

A GUIDE FOR
HEALTHCARE PROFESSIONALS

PRESCRIBING INFORMATION FOR **VENCLEXTA[®]**

(VENETOCLAX)



1. VENCLEXTA is an oral, first-in-class targeted BCL-2 inhibitor

R/R CLL: VENCLEXTA + rituximab

- VENCLEXTA is an oral medicine taken as a tablet, that works by inhibiting an anti-apoptotic protein called B cell Lymphoma 2 (BCL-2).¹
- Overexpression of BCL-2 has been demonstrated in chronic lymphocytic leukaemia (CLL) – cells and has been implicated in resistance to certain therapeutic agents.¹
- In R/R CLL, VENCLEXTA is used in combination with rituximab, a monoclonal antibody that targets the CD20 antigen expressed on the surface of pre-B and mature B-lymphocytes.^{1,2}
- VENCLEXTA is registered by Medsafe for the treatment of patients with chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL).¹
- Safety and Efficacy:
The safety and efficacy of VENCLEXTA in combination with rituximab was established in an open-label, multicentre phase 3 study vs bendamustine plus rituximab in patients with CLL who had received at least one line of prior therapy.¹

The table below provides details of the study and the relevant publications.

VENCLEXTA + rituximab clinical study overview

(This is not intended to be a comprehensive summary of all data for VENCLEXTA in R/R CLL)

STUDY NUMBER	DESCRIPTION	PUBLICATION
GO28667 (MURANO)	A randomised (1:1) Phase 3, multicentre, open label trial that evaluated the safety and efficacy of VENCLEXTA in combination with rituximab verses bendamustine with rituximab in CLL patients who had received at least one prior therapy. 389 patients were randomised.	Seymour JF et al. Venetoclax–Rituximab in Relapsed or Refractory Chronic Lymphocytic Leukemia. New England Journal of Medicine 2018; 378,1107-20.5 Kater AP et al. 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 3 study. Journal of Clinical Oncology 2019;37:269-277

