# Chronic lymphocytic leukaemia venetoclax and rituximab

**ID: 3589** v.3 **Endorsed**

**⚠ Warning: Life threatening tumour lysis syndrome with venetoclax:**
Tumour lysis syndrome (TLS), which may be life threatening or fatal, has been reported in patients treated with venetoclax.

TLS prophylaxis and stringent blood chemistry monitoring is important.

**⚠ Venetoclax azole interaction:**
Azole antifungals reduce the clearance of venetoclax. If the combination is used, the dose of venetoclax should be adjusted as outlined in the protocol below.

Patients with leukaemia should be considered for inclusion into clinical trials. Link to ALLG website and ANZCTR website.

**This protocol is not exportable and does not have a calculator.**

**Related pages:**

- Chronic lymphocytic leukaemia venetoclax DISCONTINUED

## Treatment schedule - Overview

### Titration Phase (Week 1 to 5)

| Drug | Dose | Route | Day |
|---|---|---|---|
| Venetoclax | 20 mg ONCE a day | PO | 1 to 7 (week 1) |
| Venetoclax | 50 mg ONCE a day | PO | 8 to 14 (week 2) |
| Venetoclax | 100 mg ONCE a day | PO | 15 to 21 (week 3) |
| Venetoclax | 200 mg ONCE a day | PO | 22 to 28 (week 4) |
| Venetoclax | 400 mg ONCE a day | PO | 29 to 35 (week 5) |

### Cycle 1 (Week 6 to 9)

| Drug | Dose | Route | Day |
|---|---|---|---|
| Venetoclax | 400 mg ONCE a day | PO | 1 to 28 |
| Rituximab | 375 mg/m$^2$ | IV infusion | 1 |

### Cycle 2 to 6 (Week 10 to 29)

| Drug | Dose | Route | Day |
|---|---|---|---|
| Venetoclax | 400 mg ONCE a day | PO | 1 to 28 |
| Rituximab | 500 mg/m$^2$ | IV infusion | 1 |

### Cycle 7 to 24 (Week 30 onwards)

| Drug | Dose | Route | Day |
|---|---|---|---|
| Venetoclax | 400 mg ONCE a day | PO | 1 to 28 |

**Frequency:** 28 days

**Cycles:** 24 or until disease progression or unacceptable toxicity.

**Notes:**

- Tumour lysis syndrome (TLS), which may be life threatening or fatal, has been reported in patients treated with venetoclax.
- TLS prophylaxis, stringent blood chemistry monitoring and adherence to dose modifications for toxicity is imperative. (see 'Dose modifications' section).
- Consider initiating venetoclax treatment as an inpatient for patients with high tumour burden.

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

Venetoclax is available as **10 mg, 50 mg and 100 mg** tablets

**Cost:** ~ $3,600 (titration phase) and $10,187 per month (cycle 1 to 6)

## 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.*

### Titration Phase (Week 1 to 5)

| Day 1 to 7 | | |
|---|---|---|
| Venetoclax | 20 mg (PO) | ONCE a day with food. Swallow tablets whole with a glass of water. |
| **Day 8 to 14** | | |
| Venetoclax | 50 mg (PO) | ONCE a day with food. Swallow tablet whole with a glass of water. |
| **Day 15 to 21** | | |
| Venetoclax | 100 mg (PO) | ONCE a day with food. Swallow tablet(s) whole with a glass of water. |
| **Day 22 to 28** | | |
| Venetoclax | 200 mg (PO) | ONCE a day with food. Swallow tablet(s) whole with a glass of water. |
| **Day 29 to 35** | | |
| Venetoclax | 400 mg (PO) | ONCE a day with food. Swallow tablet(s) whole with a glass of water. |

### Cycle 1 (Week 6 to 9)

| Day 1 | | |
|---|---|---|
| Venetoclax | 400 mg (PO) | ONCE a day with food. Swallow tablets whole with a glass of water. |
| Paracetamol | 1,000 mg (PO) | 60 minutes before treatment |
| Loratadine | 10 mg (PO) | 60 minutes before treatment |
| Hydrocortisone | 100 mg (IV) | 30 minutes before treatment |
| Rituximab | 375 mg/$m^2$ (IV infusion) | in 500 mL sodium chloride 0.9% as per graded administration rate |
| **Day 2 to 28** | | |

| Day 2 to 28 | | |
|---|---|---|
| Venetoclax | 400 mg (PO) | ONCE a day with food. Swallow tablets whole with a glass of water. |

### Cycle 2 to 6 (Week 10 to 29)

| Day 1 | | |
|---|---|---|
| Venetoclax | 400 mg (PO) | ONCE a day with food. Swallow tablets whole with a glass of water. |
| Paracetamol | 1,000 mg (PO) | 60 minutes before treatment |
| Loratadine | 10 mg (PO) | 60 minutes before treatment |
| Hydrocortisone | 100 mg (IV) | 30 minutes before treatment |
| Rituximab | 500 mg/$m^2$ (IV infusion) | in 500 mL sodium chloride 0.9% as per graded administration rate |

| Day 2 to 28 | | |
|---|---|---|
| Venetoclax | 400 mg (PO) | ONCE a day with food. Swallow tablets whole with a glass of water. |

### Cycle 7 to 24 (Week 30 onwards)

| Day 1 to 28 | | |
|---|---|---|
| Venetoclax | 400 mg (PO) | ONCE a day with food. Swallow tablets whole with a glass of water. |

**Frequency:** 28 days

**Cycles:** 24 or until disease progression or unacceptable toxicity.

## Indications and patient population

**Indications:**

- Chronic lymphocytic leukaemia (CLL) in patients who have received at least one prior therapy.

**Contraindication:**

- Concomitant use of venetoclax and strong CYP3A inhibitors at initiation and during the dose titration phase (see 'Interactions' section).

