Genentech
A Member of the Roche Group

RELAPSED/REFRACTORY CHRONIC LYMPHOCYTIC LEUKEMIA

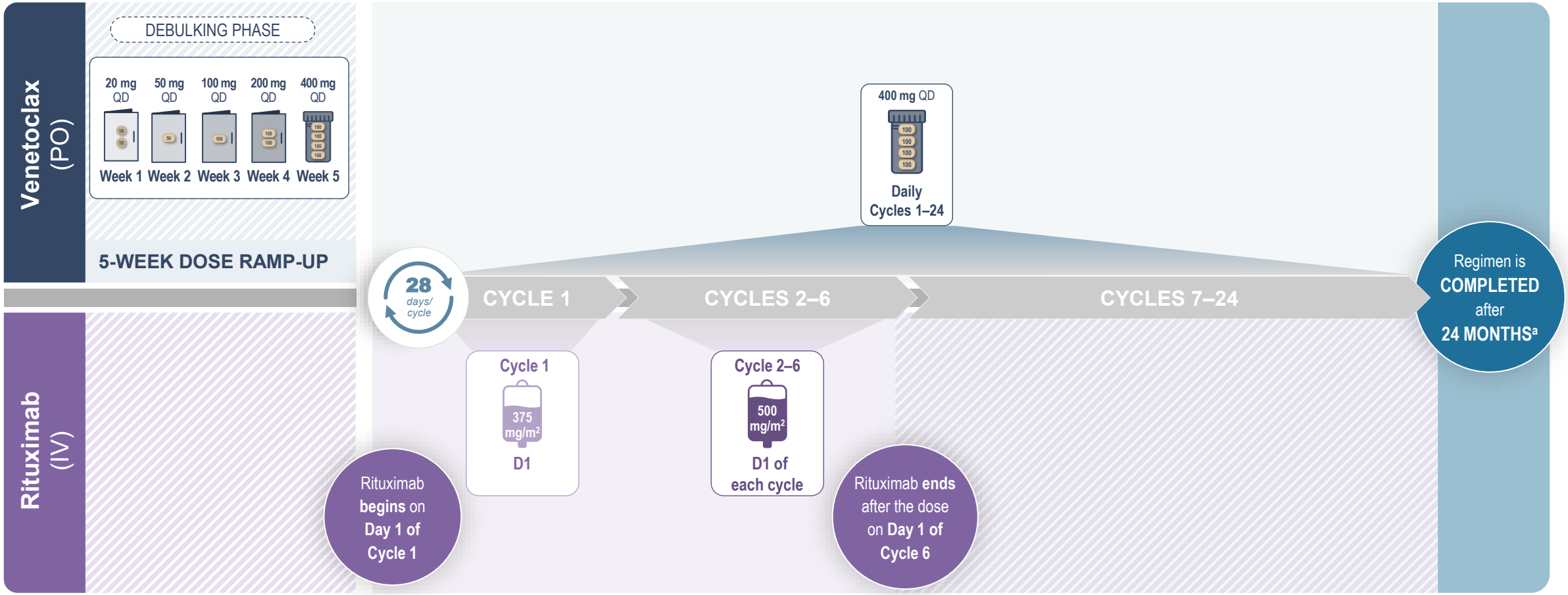
Venetoclax–Rituximab Dosing Regimen

This is a medical resource for scientific information and is intended for healthcare providers practicing in the United States

Current as of February 9, 2026

Table of Contents

VENETOCLAX–RITUXIMAB DOSING SCHEDULE OVERVIEW



Rituximab general administration guidelines (view here).