2. VENCLEXTA + rituximab: efficacy results for study G028667 (MURANO)¹

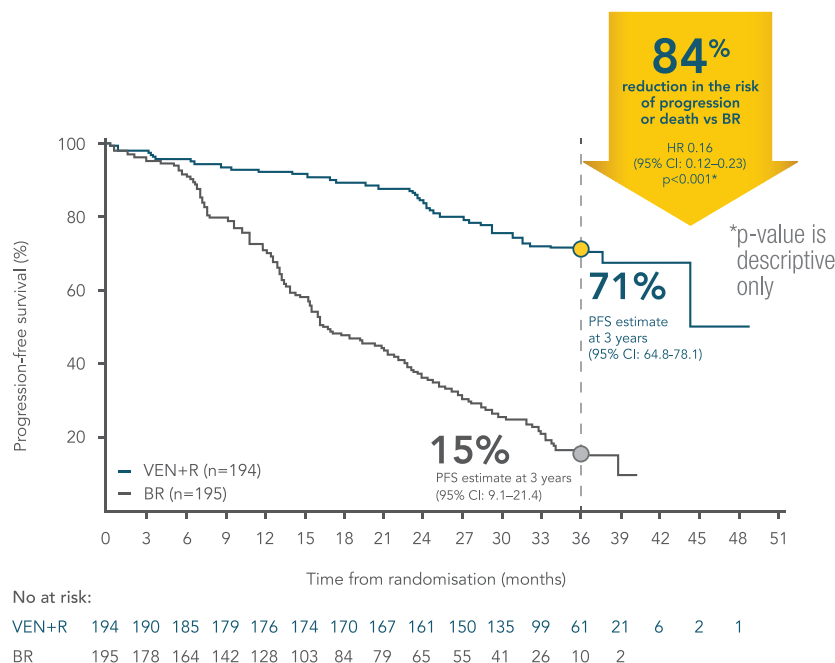
R/R CLL: VENCLEXTA + rituximab

	INV ASSESSED		IRC ASSESSED	
	Venclexta + Rituximab (N = 194)	Bendamustine + Rituximab (N = 195)	Venclexta + Rituximab (N = 194)	Bendamustine + Rituximab (N = 195)
PROGRESSION-FREE SURVIVAL				
Number of events (%)	32 (16.5)	114 (58.5)	35 (18.0)	106 (54.4)
Disease progression	21	98	26	91
Death events	11	16	9	15
Median, months, (95% CI)	Not reached	17.0 (15.5, 21.6)	Not reached	18.1 (15.8, 22.3)
HR (95% CI)	0.17 (0.11, 0.25)		0.19 (0.13, 0.28)	
p-value ^a	p < 0.0001		p < 0.0001	
12-month estimate, % (95% CI)	92.7 (89.1, 96.4)	72.5 (65.9, 79.1)	91.2 (87.2, 95.2)	74.1 (67.6, 80.7)
24-month estimate, % (95% CI)	84.9 (79.1, 90.6)	36.3 (28.5, 44.0)	82.8 (76.6, 88.9)	37.4 (29.4, 45.4)
RESPONSE RATE				
ORR, % (95% CI)	93.3 (88.8, 96.4)	67.7 (60.6, 74.2)	92.3 (87.6, 95.6)	72.3 (65.5, 78.5)
CR+CRi, (%)	26.8	8.2	8.2 ^b	3.6 ^b
PR, (%)	63.4	53.3	82.5	68.2
OVERALL SURVIVAL				
Number of deaths (%)	15 (7.7)	27 (13.8)	NA	NA
Hazard Ratio (95% CI)	0.48 (0.25, 0.90)			
TIME TO NEXT ANTI-LEUKEMIC THERAPY				
Number of events (%)	23 (11.9)	83 (42.6)	NA	NA
Median, months	Not reached	26.4	NA	NA
Hazard ratio (95% CI)	0.19 (0.12, 0.31)	NA		
EVENT-FREE SURVIVAL				
Number of events (%)	33 (17.0)	118 (60.5)	NA	NA
Median, months	Not reached	16.4	NA	NA
Hazard ratio (95% CI)	0.17 (0.11, 0.25)	NA		
CI = confidence interval; CR = complete remission; CRi = complete remission with incomplete marrow recovery; INV = investigator; IRC = independent review committee; MRD = minimal residual disease; NA = not available; nPR = nodular partial remission; ORR = overall response rate (CR + CRi + nPR + PR); PR = partial remission; HR = hazard ratio. ^a Stratified log-rank test. ^b The discrepancy between IRC- and investigator-assessed CR rate was primarily due to interpretation of residual adenopathy on CT scans. Eighteen patients in the venetoclax + rituximab arm and 3 patients in the bendamustine + rituximab arm had negative bone marrow and lymph nodes <2 cm.				

Please refer to pages 4 – 6 for important safety information on VENCLEXTA.

2. VENCLEXTA + rituximab: efficacy results for study G028667 (MURANO)

FIGURE 1. PHASE 3 MURANO TRIAL (PRIMARY ENDPOINT): KAPLAN-MEIER ESTIMATES OF INVESTIGATOR-ASSESSED PFS IN THE INTENTION-TO-TREAT POPULATION³