## Clinical information

| | |
|---|---|
| **Venous access required** | IV cannula (IVC) or central venous access device (CVAD) is required to administer this treatment.<br>Read more about central venous access device line selection |
| **Caution with oral anti-cancer drugs** | Select links for information on the safe prescribing, dispensing and administration of orally administered anti-cancer drugs.<br>Read more about the COSA guidelines and oral anti-cancer therapy |
| **Hypersensitivity/infusion related reaction** | High risk with rituximab.<br>Read more about Hypersensitivity reaction |
| **Premedication** | The product information states that premedication is required for this treatment.<br>Please refer to the treatment schedule for suggested premedication regimen. This may be substituted to reflect institutional policy. |

| | |
|---|---|
| **Emetogenicity minimal or low** | No routine prophylaxis required. If patients experience nausea and/or vomiting, consider using the low emetogenic risk regimen.<br>Read more about preventing anti-cancer therapy induced nausea and vomiting |
| **Tumour lysis risk** | Tumour lysis syndrome (TLS), including renal failure requiring dialysis and fatal events, has occurred in patients with high tumour burden or high leukaemic burden being treated with venetoclax. Consider initiating venetoclax treatment as an inpatient for at risk patients.<br>Assessment of TLS risk, prophylaxis and close monitoring is recommended.<br>See Tumour lysis prophylaxis and monitoring during venetoclax treatment .<br>If adverse events occur venetoclax interruption or discontinuation is recommended. See dose modifications section below. |
| **Rituximab rapid infusion** | This regimen is not in line with the product monograph, however published literature indicates that it can be completed safely.<br>Read more about the rapid infusion of rituximab |
| **Progressive multifocal leukoencephalopathy** | Use of monoclonal antibodies may be associated with an increased risk of progressive multifocal leukoencephalopathy (PML), a rare but potentially fatal opportunistic viral infection of the brain. Patients must be monitored for any new or worsening neurological symptoms.<br>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. |
| **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).<br>Read more about prophylaxis of pneumocystis jiroveci (carinii) in cancer patients |
| **Antiviral prophylaxis** | Antiviral prophylaxis is recommended.<br>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.<br>Access the PBS website |
| **Blood tests** | Stringent blood chemistry monitoring during titration phase is imperative.<br>Post titration phase, consider FBC, EUC, eGFR, LFTs, LDH and urate prior to each 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.<br>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.<br>Refer to the recommended schedule of vaccination for immunocompromised patients, as outlined in the Australian Immunisation Handbook.<br>Read more about COVID-19 vaccines and cancer. |
| **Fertility, pregnancy and lactation** | Cancer treatment can have harmful effects on fertility and this should be discussed with all patients of reproductive potential prior to commencing treatment. There is a risk of foetal harm in pregnant women. A pregnancy test should be considered prior to initiating treatment in females of reproductive potential if sexually active. It is important that all patients of reproductive potential use effective contraception whilst on therapy and after treatment finishes. Effective contraception methods and adequate contraception timeframe should be discussed with all patients of reproductive potential. Possibility of infant risk should be discussed with breastfeeding patients.<br>Read more about the effect of cancer treatment on fertility |

## Dose modifications

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

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

**Note on venetoclax:**

- If a dose interruption is greater than 1 week during the first 5 weeks of the dose titration phase, or greater than 2 weeks after completing the dose titration phase, the risk of tumour lysis syndrome needs to be reassessed to determine if re-initiation with a reduced dose is necessary.
- Dose reductions are calculated as a percentage of the starting dose or using the venetoclax dose reduction table where specified.

| Venetoclax dose reduction table | | | | | | |
|---|---|---|---|---|---|---|
| **Current dose at point of dose interruption** | 400 mg | 300 mg | 200 mg | 100 mg | 50 mg | 20 mg |
| **Restart dose at** | 300 mg | 200 mg | 100 mg | 50 mg | 20 mg | 10 mg |

| Tumour lysis syndrome (TLS) | |
|---|---|
| Blood chemistry suggestive of TLS | Withhold the next day's venetoclax dose and if resolution occurs within 24 to 48 hours of last dose resume at the same dose. |
| Clinical TLS<br><br>OR<br><br>Blood chemistry changes for more than 48 hours | Delay treatment until recovery.<br><br>Resume at lower venetoclax dose as per venetoclax dose reduction table above (depending on when dose interruption occurs).<br><br>Continue the reduced dose for 1 week before increasing the dose. Consider ceasing treatment if dose reductions to less than 100 mg occur for more than 2 weeks.<br><br>Read more about Tumour lysis prophylaxis and monitoring during venetoclax treatment |

| Haematological toxicity | |
|---|---|
| **ANC x $10^9$/L** | |
| Less than 1.0 with infection or fever<br>OR<br>Less than 0.5 | Delay venetoclax treatment until recovery. Consider adding G-CSF if clinically indicated.<br><br>1st occurrence: resume at the same venetoclax dose.<br><br>2nd and subsequent occurrence: Resume at lower venetoclax dose as per venetoclax dose reduction table above (depending on when dose interruption occurs). Continue the reduced dose for 1 week before increasing the dose.<br><br>A larger venetoclax dose reduction may be necessary at the discretion of the physician. Consider ceasing treatment if dose reductions to less than 100 mg occur for more than 2 weeks. |

| Haematological toxicity | |
|---|---|
| **Platelets x $10^9$/L** | |
| Less than 25 or symptomatic bleeding[1] | Delay venetoclax treatment until recovery (platelet count greater than 50 x $10^9$/L without transfusional support for 5 days).[1]<br><br>1st occurrence: resume at the same venetoclax dose.<br><br>2nd and subsequent occurrence: resume at lower venetoclax dose as per venetoclax dose reduction table above (depending on when dose interruption occurs). Continue the reduced dose for 1 week before increasing the dose.<br><br>A larger venetoclax dose reduction may be necessary at the discretion of the physician. Consider ceasing treatment if dose reductions to less than 100 mg occur for more than 2 weeks. |

| Renal impairment | |
|---|---|
| **Creatinine clearance (mL/min)** | |
| 30 to 50 | No dose adjustments necessary. |
| Less than 30 | There is no data for venetoclax in patients with severe renal impairment.<br><br>Updated pharmacokinetic studies included in the product information for venetoclax suggest no dose modifications are required if CrCl >15 mL/min. |

| Hepatic impairment | |
|---|---|
| **Hepatic dysfunction** | |
| Moderate | No dose adjustments necessary. |
| Severe | Reduce venetoclax dose by 50% and monitor for signs of toxicity. |

| Concomitant use with CYP3A4 inhibitor | |
|---|---|
| **Dose titration phase** | |
| Strong CYP3A4 inhibitor (e.g. azole antifungals) | Concomitant use with venetoclax is contraindicated. |
| Moderate CYP3A4 inhibitor | Reduce venetoclax dose by at least 50%. |
| **Week 6 onwards (post titration phase)** | |
| Strong CYP3A4 inhibitor (e.g. azole antifungals) | Reduce venetoclax dose by at least 75%. |
| Moderate CYP3A4 inhibitor | Reduce venetoclax dose by at least 50%. |

| Non-Haematological toxicity | |
|---|---|
| Greater than or equal to grade 3 | Delay venetoclax treatment until recovery.<br><br>1st occurrence: resume at the same venetoclax dose.<br><br>2nd and subsequent occurrence: resume at lower venetoclax dose as per venetoclax dose reduction table above (depending on when dose interruption occurs). Continue the reduced dose for 1 week before increasing the dose.<br><br>A larger venetoclax dose reduction may be necessary at the discretion of the physician. Consider ceasing treatment if dose reductions to less than 100 mg occur for more than 2 weeks. |