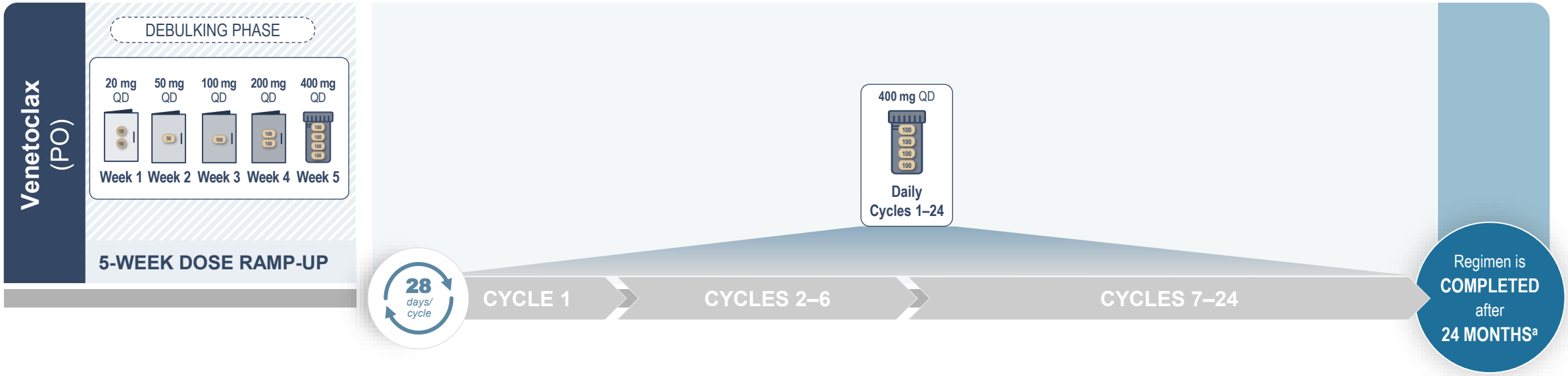
[a]From Cycle 1, Day 1, of rituximab.
Graphic is not to scale. Each cycle is 28 days.
D=day; IV=intravenous; PO=oral; QD=once daily.

1. Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024. 2. Seymour JF, et al. *N Engl J Med*. 2018;378:1107–1120 (suppl).

Genentech
A Member of the Roche Group

VENETOCLAX RAMP-UP

VENETOCLAX RAMP-UP



[a]Following the venetoclax 5-week ramp up. Cycle 1, Day 1 of rituximab

Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024.

PREPARING FOR VENETOCLAX RAMP-UP

All patients

TLS risk assessment

Reassess tumor burden (repeat ALC) and recategorize TLS risk as appropriate

Hydration

Ensure adequate hydration every day during venetoclax ramp-up and with resumption after an interruption

Blood chemistry

Assess blood chemistry (potassium, uric acid, phosphorus, calcium, and creatinine) and correct pre-existing abnormalities

Drug interactions

Determine if the patient is taking any medications that interact with venetoclax, which may require an alternative medication or venetoclax dose modification

Patients with hepatic impairment (Child-Pugh class C)

Dose modification

Determine if venetoclax daily dose should be reduced by 50% for patients with hepatic impairment

Please see **additional TLS prophylaxis considerations** for rituximab administration.

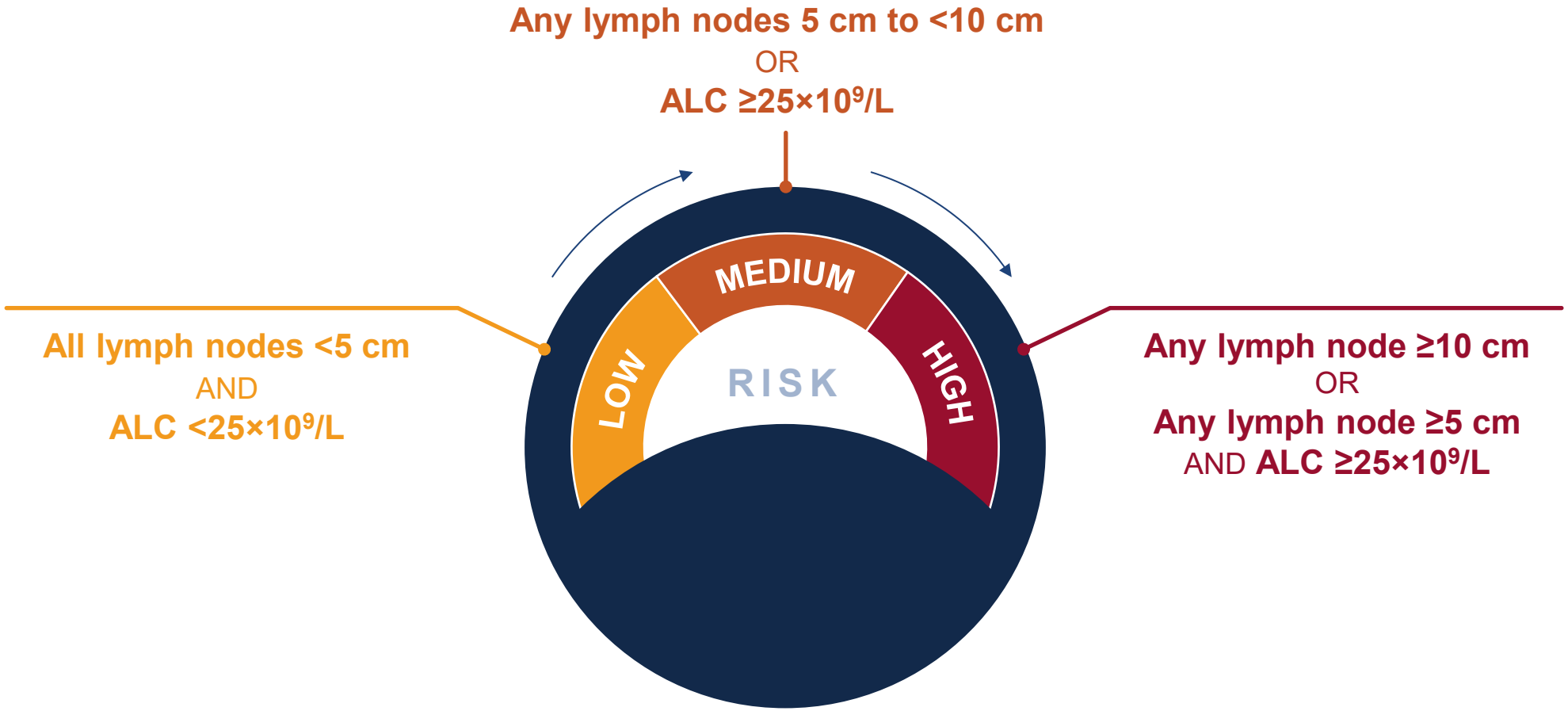
- Low/medium tumor burden/TLS risk
- High tumor burden/TLS risk