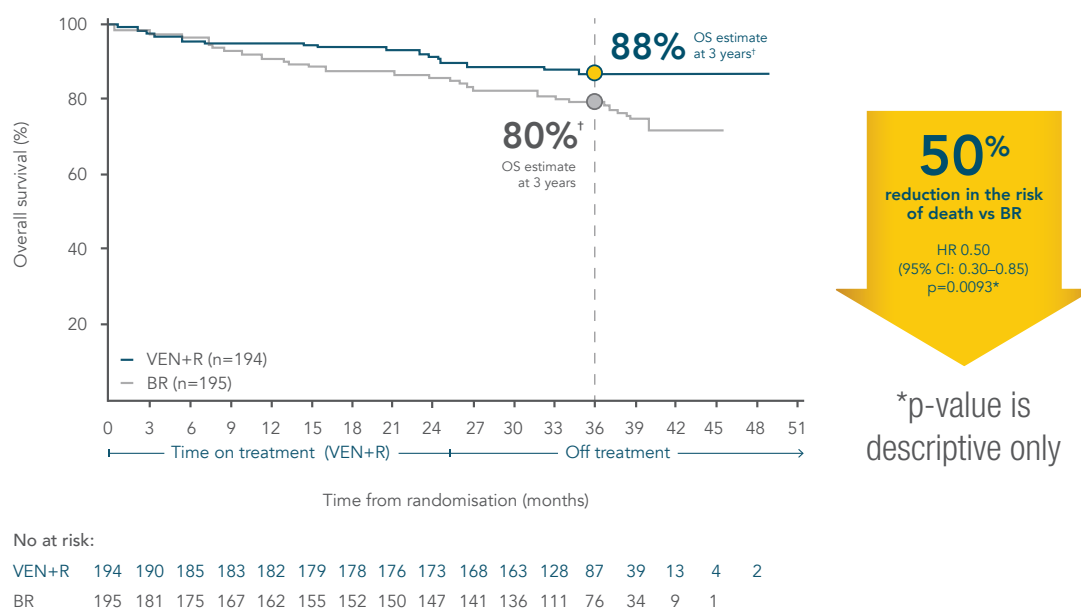


Adapted from Kater AP et al, 2019.³ 36 months of median follow-up. PFS was assessed by investigators using the International Workshop for Chronic Lymphocytic Leukaemia (iwCLL) updated National Cancer Institute-sponsored Working Group (NCI-WG) guidelines (2008).

PRESPECIFIED SUBGROUP ANALYSIS

Bendamustine is not registered or reimbursed in NZ for relapsed refractory CLL.

FIGURE 2. PHASE 3 MURANO TRIAL (SECONDARY ENDPOINT): KAPLAN-MEIER ESTIMATES OF OS IN THE INTENTION-TO-TREAT POPULATION³



Adapted from Kater AP et al, 2019.³†CI not stated. 36 months of median follow-up.

After 48 months follow-up, PFS and OS benefits were sustained with time-limited VenR compared with BR, with no new safety concerns.⁴

3. VENCLEXTA + rituximab: An established and manageable safety profile¹

R/R CLL: VENCLEXTA + rituximab

3.1 SAFETY PROFILE OF VENCLEXTA IN COMBINATION WITH RITUXIMAB¹

Summary of Adverse Reactions Reported in $\geq 10\%$ Incidence and $\geq 5\%$ higher [All Grades] OR $\geq 2\%$ higher [Grade 3 or 4] in Patients treated with VENCLEXTA plus rituximab compared with Bendamustine plus rituximab.

ADVERSE REACTION BY BODY SYSTEM	VENETOCLAX + RITUXIMAB (N=194)		BENDAMUSTINE + RITUXIMAB (N=188)	
	All Grades % (Frequency)	Grade 3 or 4 %	All Grades %	Grade 3 or 4 %
Blood & lymphatic system disorders				
Neutropenia	61 (Very common)	58	44	39
Gastrointestinal disorders				
Diarrhoea	40 (Very common)	3	17	1
Infections & infestations				
Upper respiratory tract infection	22 (Very common)	2	15	1
Metabolism and nutrition disorders				
Tumour lysis syndrome	3 (Common)	3	1	1

Based on the existing safety profile of VENCLEXTA, other adverse reactions reported in the VENCLEXTA + rituximab arm of Study GO28667 include:

Blood & lymphatic system disorders: anemia (16%), febrile neutropenia (4%), lymphopenia (0%; considered an adverse reaction based on the mechanism of action)

Gastrointestinal disorders: nausea (21%), constipation (14%), vomiting (8%)

General disorders and administration site conditions: fatigue (18%)

Infections & infestations: pneumonia (9%), urinary tract infections (6%), sepsis (1%)

Investigations: blood creatinine increase (3%)

Metabolism and nutrition disorders: hyperkalemia (6%), hyperphosphatemia (5%), hyperuricemia (4%), hypocalcemia (2%).

3. VENCLEXTA + rituximab: An established and manageable safety profile¹

3.2 ADVERSE REACTIONS IN PATIENTS WITH CLL TREATED WITH VENCLEXTA¹

- Neutropenia is an identified risk associated with VENCLEXTA treatment.
 - In Study GO28667, neutropenia (all grades) was reported in 61% of patients on the VENCLEXTA + rituximab arm.
 - 43% percent of patients treated with VENCLEXTA + rituximab experienced dose interruption and 3% of patients discontinued VENCLEXTA due to neutropenia.
- Discontinuations due to adverse events occurred in 16% of patients on VENCLEXTA + rituximab.
- Dosage adjustments due to adverse events occurred in 15% of patients on VENCLEXTA + rituximab.
- 71% of patients on VENCLEXTA + rituximab and had dose interruptions due to adverse reactions.