## 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*

| Rituximab | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Antihypertensives** | Additive hypotensive effect | Consider withholding antihypertensive medications 12 hours prior to the rituximab infusion |

| Venetoclax | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **CYP3A4 inhibitors (e.g. aprepitant, azole antifungals, clarithromycin, erythromycin, fluvoxamine, grapefruit juice, ritonavir, seville oranges etc.)** | Increased toxicity of venetoclax possible due to reduced clearance | *Dose titration phase:*<br>• Concomitant administration with a strong CYP3A4 inhibitor (e.g. ritonavir, vorinconazole, posaconazole) is contraindicated.<br>• Concomitant administration with a moderate CYP3A4 inhibitor (e.g. ciprofloxacin, fluconazole) should be avoided or alternative treatments considered. If a moderate CYP3A4 inhibitor must be used, venetoclax dose should be reduced by at least 50%.<br><br>*Week 6 onwards*<br><br>Once titration phase is complete and steady daily dose achieved venetoclax dose should be:<br>• Reduced by at least 75% when administered with a strong CYP3A4 inhibitor.<br>• Reduced by at least 50% when administered concomitantly with a moderate CYP3A4 inhibitor. |
| **CYP3A4 inducers (e.g. carbamazepine, phenytoin, phenobarbitone, rifampicin, St Johns wort etc.)** | Reduced efficacy of venetoclax due to increased clearance | Avoid combination with strong or moderate CYP3A4 inducers, or consider alternative agents with less CYP3A4 induction. |
| **P-glycoprotein inhibitors (e.g. verapamil, ciclosporin)** | Increased toxicity of venetoclax possible due to reduced clearance | Avoid combination.<br>If combination must be used monitor patients closely |
| **P-glycoprotein and BCRP substrates (e.g. digoxin, morphine, topotecan)** | Venetoclax may alter the absorption of the substrate | Avoid combination with narrow therapeutic index drugs.<br>If combination must be used administer at least 6 hours before |

| Venetoclax | | |
|---|---|---|
| | | venetoclax |
| **Warfarin** | Increased risk of bleeding | Monitor international normalised ratio (INR) closely when used in combination |

| General | | |
|---|---|---|
| | **Interaction** | **Clinical management** |
| **Antiepileptics** | Both altered antiepileptic and anti-cancer drug levels may occur, possibly leading to loss of efficacy or toxicity. | Where concurrent use of an enzyme-inducing antiepileptic cannot be avoided, monitor antiepileptic serum levels for toxicity, as well as seizure frequency for efficacy; adjust dosage as appropriate. Also monitor closely for efficacy of the anti-cancer therapy. |
| **Antiplatelet agents and NSAIDs** | Increased risk of bleeding due to treatment related thrombocytopenia. | Avoid or minimise combination.<br>If combination deemed essential, (e.g. low dose aspirin for ischaemic heart disease) monitor for signs of bleeding. |
| **Serotonergic drugs, including selective serotonin reuptake inhibitors (SSRIs e.g. paroxetine) and serotonin noradrenaline reuptake inhibitors (SNRIs e.g. venlafaxine)** | Increased risk of serotonin syndrome with concurrent use of 5-HT3 receptor antagonists (e.g. palonosetron, ondansetron, granisetron, tropisetron, dolasetron, etc.) | Avoid combination.<br>If combination is clinically warranted, monitor for signs and symptoms of serotonin syndrome (e.g. confusion, agitation, tachycardia, hyperreflexia).<br>For more information link to TGA Medicines Safety Update. |
| **Vaccines** | Diminished response to vaccines and increased risk of infection with live vaccines. | Live vaccines (e.g. BCG, MMR, zoster and varicella) are contraindicated in patients on immunosuppressive therapy. Use with caution in patients on non-immunosuppressive therapy.<br>For more information; refer to the recommended schedule of vaccination for cancer patients, as outlined in the Australian Immunisation Handbook 10th Edition (updated 2018) |

## Administration Titration phase (Week 1 to 5)

*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.*

### Days 1 to 35

**This is an oral treatment**

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

- baseline weight
- dipstick urinalysis each visit

### Treatment - Time out

#### Venetoclax

- administer orally ONCE daily with food
- to be swallowed whole with a glass of water; do not break, crush or chew

**Note**: if a dose is missed and within 8 hours of the usual dose time, it should be taken as soon as the patient remembers. If it is more than 8 hours 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

#### Venetoclax tablets

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

#### Antiemetics

- Antiemetics if required or prescribed.

#### Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. antivirals, tumour lysis prophylaxis, PJP prophylaxis and medication for constipation.

#### Patient information

- Ensure patient receives patient information sheet.

# Administration cycles 1 to 6 (Week 6 to 29)

*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.*

## Day 1

**Approximate treatment time: 4 to 6 hours (initial); 3 to 4 hours (subsequent)**

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

- baseline weight
- dipstick urinalysis prior to treatment

Insert IV cannula or access TIVAD or CVAD.

### Treatment - Time out

#### Venetoclax

- administer orally ONCE daily with food
- to be swallowed whole with a glass of water; do not break, crush or chew

**Note**: if a dose is missed and within 8 hours of the usual dose time, it should be taken as soon as the patient remembers. If it is more than 8 hours the patient should not take the missed dose.