Click for details on prophylaxis and monitoring by tumor burden/TLS risk.

ALC=absolute lymphocyte count; TLS=tumor lysis syndrome.

1. Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024. 2. Seymour JF, et al. *N Engl J Med.* 2018;378:1107–1120 (protocol).

TUMOR BURDEN AND TLS RISK ASSESSMENT



1. Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024. 2. Seymour JF, et al. *N Engl J Med.* 2018;378:1107–1120 (protocol).

VENETOCLAX RAMP-UP: LOW OR MEDIUM TUMOR BURDEN/TLS RISK

5-WEEK DOSE RAMP-UP

	20 mg QD Week 1	50 mg QD Week 2	100 mg QD Week 3	200 mg QD Week 4	400 mg QD Week 5
TLS prophylaxis					
Hydration	1.5–2.0 L/d PO[a] throughout the ramp-up phase beginning **at least** 2 days prior to and continuing for at least 24 hours after the first dose of each dose level. **For patients with medium tumor burden:** Consider IV hydration in addition to oral hydration during outpatient stay for the first doses of 20 mg and 50 mg.				
Antihyperuricemic	Allopurinol 300 mg/d beginning **at least** 2 days prior to initiation of venetoclax and continuing until ramp-up is completed.				
Laboratory monitoring on the first day of each dose level					
Setting	Outpatient **For patients with medium tumor burden and CrCl <80 mL/min:** Consider hospitalization for the first venetoclax doses of 20 mg and 50 mg. For these patients, follow the TLS prophylaxis and monitoring plan for high tumor burden.				
Blood chemistry tests	Predose, 6−8 hours, and 24 hours	Predose, 6−8 hours, and 24 hours	Predose	Predose	Predose

[a]Administer IV hydration to any patient who cannot tolerate oral hydration.
CrCl=creatinine clearance.
Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024.

VENETOCLAX RAMP-UP: HIGH TUMOR BURDEN/TLS RISK

5-WEEK DOSE RAMP-UP

	Week 1	Week 2	Week 3	Week 4	Week 5
	20 mg QD	50 mg QD	100 mg QD	200 mg QD	400 mg QD
TLS prophylaxis					
Hydration	1.5–2.0 L/d PO[a] throughout the ramp-up phase beginning **at least** 2 days prior to and continuing for at least 24 hours after the first dose of each dose level. *AND* IV hydration 150−200 mL/h as tolerated prior to the first dose of each dose level.				
Antihyperuricemic	Allopurinol 300 mg/d beginning **at least** 2 days prior to initiation of venetoclax and continuing until ramp-up is completed. Consider rasburicase for elevated uric acid (>8 mg/dL).				
Laboratory monitoring on the first day of each dose level					
Setting	Hospital		Outpatient		
Blood chemistry tests	Predose, 4, 8, 12, and 24 hours	Predose, 4, 8, 12, and 24 hours	Predose, 8 hours, and 24 hours	Predose, 8 hours, and 24 hours	Predose, 8 hours, and 24 hours

[a]Administer IV hydration to any patient who cannot tolerate oral hydration.

1. Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024. 2. Seymour JF, et al. *N Engl J Med.* 2018;378:1107–1120 (protocol).

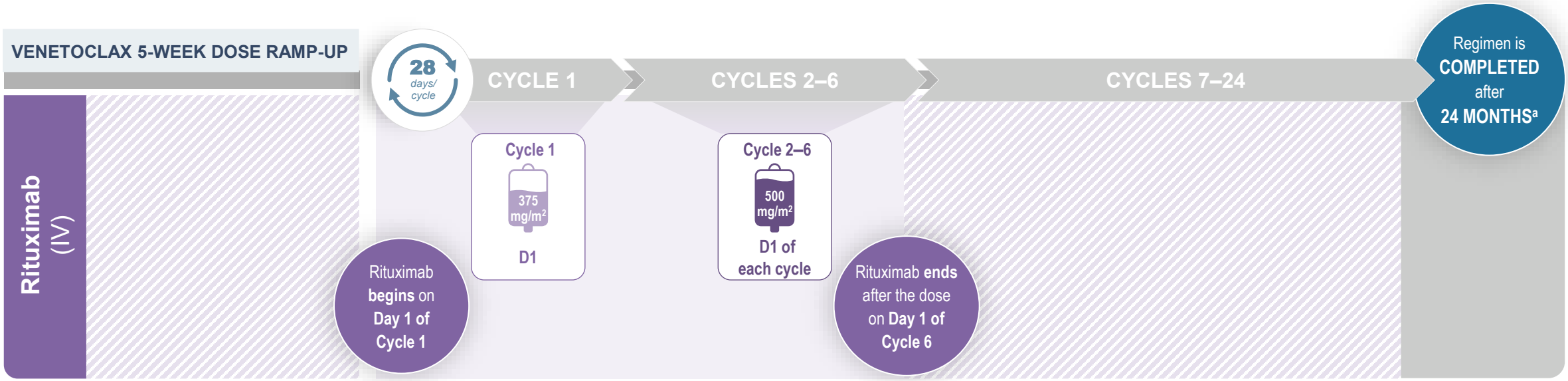
Genentech
A Member of the Roche Group

RITUXIMAB INFUSIONS

WARNING: FATAL INFUSION-RELATED REACTIONS, SEVERE MUCOCUTANEOUS REACTIONS, HEPATITIS B VIRUS REACTIVATION AND PRORESSIVE MULTIFOCAL LEUKOENCEOPHALOPATHY

Please refer to the full prescribing information for additional details.

CYCLES 1 THROUGH 6: RITUXIMAB INFUSIONS



Tumor Lysis Syndrome Prophylaxis | Infection Prophylaxis | Premedications to Reduce IRR | Dosing Schedule and Infusion Rates | IRR Management

[a]From Cycle 1, Day 1, of rituximab. IRR=infusion-related reaction.

1. Rituxan (rituximab) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2021. 2. Seymour JF, et al. *N Engl J Med*. 2018;378:1107–1120 (suppl).

TUMOR LYSIS SYNDROME PROPHYLAXIS

A high number of circulating malignant cells (≥25,000/mm^3) or high tumor burden confers a greater risk of TLS and should receive prophylaxis

TLS PROPHYLAXIS

ADEQUATE HYDRATION

ANTI-HYPERURICEMICS

LABORATORY PARAMETERS

Monitor laboratory parameters of **patients considered at risk for TLS** during **initial days of treatment**

FOR PATIENTS WITH TLS

Correct electrolyte abnormalities, monitor renal function and fluid balance, and administer supportive care, including dialysis as indicated.

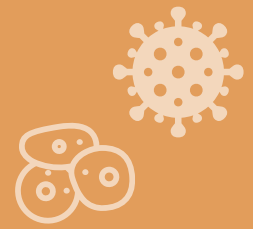
Please see **additional TLS prophylaxis considerations** for venetoclax administration.

1. Rituxan (rituximab) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2021. 2. Seymour JF, et al. *N Engl J Med*. 2018;378:1107–1120 (suppl).

