 35).[12] At a median follow up of 26.2 months, the median progression-free survival (PFS) had not been reached in group A or B, however PFS was improved in group A compared to group B with a hazard ratio of 0.42 (p<0.0001).[12]

Efficacy

In the ALPINE trial, the overall response rate in the zanubrutinib group was 83.5%, compared with 74.2% in the ibrutinib group. A higher percentage of patients achieved at least a partial response (PR) with zanubrutinib (89.9%) than ibrutinib (82.5%). The higher response to zanubrutinib was observed in high-risk subgroups such as 17p deletion and/or TP53 mutation. The duration of response has not yet been reached in the zanubrutinib arm. Longer PFS was also seen in the zanubrutinib group compared to the ibrutinib group; at 24 months, PFS rates were 78.4% and 65.9% respectively. The median overall survival (OS) has not been reached in either group.[10]

Moreover, in the SEQUOIA study, patients with CLL/SLL with del(17p) treated with zanubrutinib (group C) had an overall response rate of 94.5% at a median follow up of 18.2 months. The estimated PFS rate was 88.6% (95% CI 79-94%) with an OS rate of 95.1% (95% CI 88-98%). 7 patients from this group discontinued due to progressive disease.[13]

Toxicity

A summary of the safety data in the RR CLL/SLL cohort from the ALPINE study can be seen in table 1.[10] The most common adverse effects of both BTK inhibitors were diarrhoea (16% in the zanubrutinib group vs 24.1% in the ibrutinib group), hypertension (21.9% vs 19.8%), neutropenia (22.8% vs 18.2%) and infections including COVID-19 (23.1% vs 17.9%). The reported incidence of cardiac disorders was lower in the zanubrutinib group (21.3% vs 29.6%).

Atrial fibrillation or flutter was studied as a key secondary outcome, and at any grade was found to be lower in the zanubrutinib group (5.2%) than the ibrutinib group (13.3%). Neutropenia of any grade was higher in the zanubrutinib group (29.3% vs 24.4%), however similar rates of grade ≥3 neutropenia, febrile neutropenia and infections were observed between groups. Haemorrhagic events were of a similar frequency between the two groups.

Table 1: Adverse events that occurred during treatment with zanubrutinib and ibrutinib.[10]

Adverse Events that Occurred during Treatment (Safety Population).*		
Event	**Zanubrutinib (N=324)**	**Ibrutinib (N=324)**
	number of patients (percent)	
≥1 adverse event	318 (98.1)	321 (99.1)
Grade ≥3 adverse events	218 (67.3)	228 (70.4)
Grade ≥3 adverse events reported in >2% of the patients in either trial group		
Neutropenia	52 (16.0)	45 (13.9)
Hypertension	48 (14.8)	36 (11.1)
Covid-19–related pneumonia	23 (7.1)	13 (4.0)
Covid-19	22 (6.8)	16 (4.9)
Pneumonia	19 (5.9)	26 (8.0)
Decreased neutrophil count	17 (5.2)	14 (4.3)
Syncope	9 (2.8)	4 (1.2)
Thrombocytopenia	9 (2.8)	12 (3.7)
Anemia	7 (2.2)	8 (2.5)
Atrial fibrillation	6 (1.9)	12 (3.7)
Increased blood pressure	4 (1.2)	10 (3.1)
Serious adverse events		
All serious adverse events	136 (42.0)	162 (50.0)
Events leading to dose reduction	40 (12.3)	55 (17.0)
Events leading to dose interruption	162 (50.0)	184 (56.8)
Events leading to treatment discontinuation	50 (15.4)	72 (22.2)
Events leading to death	33 (10.2)	36 (11.1)

* The safety population consisted of all the patients who received at least one dose of a trial drug. Shown are all adverse events with an onset from the time of the first dose of trial drug up to 30 days after the last dose of trial drug or to the day before initiation of a new therapy for chronic lymphocytic leukemia or small lymphocytic lymphoma, whichever occurred first. Covid-19 denotes coronavirus disease 2019.