This is not a complete summary of all safety information. See VENCLEXTA Data Sheet at www.medsafe.govt.nz.








3.3 TUMOUR LYSIS SYNDROME (TLS) AND VENCLEXTA

- VENCLEXTA can cause rapid tumour reduction and thus poses a risk for TLS at initiation and during the dose titration phase.¹ TLS can be life threatening or fatal.⁵
- The dose titration schedule is designed to gradually reduce tumour burden (debulking) and decrease the risk of TLS.¹
- Changes in electrolytes consistent with TLS that require prompt management can occur as early as 6 to 8 hours following the first dose of VENCLEXTA and at each dose increase.¹

Clinical symptoms associated with TLS:⁵

FEVER OR CHILLS	NAUSEA OR VOMITING	CONFUSION
SHORTNESS OF BREATH	IRREGULAR HEART BEAT	FITS AND SEIZURES
DARK OR CLOUDY URINE	UNUSUAL TIREDNESS	MUSCLE PAIN OR JOINT DISCOMFORT

- The risk of TLS is a continuum based on multiple factors, including tumour burden and comorbidities.¹
- All patients should be assessed for TLS risk prior to commencing treatment and at each dose change:¹
 - Evaluate tumour burden, including radiographic evaluation (i.e., CT scan).
 - Assess blood chemistry (potassium, uric acid, phosphorus, calcium, and creatinine) in all patients and correct pre-existing abnormalities prior to initiation of treatment with VENCLEXTA.
 - Reduced renal function (CrCl <80 mL/min) further increases the risk. Consider hospitalisation for patients with CrCl <80 mL/min at first dose of 20 mg and 50 mg.
 - Interrupt dosing if needed.
 - Employ more intensive measures (IV hydration, frequent monitoring, hospitalisation) as overall risk increases.
 - Concomitant use of VENCLEXTA with strong CYP3A inhibitors at initiation and during the dose titration phase is contraindicated.

STEP 1: ASSESS LARGE TUMOURS PRESENT GREATER RISK ¹	STEP 2: PREPARE 2-3 DAYS PRIOR TO FIRST DOSE ¹	STEP 3: INITIATE FIRST 5 WEEKS OF TREATMENT ¹
Tumour burden assessment	Anti-hyperuricaemics* Hydration [†]	Blood chemistry monitoring [‡]
LOW TUMOUR BURDEN All LN <5 cm AND ALC <25 x 10 ⁹ /L	 Allopurinol	Oral (1.5-2 L)  Outpatient <ul style="list-style-type: none"> For first dose of 20 mg and 50 mg: Pre-dose, 6 to 8 hours, 24 hours For subsequent titration doses: Pre-dose[§]
MEDIUM TUMOUR BURDEN Any LN 5 cm to <10 cm OR ALC ≥25 x 10 ⁹ /L For patients with CrCl <80 mL/min and medium tumour burden, consider management as high risk for TLS	 Allopurinol	Oral (1.5-2 L)  Consider additional IV Outpatient <ul style="list-style-type: none"> For first dose of 20 mg and 50 mg: Pre-dose, 6 to 8 hours, 24 hours For subsequent titration doses: Pre-dose[§] For first dose of 20 mg and 50 mg: Consider hospitalisation for patients with CrCl <80 mL/min; see below for monitoring in hospital
HIGH TUMOUR BURDEN Any LN ≥10 cm OR Any LN ≥5 cm AND ALC ¹³ ≥25 x 10 ⁹ /L	 Allopurinol Consider rasburicase if baseline uric acid is elevated	Oral (1.5-2 L)  and  IV (150-200 mL/h as tolerated) In hospital <ul style="list-style-type: none"> For first dose of 20 mg and 50 mg: Pre-dose, 4, 8, 12, and 24 hours Outpatient <ul style="list-style-type: none"> For subsequent titration doses: Pre-dose, 6 to 8 hours, 24 hours[§]

The risk of TLS may decrease as tumour burden decreases

*Start allopurinol or xanthine oxidase inhibitor 2 to 3 days prior to initiation of VENCLEXTA.