#### Rituximab

**Prior to administration:**

- check baseline observations

- check for previous adverse events during previous infusions
- verify premedication has been taken. If not, administer 30 to 60 minutes prior to rituximab administration:
  - paracetamol 1000 mg orally AND
  - loratadine 10 mg orally (or similar antihistamine)
  - a steroid may also be included as a premed according to local guidelines

#### Initial infusion:

- **commence rituximab** infusion at 50 mg/hr for 30 minutes
- repeat observations prior to each rate increase
- **increase rate** by 50 mg/hr every 30 minutes, up to a maximum of 400 mg/hr if observations are stable
- flush with ~ 50 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have completely resolved, recommence the infusion at half the rate prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Transient hypotension may occur. Consider withholding antihypertensive medication for 12 hours before and during infusion.

#### Subsequent infusions:

If an adverse event was experienced with initial infusion recommence infusion at the same rate as initial infusion

- **commence** rituximab infusion at 100 mg/hr
- repeat observations prior to each rate increase
- increase rate by 100 mg/hr increments every 30 minutes to a maximum of 400 mg/hr if observations are stable
- flush with ~ 50 mL of sodium chloride 0.9%

If an infusion reaction occurs, temporarily discontinue the infusion and notify medical officer

- when symptoms have resolved, recommence the infusion at **half the rate** prior to the reaction
- for severe reactions **stop** infusion and manage as per emergency

Read more about rapid infusion rituximab

Remove IV cannula and/or deaccess TIVAD or CVAD.

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

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## Days 2 to 28

**This is an oral treatment**

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

- dipstick urinalysis each visit

### Treatment - Time out

### Venetoclax

- administer orally ONCE daily with food
- to be swallowed whole with a glass of water; do not break, crush or chew

**Note**: if a dose is missed and within 8 hours of the usual dose time, it should be taken as soon as the patient remembers. If it is more than 8 hours the patient should not take the missed dose.

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

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## Discharge information

#### Venetoclax tablets

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

#### Antiemetics

- Antiemetics if required or prescribed.

#### Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. antivirals, tumour lysis prophylaxis, PJP prophylaxis and medication for constipation.

#### Patient information

- Ensure patient receives patient information sheet.

## Administration cycles 7 to 24 (Week 30 onwards)

*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.*

### Days 1 to 28

**This is an oral treatment**

Safe handling and waste management (reproductive risk only)

Safe administration

General patient assessment prior to each day of treatment.

- dipstick urinalysis each visit

### Treatment - Time out

#### Venetoclax

- administer orally ONCE daily with food
- to be swallowed whole with a glass of water; do not break, crush or chew

**Note**: if a dose is missed and within 8 hours of the usual dose time, it should be taken as soon as the patient remembers. If it is more than 8 hours 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

#### Venetoclax tablets

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

#### Antiemetics

- Antiemetics if required or prescribed.

#### Prophylaxis medications

- Prophylaxis medications (if prescribed) i.e. antivirals, tumour lysis prophylaxis, PJP prophylaxis and medication for constipation.

#### 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) | |
|---|---|
| **Flu-like symptoms** | Symptoms include fever, chills, rigors, diaphoresis, malaise, myalgia, arthralgia, loss of appetite, dry cough and headache. |
| **Hypersensitivity reaction** | Anaphylaxis and infusion related reactions can occur with this treatment.<br>Read more about hypersensitivity reaction |
| **Metabolism and electrolyte imbalance** | Tumour lysis syndrome, hyperphosphataemia, hyperkalaemia, hypocalcaemia and hyperuricaemia may occur with venetoclax. |
| **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.<br>Read more about immediate management of neutropenic fever |
| **Thrombocytopenia** | A reduction in the normal levels of functional platelets, increasing the risk of abnormal bleeding.<br>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.<br>Read more about arthralgia and myalgia |
| **Atrial fibrillation** | |
| **Constipation** | |
| **Diarrhoea** | Read more about treatment induced diarrhoea |
| **Fatigue** | Read more about fatigue |
| **Fever** | |
| **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.<br>Read more about skin rash |
| **Respiratory tract infection** | |

| Late (onset weeks to months) | |
|---|---|
| **Anaemia** | Abnormally low levels of red blood cells (RBCs) or haemoglobin in the blood.<br>Read more about anaemia |
| **Progressive multifocal leukoencephalopathy (PML)** | A rare opportunistic viral infection of the brain, usually leading to death or severe disability, can occur with monoclonal antibodies (e.g. rituximab, obinutuzumab, ofatumumab, brentuximab vedotin) and other targeted therapies (e.g. ibrutinib, ruxolitinib, idelalisib). Onset may occur up to months after the final dose.<br>Read more about progressive multifocal leukoencephalopathy (PML) |

## Evidence

The evidence supporting this protocol is provided by a phase III multicentre international, open label randomised trial (MURANO) involving 389 patients comparing venetoclax plus rituximab with bendamustine plus rituximab in patients with relapsed or refractory chronic lymphocytic leukaemia (CLL).[1]

Between March 31, 2014 and September 23, 2015, 389 patients were randomised in a 1:1 ratio. 194 received venetoclax-rituximab and 195 received bendamustine-rituximab. Venetoclax was administered in a 5-week schedule with gradual ramp up from 20 mg daily to 400 mg daily. Rituximab was commenced after the venetoclax ramp-up period (cycle 1: 375 mg/m$^2$; cycle 2 to 6: 500 mg/m$^2$) at 28-day treatment cycles. Venetoclax 400 mg was administered daily continuously for 2 years unless disease

progression or toxicity occurred. In the bendamustine-rituximab arm, bendamustine was administered at 70 mg/m$^2$ on day 1 and 2 of 28-day treatment cycles for a total of 6 cycles in combination with the same aforementioned rituximab dosing schedule.[1]

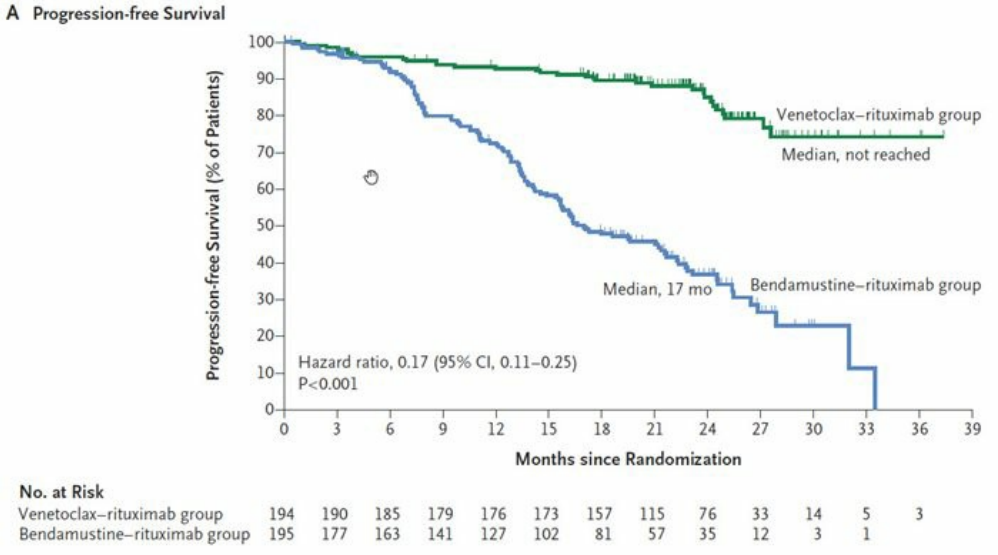
There was no crossover to venetoclax after disease progression.