In use as frontline treatment for CLL/SLL, the most frequent grade 3 or worse adverse event was neutropenia, and the incidence of this was markedly reduced in the groups receiving zanubrutinib (groups A and C, 11-15%) compared to bendamustine-rituximab (group B, 51%). Death related to adverse events occurred in 5% in group A, 5% in group B and 3% in group C and were secondary to COVID-19 infection, diarrhoea and aspiration pneumonia.[11]

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History

Version 2

Date	Summary of changes
19/10/2023	New indication added to include chronic lymphocytic leukaemia and small lymphocytic lymphoma. Evidence supporting the new indication updated.Version changed to 2. Review in 1 year.

Version 1

Date	Summary of changes
15/06/2022	New protocol developed out of session as a result of TGA approval. Approved electronically by the Haematology Reference Committee. Protocol published as version number v.1. Review in 1 year.
19/07/2022	Zanubrutinib drug status updated - PBS approved for both indications.
11/11/2022	Protocol reviewed electronically by the Haematology Reference Committee, nil changes. Review in 1 years

First approved: 15 June 2022
Last reviewed: 19 October 2023
Review due: 31 December 2024

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https://www.eviq.org.au/p/4081
23 Nov 2023

Patient information - Zanubrutinib

Patient's name:

Your treatment

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

Zanubrutinib		
This treatment is continuous. Your doctor will advise you how long to take the treatment.		
Day	**Treatment**	**How it is given**
Continuous	**Zanubrutinib** (*zan-oo-broo-ti-nib*)	Take orally TWICE a day with or without food. Swallow whole, do not open, break or chew the capsules. 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, take it as soon as you remember on the same day. If it is a different day, skip the missed dose and take your normal dose the next time it is due. Do not take an extra dose.

Note: Your doctor may prescribe you a ONCE daily dose of zanubrutinib. Check with your doctor, nurse or pharmacist if you are unsure.

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.

Surgery and wound healing

This treatment may affect wound healing. Tell your doctor if you are planning to have surgery or have a wound that has not healed.

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.
- **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.

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)	
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.**
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.**
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.**
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.
Heart palpitations	• You may get: ◦ chest pain ◦ a pounding or fluttering heart (palpitations) ◦ shortness of breath ◦ dizzy or light-headed ◦ confused ◦ more tired than usual. • Tell your doctor if you have any heart problems or are on any heart medications. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

Heart problems	• You may get:
	  ◦ chest pain or tightness
	  ◦ shortness of breath
	  ◦ swelling of your ankles
	  ◦ an abnormal heartbeat.
	• Heart problems can occur months to years after treatment.
	• Tell your doctor if you have a history of heart problems or high blood pressure.
	• Before or during treatment, you may be asked to have a test to see how well your heart is working.
	• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the symptoms listed above.**

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.**

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.**
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.**
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.**

Fever	• You may feel warm. • Tell your doctor or nurse if you get this symptom.
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.**
Bleeding (haemorrhage)	• Tell your doctor or nurse if you have a wound that does not heal. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:** ◦ **unusual bleeding or bruising** ◦ **bright red or black, tarry bowel motions (stools, poo)** ◦ **stomach pain** ◦ **slurred speech** ◦ **shortness of breath** ◦ **a fast heartbeat.**
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.**
High blood pressure (hypertension)	• You may not have any signs or symptoms if you have high blood pressure. • If it is severe you may get headaches, shortness of breath or feel dizzy. • Your blood pressure will be taken regularly during your treatment. • **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the signs or symptoms listed above.**
Low blood calcium or phosphate levels (hypocalcaemia, hypophosphataemia), high or low blood potassium levels (hyperkalaemia, hypokalaemia), high blood sugar level (hyperglycaemia)	• This may be found from your routine blood tests and treated by your doctor. • If it is severe you may get: ◦ muscle cramps, twitches or weakness ◦ bone pain ◦ numbness or tingling in your fingers, toes or around your mouth ◦ constipation ◦ an irregular heartbeat ◦ sleepy, drowsy or confused • You may feel thirsty and need to urinate more often than normal. • You may get repeated infections, especially thrush. • If you are a diabetic, you will need to have your blood sugar levels checked more often. You may also need to have your diabetes medication increased. • **Tell your doctor or nurse as soon as possible if you get any of the signs or symptoms listed above.**

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**
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.**

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.**

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.
- Seville oranges, 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

Additional notes:

First approved: 15 June 2022
Last reviewed: 19 October 2023
Review due: 31 December 2024

The currency of this information is guaranteed only up until the date of printing, for any updates please check:
https://www.eviq.org.au/pi/4081
23 Nov 2023