[†]1.5-2 L of water (6-8 glasses) should be consumed every day starting 2 days before the first dose and throughout the dose titration phase, especially the first day of each dose increase. Administer intravenous hydration for any patient who cannot tolerate oral hydration.

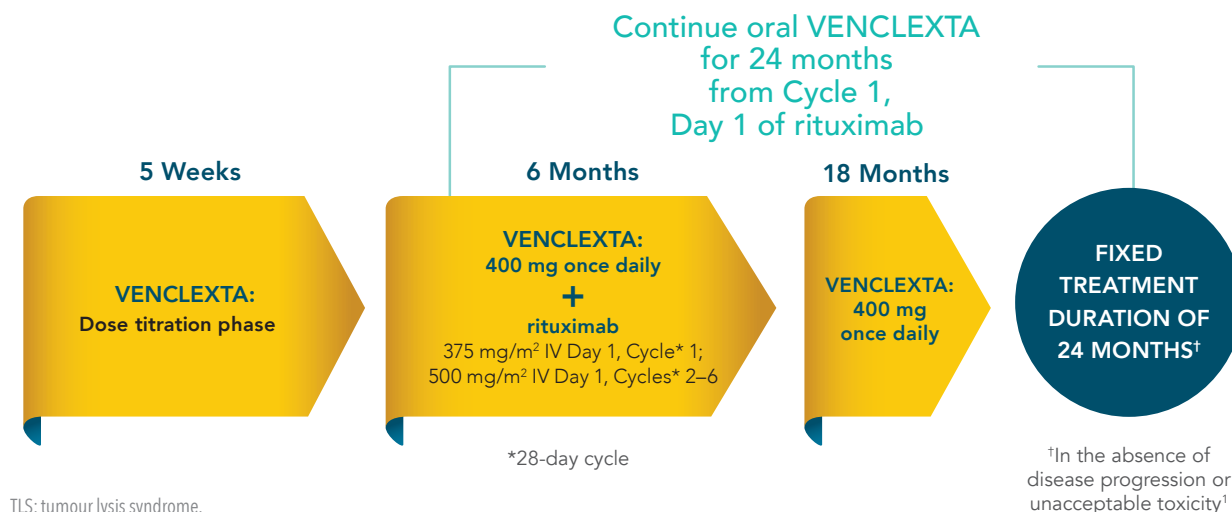
[‡]Blood Chemistry Monitoring: Potassium, calcium, creatinine, phosphorus, uric acid (review in real time).

[§]For patients at risk of TLS, monitor blood chemistries at 6 to 8 hours and at 24 hours at each subsequent dose titration.

No patient is typical. Please refer to the full VENCLEXTA Data Sheet when making treatment decisions.

4. How to prescribe VENCLEXTA + rituximab

VENCLEXTA + R is dosed in 3 general phases in CLL¹



Please refer to VENCLEXTA Approved Data Sheet for complete information on TLS prophylaxis and dose modification or interruption due to neutropenia or other toxicities.¹

Phase 1: VENCLEXTA 5 week dose titration¹

- The 5-week dose titration schedule has been designed to gradually reduce tumour burden (debulking) and decrease the risk of TLS.
- The starting pack provides colour coded weekly wallet blister packs for the first 4 weeks according to the titration schedule.
- Patients should be instructed to take VENCLEXTA tablets with a meal and water at approximately the same time each day.
- Patients should be adequately hydrated during the dose titration phase to reduce the risk of TLS.
- Tablets should be swallowed whole and not chewed or crushed or broken.
- If the patient vomits during dosing, no additional dose should be taken that day. The next prescribed dose should be taken at the usual time.

4. How to prescribe VENCLEXTA + rituximab

R/R CLL: VENCLEXTA + rituximab

Dosing titration designed to reduce the risk of TLS¹



Phase 2: VENCLEXTA in combination with rituximab for 6 months¹.

Start rituximab administration after the patient has completed the dose titration schedule with VENCLEXTA and has received the 400 mg dose of VENCLEXTA for 7 days. Each cycle of rituximab is 28 days.

Phase 3: VENCLEXTA monotherapy for 18 months¹.