The primary end point was investigator-assessed progression free survival, defined as the time from randomisation to first occurrence of disease progression, relapse or death of any cause. Secondary efficacy end point included independent review committee-assessed progression free survival, investigator-assessed and independent review committee-assessed progression free survival in patients with chromosome 17p deletion, investigator-assessed and independent review committee-assessed overall response rate and complete response rate, overall survival, rates of clearance of minimal residual disease, duration of response, event free survival, and time to next treatment for CLL.[1]

## Efficacy

After a median follow up of 23.8 months, the median progression-free survival (PFS) as assessed by the investigator was 17 months in the bendamustine-rituximab arm and not reached in the venetoclax-rituximab group (Figure 1). The 2-year investigator-assessed PFS was 84.9% (95% CI, 79.1 to 90.6) in the venetoclax-rituximab group and 36.3% (95% CI, 28.5 to 44.0) in the bendamustine-rituximab group (HR for progression or death, 0.17; 95% CI ,0.11 to 0.25 p<0.001).

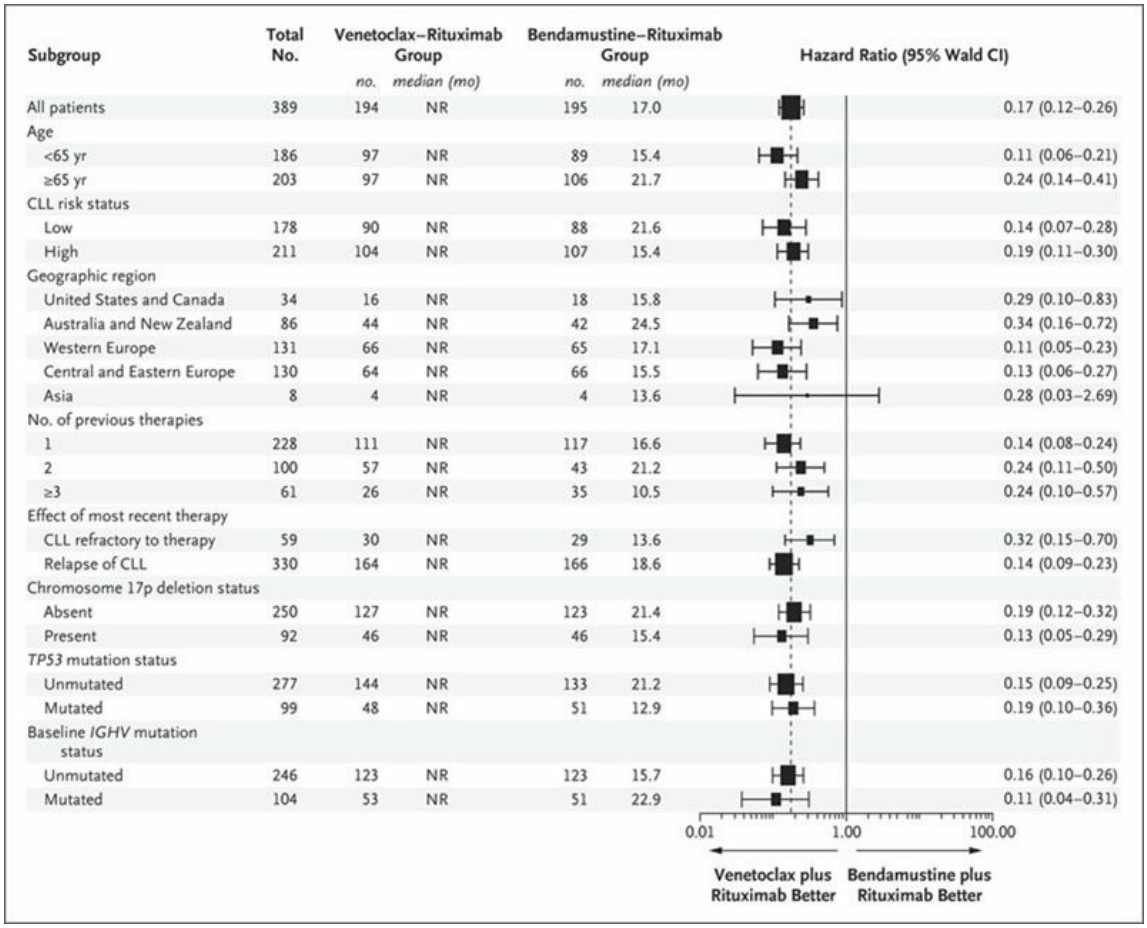
**Figure 1: Kaplan Meier estimates of investigator-assessed PFS**[1]






There was consistent benefit in the venetoclax-rituximab group in pre-specified subgroups (Figure 2), including 17p deletion, with 2-year investigator-assessed PFS being higher in the venetoclax-rituximab group than the bendamustine-rituximab group (81.5% vs 27.8%; HR 0.13; 95%CI, 0.05 to 0.29). Overall survival was higher in the venetoclax-rituximab group than in the bendamustine-rituximab group, with 2-year survival being 91.9% and 86.6%, respectively (HR, 0.48; 95% CI, 0.25 to 0.90).

**Figure 2: Pre-specified subgroup analysis of investigator-assessed PFS**[1]






The investigator-assessed overall response rate (ORR) was 93.3% in the venetoclax-rituximab group and 67.7% in the bendamustine-rituximab group. The rate of investigator-assessed complete response (CR) or complete response with incomplete haematologic recovery (CRi) was 26.8% in the venetoclax-rituximab group and 8.2% in the bendamustine-rituximab group. Of the 68 patients across the CR/CRi groups, 50 were classified as partial response and one as having stable disease (as assessed by the independent review committee). The main reason for discordance in the rate of CR/CRi was due to divergent interpretation of residual adenopathy on computed tomography (Figure 3).

**Figure 3: Reasons for the lower independent review committee CR/CRi rate relative to the investigator-assessed CR/CRi rate**[1]

| Reason for discrepancy | Venetoclax plus rituximab n=42 | Bendamustine plus rituximab n=9 |
|---|---|---|
| CT scan (all reasons) | 33 | 7 |
| Lesions 16–20 mm | 18 | 3 |
| Lesions 21–30 mm | 10 | 2 |
| Lesions >30 mm | 1 | 2 |
| Anatomy missing | 3 | 0 |
| Spleen enlarged | 1 | 0 |
| Bone marrow, elements missing | 4 | 2 |
| Growth factor use | 2 | 0 |
| Spleen size /ALC fluctuation | 2 | 0 |
| Adverse event – secondary malignancy[a] | 1 | 0 |

The IRC-adjudicated reduction in CR/CRi rates was proportional in the two treatment arms.

[a] Omental and peritoneal nodules likely related to metastatic lung cancer rather than CLL. No biopsy available.

ALC, absolute lymphocyte count; CR, complete response; CRi, complete response with incomplete hematologic recovery; PR, partial response.



## Toxicity

379 patients (99.2%) had at least one adverse event. 100% in the venetoclax-rituximab group and 98.4% in the bendamustine-rituximab group. Grade 3 or 4 adverse events were reported in 82% of the venetoclax-rituximab group and 70.2% of the bendamustine-rituximab group. The most common grade 3 or 4 adverse event was neutropenia with a higher incidence in the venetoclax-rituximab group than in the bendamustine-rituximab group (57.7% vs 38.8%). However, the incidence of grade 3 or 4

febrile neutropenia and infections was lower in the venetoclax-rituximab group. Grade 3 or 4 tumour lysis syndrome was reported in 6 patients (3.1%) in the venetoclax-rituximab group and in 2 patients (1.1%) in the bendamustine-rituximab group.

**Adverse events - MURANO study**[1]

**Table 2. Adverse Events.***

| Event | Venetoclax–Rituximab Group (N=194) | Bendamustine–Rituximab Group (N=188) |
|---|---|---|
| Grade 3 or 4 adverse event — no. of patients (%) | 159 (82.0) | 132 (70.2) |
| Total no. of events | 335 | 255 |
| Grade 3 or 4 adverse events with at least 2% difference in incidence between groups — no. of patients (%) | 130 (67.0) | 104 (55.3) |
| Neutropenia† | 112 (57.7) | 73 (38.8) |
| Infections and infestations | 34 (17.5) | 41 (21.8) |
| Anemia | 21 (10.8) | 26 (13.8) |
| Thrombocytopenia | 11 (5.7) | 19 (10.1) |
| Febrile neutropenia | 7 (3.6) | 18 (9.6) |
| Pneumonia | 10 (5.2) | 15 (8.0) |
| Infusion-related reaction | 3 (1.5) | 10 (5.3) |
| Tumor lysis syndrome‡ | 6 (3.1) | 2 (1.1) |
| Hypotension | 0 | 5 (2.7) |
| Hyperglycemia | 4 (2.1) | 0 |
| Hypogammaglobulinemia | 4 (2.1) | 0 |
| Serious adverse events with at least 2% incidence in either group — no. of patients (%) | 90 (46.4) | 81 (43.1) |
| Pneumonia | 16 (8.2)§ | 15 (8.0) |
| Febrile neutropenia | 7 (3.6) | 16 (8.5) |
| Pyrexia | 5 (2.6) | 13 (6.9) |
| Anemia | 3 (1.5) | 5 (2.7) |
| Infusion-related reaction | 1 (0.5) | 6 (3.2) |
| Sepsis | 1 (0.5) | 4 (2.1) |
| Tumor lysis syndrome | 4 (2.1) | 1 (0.5) |
| Hypotension | 0 | 5 (2.7) |
| Fatal adverse events — no. of patients (%) | 10 (5.2)§ | 11 (5.9) |

* Before the initiation of a trial drug, only serious adverse events that were considered to have been caused by a protocol-mandated intervention were reported (e.g., serious adverse events related to invasive procedures, such as biopsies). After the initiation of a trial drug, all adverse events, regardless of the relationship to the trial drug, were reported through 28 days after the last dose of trial drug (a maximum of 2 years for the venetoclax–rituximab group) or through 90 days after the last dose of rituximab, whichever was longer. After this period, investigators were to report any deaths, serious adverse events, or other adverse events of concern that were believed to be related to previous treatment with the trial drug.
† A higher percentage of new-onset events of neutropenia occurred during the combination-treatment period than during the venetoclax monotherapy phase (54.1% vs. 11.1%). Protocol-mandated dose interruption for all grade 3 or 4 events of neutropenia occurred in 43.3% of the patients in the venetoclax–rituximab group. In total, 47.9% of the patients in the venetoclax–rituximab group and 43.1% of the patients in the bendamustine–rituximab group received growth factor.
‡ Additional information on the events of the tumor lysis syndrome can be found in Table S12 in the Supplementary Appendix.
§ Two serious adverse events of pneumonia that resulted in death occurred in patients who had both disease progression and confirmed Richter's transformation (i.e., conversion into an aggressive lymphoma, typically diffuse large B-cell lymphoma).



Richter's transformation was confirmed in 6 patients in the venetoclax-rituximab group and in 5 patients in the bendamustine-rituximab group.

Death occurred in 10 (5.2%) patients in the venetoclax-rituximab group and in 11 (5.9% in the bendamustine-rituximab group (4 fatal infections in each group).

48 patients discontinued venetoclax and 13 patients discontinued rituximab in the venetoclax-rituximab arm while 27 patients discontinued bendamustine-rituximab.