Once the patient has completed 6 cycles of rituximab in combination with VENCLEXTA, VENCLEXTA is continued as monotherapy for 18 months.

DOSE HOLD PACKS¹

Dose hold packs are available in the following strength and size for patients who need dose adjustments.

10 mg wallet	14 x 10 mg tablets
50 mg wallet	7 x 50 mg tablets



4. How to prescribe VENCLEXTA + rituximab

Dose modifications or interruptions can help manage potential adverse reactions¹

TLS			
Blood chemistry changes suggestive of TLS	Withhold the following day's VENCLEXTA dose until resolved	If resolved within 24-48 hours of last dose	Resume at same dose
		If events of clinical TLS occur or blood chemistry requires more than 48 hours to resolve	Resume at reduced dose according to dose reduction guidelines
Other toxicities			
Grade 3 or 4 non-haematologic toxicities	Interrupt VENCLEXTA treatment	First occurrence	Once the toxicity has resolved to grade 1 or baseline level, resume VENCLEXTA at the same dose
*Grade 3 neutropenia with infection or fever			
*Grade 4 haematologic toxicities (except lymphopenia)		Second and subsequent occurrences	Resume at reduced dose according to dose reduction guidelines. A larger reduction may occur at the discretion of the physician
*Consider using granulocyte-colony stimulating factor (G-CSF) as clinically indicated for Grade 3 neutropenia with infection or fever or Grade 4 haematologic toxicities (except lymphopenia). Please see Data Sheet for more information.			
When a dose interruption or reduction is required			
Dosing interruptions lasting longer than 1 week during the first 5 weeks of dose titration	Reassess for risk of TLS to determine if restarting at reduced dose (repeating some/all levels of dose-titration phase) is required		
Dosing interruptions lasting longer than 2 weeks after completing the dose titration phase			

Dose reduction guidelines¹

Dose at interruption (mg)	Restart dose (mg)
400	300
300	200
200	100
100	50
50	20
20	10

Consider discontinuing VENCLEXTA for patients who require dose reductions to less than 100 mg for more than 2 weeks.¹

The reduced dose should be continued for 1 week before increasing the dose.¹

TLS=tumour lysis syndrome.

Contraindications

- Hypersensitivity to the active substance or to any of the excipients
- Concomitant use of strong CYP3A inhibitors at initiation and during the dose-titration phase

Renal impairment

- Patients with reduced renal function (CrCl <80 mL/min) may require more intensive prophylaxis and monitoring to reduce the risk of TLS when initiating treatment with VENCLEXTA.
- Safety in patients with severe renal impairment (CrCl <30 mL/min) or on dialysis has not been established, and a recommended dose for these patients has not been determined.

Hepatic impairment:

- No dose adjustment is recommended in patients with mild or moderate hepatic impairment.
- A 50% dose reduction throughout treatment is recommended for patients with severe hepatic impairment; monitor these patients more closely for signs of toxicity.

Potential Effects of Other Medicines on VENCLEXTA

VENCLEXTA is predominantly metabolised by CYP3A4.

CYP3A Inhibitors

For patients requiring concomitant use of VENCLEXTA with strong CYP3A inhibitors (e.g., itraconazole, ketoconazole, posaconazole, voriconazole, clarithromycin, ritonavir) or moderate CYP3A inhibitors (e.g., ciprofloxacin, diltiazem, erythromycin, dronedarone, fluconazole, verapamil)

INHIBITORS	INITIATION AND DOSE-TITRATION PHASE	STEADY DAILY DOSE (AFTER DOSE-TITRATION PHASE) ^a
Strong CYP3A inhibitor	Contraindicated	Avoid inhibitor use or reduce the VENCLEXTA dose by at least 75% of the original dose
Moderate CYP3A inhibitor	Avoid inhibitor use or reduce the VENCLEXTA dose by at least 50% of the original dose	

^aAvoid concomitant use of VENCLEXTA with strong or moderate CYP3A inhibitors. Consider alternative medications or reduce the VENCLEXTA dose as described in this table.

administer VENCLEXTA dose according to the table below. Patients should be monitored more closely for signs of VENCLEXTA toxicities.

Avoid grapefruit products, Seville oranges, and starfruit during treatment with VENCLEXTA, as they contain inhibitors of CYP3A.

OATP1B1/1B3 and P-gp Inhibitors

Avoid concomitant use of VENCLEXTA with P-gp inhibitors (e.g., amiodarone, captopril, carvedilol, ciclosporin, felodipine, quercetin, quinidine, ranolazine, ticagrelor) at initiation and during the dose titration phase; if a P-gp inhibitor must be used, patients should be monitored closely for signs of toxicities.

Azithromycin

No dose adjustment is needed when VENCLEXTA is co-administered with azithromycin.

CYP3A Inducers

Concomitant use of VENCLEXTA with strong CYP3A inducers (e.g., carbamazepine, phenytoin, rifampicin, St. John's wort (*Hypericum perforatum*)) or moderate CYP3A inducers (e.g., bosentan, efavirenz, etravirine, modafinil, nafcillin) should be avoided. Alternative treatments with less CYP3A induction should be considered.

Potential Effects of VENCLEXTA on Other Medicines

Warfarin

It is recommended that the international normalised ratio (INR) be monitored closely in patients receiving warfarin.

P-gp Substrates

Coadministration of narrow therapeutic index P-gp substrates (e.g., digoxin, everolimus, and sirolimus) with VENCLEXTA should be avoided. If a narrow therapeutic index P-gp substrate must be used, it should be taken at least 6 hours before VENCLEXTA.

Summary of medicines that interact with VENCLEXTA¹

Strong CYP3A inhibitors include:	Moderate CYP3A inhibitors include:	P-gp inhibitors	Strong CYP3A inducers include:	Moderate CYP3A inducers include:	Narrow therapeutic index P-gp substrates include:	Monitor closely:
Itraconazole Ketoconazole Posaconazole Voriconazole Clarithromycin Ritonavir	Ciprofloxacin Diltiazem Dronedaron Erythromycin Fluconazole Verapamil	Amiodarone Captopril Carvedilol Ciclosporin Felodipine Quercetin Quinidine Ranolazine Ticagrelor	Carbamazepine Phenytoin Rifampicin St John's wort (<i>Hypericum perforatum</i>)	Bosentan Efavirenz Etravirine Modafinil Nafcillin	Digoxin Everolimus Sirolimus	Warfarin

Please refer to the VENCLEXTA Data Sheet for full list.

Find out more at venclexta.co.nz

Log in to the Healthcare Professional portal by typing **CLL** for both the username and password.

References:

1. VENCLEXTA approved Data Sheet 2. Mabthera (rituximab) approved Data Sheet 3. Kater AP et al 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; Post-Treatment Follow-Up of the MURANO Phase III Study. J of Clinical Oncology 2019;37:269-277 4. Seymour et al 2019. Poster #2266, Presented at XVIII International Workshop on CLL (iwCLL), Edinburgh, United Kingdom, 20–23 September 2019 5. VENCLEXTA Consumer Medical Information.

VENCLEXTA in combination with rituximab is fully funded for relapsed refractory chronic lymphocytic leukaemia (CLL). Special authority criteria apply. Refer to the PHARMAC website for full authority information.

Please review full Data Sheet before prescribing. Full Data Sheet is available on request from AbbVie Limited by calling 0800 900 030, or on the Medsafe website. <http://www.medsafe.govt.nz/profs/Datasheet/v/venclexatab.pdf>

VENCLEXTA is a Prescription Medicine containing venetoclax 10 mg, 50 mg or 100 mg for oral use.