Follow up data from subsequent publication from Kater et al showed that 130 of the 194 patients randomised to venetoclax-rituximab arm (67%) completed two years of planned venetoclax. 11% had progressive disease, 1% died without progressive disease, 15% withdrew due to adverse events and 6% for other reasons.[2]

Adverse events (AEs) that led to withdrawal during combination therapy were neutropenia (2.1%), thrombocytopenia (1.5%), neoplasm (1%), febrile neutropenia, anaemia, autoimmune haemolytic anaemia, acute respiratory failure, appendicitis, peritoneal tuberculosis, pneumonia, pyrexia, status epilepticus and sudden cardiac death, all accounting for 0.5% each. AEs that led to withdrawal during single agent therapy were neoplasms (2.6%), neutropenia (1.5%), thrombocytopenia (1%); whilst an increase in

ALT, ascites, asthenia, autoimmune haemolytic anaemia, Crohn's disease, diarrhoea, immune thrombocytopenic purpura, hydrothorax, pneumonia, sudden death and vertigo all accounted for 0.5% each.[2]

Updated follow-up results at a median of 22 months post-completion of venetoclax therapy demonstrated no new SAEs related to study drug, with only 3 additional non-melanomatous skin cancers detected (bendamustine-rituximab, n=1, melanoma; venetoclax-rituximab, n=2, melanoma and breast cancer). There were no additional reports of Richter's transformation.[3]

## References


1 Seymour, J. F., T. J. Kipps, B. Eichhorst, et al. 2018. "Venetoclax-Rituximab in Relapsed or Refractory Chronic Lymphocytic Leukemia." N Engl J Med 378(12):1107-1120.

2 Kater, A. P., J. F. Seymour, P. Hillmen, et al. 2019. "Fixed Duration of Venetoclax-Rituximab in Relapsed/Refractory Chronic Lymphocytic Leukemia Eradicates Minimal Residual Disease and Prolongs Survival: Post-Treatment Follow-Up of the MURANO Phase III Study." J Clin Oncol 37(4):269-277.

3 Kater, A. P., J. Q. Wu, T. Kipps, et al. 2020. "Venetoclax Plus Rituximab in Relapsed Chronic Lymphocytic Leukemia: 4-Year Results and Evaluation of Impact of Genomic Complexity and Gene Mutations From the MURANO Phase III Study." J Clin Oncol 38(34): 4042-4054.


## History

### Version 3

| Date | Summary of changes |
|---|---|
| **28/04/2023** | Subcutaneous rituximab information removed from the following sections - treatment schedule, clinical information, administration, patient information. Increased to version 3. |

### Version 2

| Date | Summary of changes |
|---|---|
| **27/03/2020** | Protocol reviewed at Haematology Reference Committee meeting. Severe renal impairment dose modification recommendations added as per product information. Version number increased to v.2. Review in 2 years. |
| **01/10/2021** | Drug status updated: rituximab SC is TGA registered but no longer PBS listed. |
| **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. |
| **02/06/2022** | Protocol reviewed electronically by the Haematology Reference Committee, updates include:<br>• addition of venetoclax-azole interaction flag<br>• minor change to dose modifications<br>• evidence update.<br><br>Review in 4 years. |
| **19/12/2022** | Dose modifications section reformatted. |

### Version 1

| Date | Summary of changes |
|---|---|
| **29/07/2019** | Protocol developed out of session. Circulated to Haematology Reference Committee members for review via email.<br><br>Approved and published on eviQ. Version number v.1. |

**First approved:** 29 July 2019
**Last reviewed:** 28 April 2023
**Review due:** 30 June 2026

***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/3589*
*19 Sep 2023*

# Patient information - Chronic lymphocytic leukaemia (CLL) - Venetoclax and rituximab

**Patient's name:**

## Your treatment

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

| Venetoclax and rituximab | | | |
|---|---|---|---|
| The first 5 weeks of treatment is a titration phase where the dose of venetoclax is gradually increased. From week 6 onwards, rituximab is added to the schedule and this treatment cycle is repeated every 28 days. You will have up to 6 cycles. Your doctor will advise you how long to take the tablets. | | | |
| **Day** | **Treatment** | **How it is given** | **How long it takes** |
| Continuous<br><br>(Titration phase for 5 weeks and then for up to 24 months from cycle 1 day 1) | **Venetoclax** (*ven-ET-oh-klax*) | Take orally ONCE a day with food. Swallow the tablet(s) whole with a glass of water, do not break, crush or chew.<br><br>If you vomit a tablet(s), take your normal dose the next time it is due. Do not take an extra dose.<br><br>If you forget to take a dose, and it is less than 8 hours late, take it as soon as you remember. If it is more than 8 hours late, skip that dose and take your normal dose the next time it is due. Do not take an extra dose. | |
| Cycles 1 to 6: Day 1<br><br>(Commencing week 6 onwards) | **Rituximab** (*ri-TUX-i-mab*) | By a drip into a vein | **1st dose:** About 4 to 6 hours<br><br>**Doses thereafter:** About 3 to 4 hours |

## 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**<br><br>Ask your doctor or nurse from your treating team who to contact if you have a problem |
|---|---|
| • a temperature of 38°C or higher<br>• chills, sweats, shivers or shakes<br>• shortness of breath | Daytime:.....<br>Night/weekend:.....<br>Other instructions:..... |

- uncontrolled vomiting or diarrhoea
- pain, tingling or discomfort in your chest or arms
- you become unwell.

**During your treatment immediately** tell the doctor or nurse looking after you if you get any of the following problems:

- leaking from the area where the drugs are being given
- pain, stinging, swelling or redness in the area where the drugs are being given or at any injection sites
- a skin rash, itching, feeling short of breath, wheezing, fever, shivers, or feeling dizzy or unwell in any way (allergic reaction).

## Other information about your treatment

### Tumour lysis syndrome

Some people having treatment for cancer can develop Tumour Lysis Syndrome (TLS), which results from the fast breakdown of cancer cells especially during the first couple of weeks of treatment. As the cancer cells are destroyed, they break open and the content of the cancer cell (uric acid, potassium, phosphorus) gets into the blood. This can lead to changes in kidney function, sudden kidney failure or even death.

If you do not have any heart or kidney problems, keep your fluids up by drinking at least 8 to 10 glasses of fluid daily. It is also important for you to keep your scheduled appointments for blood tests.

### 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.

### Central venous access devices (CVADs)

This treatment may involve having chemotherapy through a central venous access device (CVAD). Your doctor or nurse will explain this to you. For more information, see the eviQ patient information sheets on CVADs.

### 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.

### Medications for blood pressure

Rituximab may lower your blood pressure. Tell your doctor if you are taking any blood pressure medications. Your doctor may advise you to temporarily stop your blood pressure medications before your rituximab infusions.

### Other medications given during this treatment

- **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.
- **Rituximab premedication:** before your treatment with rituximab you will need to take some tablets called a premedication to help prevent you from having a reaction to the rituximab.
- **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) | |
|---|---|
| **Flu-like symptoms** | • You may get:<br>◦ a fever<br>◦ chills or sweats<br>◦ muscle and joint pain<br>◦ a cough<br>◦ headaches.<br>• These symptoms are caused by the drug rituximab.<br>• Tell your doctor or nurse **immediately** if you get any of the symptoms listed above. |
| **Allergic reaction** | • Allergic reactions are uncommon but can be life threatening.<br>• **If you feel unwell during the infusion or shortly after it, or:**<br>◦ **get a fever, shivers or shakes**<br>◦ **feel dizzy, faint, confused or anxious**<br>◦ **start wheezing or have difficulty breathing**<br>◦ **have a rash, itch or redness of the face**<br><br>**<u>While you are in hospital:</u> Tell your doctor or nurse immediately.**<br>**<u>After you leave:</u> Contact your doctor or nurse immediately, or go to the nearest hospital Emergency Department.** |
| **Nausea and vomiting** | • You may feel sick (nausea) or be sick (vomit).<br>• Take your anti-sickness medication as directed even if you don't feel sick.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat small meals more frequently.<br>• Try food that does not require much preparation.<br>• Try bland foods like dry biscuits or toast.<br>• Gentle exercise may help with nausea.<br>• Ask your doctor or nurse for eviQ patient information - Nausea and vomiting during cancer treatment.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you have uncontrolled vomiting or feel dizzy or light-headed.** |
| **Early (onset days to weeks)** | |

| | |
|---|---|
| **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.<br>• Wash your hands often.<br>• Keep a thermometer at home and take your temperature regularly, and if you feel unwell.<br>• Do your mouth care regularly.<br>• Inspect your central line site (if you have one) daily for any redness, pus or swelling.<br>• Limit contact with people who are sick.<br>• Learn how to recognise the signs of infection.<br>• Ask your doctor or nurse for eviQ patient information - Infection during cancer treatment.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following signs or symptoms:**<br>◦ **a temperature of 38°C or higher**<br>◦ **chills, shivers, sweats or shakes**<br>◦ **a sore throat or cough**<br>◦ **uncontrolled diarrhoea**<br>◦ **shortness of breath**<br>◦ **a fast heartbeat**<br>◦ **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.<br>• Try not to bruise or cut yourself.<br>• Avoid contact sport or vigorous exercise.<br>• Clear your nose by blowing gently.<br>• Avoid constipation.<br>• Brush your teeth with a soft toothbrush.<br>• Don't take aspirin, ibuprofen or other similar anti-inflammatory medications unless your doctor tells you to.<br>• Tell your doctor or nurse if you have any bruising or bleeding.<br>• **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.<br>• Applying a heat pack to affected areas may help.<br>• 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:<br>◦ chest pain<br>◦ a pounding or fluttering heart (palpitations)<br>◦ shortness of breath<br>◦ dizzy or light-headed<br>◦ confused<br>◦ more tired than usual.<br>• Tell your doctor if you have any heart problems or are on any heart medications.<br>• **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.<br>• You may also get:<br>  ◦ bloating, cramping or pain<br>  ◦ a loss of appetite<br>  ◦ nausea or vomiting.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat plenty of fibre-containing foods such as fruit, vegetables and bran.<br>• Take laxatives as directed by your doctor.<br>• Try some gentle exercise daily.<br>• **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.<br>• You may also get bloating, cramping or pain.<br>• Take your antidiarrhoeal medication as directed by your doctor.<br>• Drink plenty of fluids (unless you are fluid restricted).<br>• Eat and drink small amounts more often.<br>• Avoid spicy foods, dairy products, high fibre foods, and coffee.<br>• Ask your doctor or nurse for eviQ patient information - Diarrhoea during cancer treatment.<br>• **Tell your doctor or nurse immediately, or go to your nearest hospital Emergency Department if your diarrhoea is not controlled, you have 4 or more loose bowel motions per day, and if you feel dizzy or light-headed.** |
| **Tiredness and lack of energy (fatigue)** | • You may feel very tired, have no energy, sleep a lot, and not be able to do normal activities or things you enjoy.<br>• Do not drive or operate machinery if you are feeling tired.<br>• Nap for short periods (only 1 hour at a time)<br>• Prioritise your tasks to ensure the best use of your energy.<br>• Eat a well balanced diet and drink plenty of fluids (unless you are fluid restricted).<br>• Try some gentle exercise daily.<br>• Allow your friends and family to help.<br>• **Tell your doctor or nurse if you get any of the symptoms listed above.** |
| **Fever** | • You may feel warm.<br>• Tell your doctor or nurse if you get this symptom. |
| **Skin rash** | • You may get a red, bumpy rash and dry, itchy skin.<br>• Moisturise your skin with a gentle non-perfumed moisturising cream like sorbolene or aqueous cream.<br>• Do not scratch your skin.<br>• Protect your skin from the sun by wearing sun-protective clothing, a wide-brimmed hat, sunglasses and sunscreen of SPF 50 or higher.<br>• **Talk to your doctor or nurse about other ways to manage your skin rash.** |
| **Chest infection** | • You can develop a chest infection whilst receiving this treatment.<br>• **Tell your doctor or nurse as soon as possible if you get any of the following symptoms:**<br>  ◦ **shortness of breath**<br>  ◦ **difficulty breathing**<br>  ◦ **wheezing**<br>  ◦ **coughing up mucus** |

| Late (onset weeks to months) | |
|---|---|
| **Low red blood cells (anaemia)** | • You may feel dizzy, light-headed, tired and appear more pale than usual.<br>• Tell your doctor or nurse if you have any of these signs or symptoms. You might need a blood transfusion.<br>• **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.** |
| **Changes in the way your brain works [progressive multifocal leukoencephalopathy (PML)]** | • This treatment can affect your central nervous system. This can be very serious.<br>• **Tell your doctor or nurse immediately, or go to the nearest hospital Emergency Department if you get any of the following symptoms:**<br>◦ **trouble with your speech or vision**<br>◦ **confusion or memory loss**<br>◦ **changes in your personality**<br>◦ **weakness in your arms and legs**<br>◦ **poor balance or coordination**<br>◦ **fits (seizures).** |

## 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:**



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