THERAPEUTIC INDICATIONS: VENCLEXTA is indicated for the treatment of patients with chronic lymphocytic leukaemia (CLL) or small lymphocytic lymphoma (SLL). **DOSE AND METHOD OF ADMINISTRATION:** VENCLEXTA should be taken orally once daily, with a meal and water. The starting dose (week 1) is 20 mg once daily for 7 days. Dose must be administered according to a weekly dose titration schedule to the recommended daily dose of 400 mg over a period of 5 weeks. Week 2 daily dose is 50 mg, week 3 daily dose is 100 mg, week 4 daily dose is 200 mg, week 5 daily dose is 400 mg. The 5-week dose titration schedule is designed to gradually reduce tumour burden and decrease risk of Tumour Lysis Syndrome (TLS). First line CLL/SLL Combination Therapy with obinutuzumab When VENCLEXTA is used in combination with obinutuzumab it should be given for a total of 12 cycles (28 days in each cycle): 6 cycles in combination with obinutuzumab, followed by 6 cycles of VENCLEXTA as a single agent. On Cycle 1 Day 1, start obinutuzumab administration at 1000 mg (dose may be split as 100 mg and 900 mg on Days 1 and 2, respectively). Administer 1000 mg on Days 8 and 15 of Cycle 1, and on Day 1 of five subsequent cycles (total of 6 cycles, 28 days each). On Cycle 1 Day 22, start VENCLEXTA according to the 5-week dose titration schedule, continuing through Cycle 2 Day 28. After completing the dose titration schedule, patients should continue VENCLEXTA 400 mg once daily from Cycle 3 Day 1 of obinutuzumab to the end of Cycle 12. Previously treated CLL/SLL Combination Therapy with rituximab When VENCLEXTA is used in combination with rituximab, start rituximab administration after the 5-week dose titration schedule has been completed and the patient has received the 400 mg dose of VENCLEXTA for 7 days. The daily dose of 400 mg is to continue for up to 24 months from Cycle 1 Day 1 of rituximab in the absence of disease progression or unacceptable toxicity. **Monotherapy** When VENCLEXTA is used as a single agent, the recommended dose is 400 mg once daily after patient has completed the 5-week dose titration schedule. Treatment is to continue until disease progression or no longer tolerated by patient. See full DS for additional information on duration of treatment, risk assessment and prophylaxis for TLS as well as dose modifications based on toxicities, use with CYP3A and P-gp inhibitors and use in patients with severe hepatic impairment. **CONTRAINDICATIONS:** Hypersensitivity to venetoclax, or to any of the excipients. In patients with CLL or SLL, concomitant use with strong CYP3A inhibitors (i.e. itraconazole, ketoconazole, posaconazole, voriconazole, clarithromycin and ritonavir) at initiation and dose titration is contraindicated. **SPECIAL WARNINGS AND PRECAUTIONS FOR USE:** Life-threatening tumour lysis syndrome (TLS): risk of TLS is highest at initiation and during the dose titration phase; changes in electrolytes consistent with TLS can occur 6-8 hours following first dose and at each dose increase; monitor blood chemistries and promptly manage abnormalities; increased TLS risk with reduced renal function (CrCl < 80 mL/min); assess patients for risk and provide appropriate prophylaxis, including hydration and anti-hyperuricaemics. Neutropenia: monitor complete blood counts; recommend dose interruptions and reductions if severe; consider administration of granulocyte-colony stimulating factor (G-CSF) for neutropenia if clinically indicated. Serious infection: monitor for fever and symptoms of infection and treat promptly; interrupt dosing as appropriate. Live attenuated vaccines should not be administered before, during or after treatment until B-cell recovery occurs. No dose adjustment recommended for mild or moderate hepatic or renal impairment. Not recommended during pregnancy, lactation, in children and adolescents less than 18 years of age. See full DS for details. **INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION:** Potential for significant drug interactions requiring dose-adjustment or appropriate clinical monitoring with various agents, incl. ciprofloxacin, diltiazem, erythromycin, dronedarone, fluconazole, verapamil, amiodarone, captopril, carvedilol, ciclosporin, felodipine, quercetin, quinidine, ranolazine, ticagrelor, azithromycin, warfarin, digoxin, everolimus, and sirolimus. Avoid carbamazepine, phenytoin, St. John's wort (*Hypericum perforatum*), bosentan, efavirenz, etravirine, modafinil, and nafcillin. Avoid grapefruit products, Seville oranges, starfruit. **UNDESIRABLE EFFECTS:** Upper respiratory tract infection, pneumonia, neutropenia, anaemia, lymphopenia, hyperkalaemia, hyperphosphataemia, hypocalcaemia, diarrhoea, nausea, vomiting, constipation, fatigue, urinary tract infection, sepsis, febrile neutropenia, TLS, hyperuricaemia, blood creatinine increased. Version 06 **Date of Preparation:** November 2019, based on Data Sheet last updated 7 November 2019. AbbVie Limited, PO Box 11437, Manners Street, Wellington 6142, New Zealand. TAPS PP4816. NZ-VENC-190006. ONO0007. Prepared November 2019.