INFECTION PROPHYLAXIS

INFECTION PROPHYLAXIS

Provide prophylaxis for ***Pneumocystis jirovecii*** **pneumonia (PCP)** and **Herpes virus infections** during treatment and for up to 12 months following treatment as appropriate



WARNING: Hepatitis B Virus (HBV) Reactivation – HBV reactivation can occur in patients treated with rituximab, in some cases resulting in fulminant hepatitis, hepatic failure, and death. See full prescribing information for additional information.

HBV=hepatitis B virus; PCP=*Pneumocystis jirovecii* pneumonia .

1. Rituxan (rituximab) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2021. 2. Seymour JF, et al. *N Engl J Med*. 2018;378:1107–1120 (suppl).

RITUXIMAB PREMEDICATIONS TO REDUCE IRRs

ANTIPYRETIC

DOSAGE
Acetaminophen **650 mg to 1000 mg PO**

ADMINISTRATION
At least **30 minutes before rituximab infusion**

ANTIHISTAMINE

DOSAGE
Diphenhydramine **25–50 mg PO/IV** or equivalent

ADMINISTRATION
At least **30 minutes before rituximab infusion**

CORTICOSTEROID *(OPTIONAL)*[a]

DOSAGE
A single dose of hydrocortisone 100 mg or equivalent dose of methylprednisolone

ADMINISTRATION
With rituximab infusion (per institution protocol)

Cycles 1–6: All patients

Hypotension may occur during infusions. Consider withholding antihypertensive treatments for 12 hrs prior infusion.

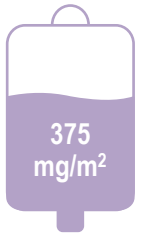
WARNING: Rituximab administration can result in serious, including fatal, infusion related reactions. Please see prescribing information for additional information.

[a]If this is usual practice at institution.

1. Rituxan (rituximab) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2021. 2. Seymour JF, et al. *N Engl J Med*. 2018;378:1107–1120 (protocol).

RITUXIMAB DOSING SCHEDULE AND INFUSION RATES

CYCLE 1 DAY 1



- Initiate infusion at a rate of 50 mg/h
  - In the absence of infusion toxicity, increase infusion rate by 50 mg/h increments every 30 minutes, to a maximum of 400 mg/h
- If an IRR develops, stop or slow the infusion
  - Administer infusion-reaction medications and supportive care in accordance with institutional guidelines
  - If the reaction resolves, resume the infusion at a 50% reduction in rate[a]

CYCLES 2–6 DAY 1

- Initiate infusion at a rate of 100 mg/h
  - In the absence of infusion toxicity, increase infusion rate by 100 mg/h increments at 30 minute intervals, to a maximum of 400 mg/h
- If the patient experienced an infusion-related or hypersensitivity reaction during the prior infusion, begin infusion at an initial rate of 50 mg/h and follow instructions for first infusion (Cycle 1, Day 1)
- If an IRR develops, stop or slow the infusion
  - Administer infusion-reaction medications and supportive care in accordance with institutional guidelines
  - If the reaction resolves, resume the infusion at a 50% reduction in rate[a]

[a]For example, resume infusion at 50% of the rate used at the time that the reaction occurred.

1. Rituxan (rituximab) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2021. 2. Seymour JF, et al. *N Engl J Med*. 2018;378:1107–1120 (protocol).

MANAGEMENT OF RITUXIMAB INFUSION–RELATED REACTIONS

Grade of IRR	Guidance	
Grades 1–2	• First occurrence	• Manage per institution protocol
	• Subsequent occurrence	• Manage per institution protocol. Consider discontinuing rituximab if experiencing recurrent IRRs
Grade 3	• First occurrence	• Manage per institution protocol
	• Subsequent occurrence	• Discontinue rituximab permanently
Grade 4	• Discontinue rituximab permanently	

Seymour JF, et al. *N Engl J Med*. 2018;378:1107–1120 (protocol).

Genentech
A Member of the Roche Group

DOSE MODIFICATIONS FOR DRUG INTERACTIONS AND ADVERSE REACTIONS

VENETOCLAX DOSE MODIFICATIONS FOR DRUG INTERACTIONS

COADMINISTERED DRUG	INITIATION AND RAMP-UP PHASE	STEADY DAILY DOSE (post ramp-up phase)[a]
Posaconazole	Contraindicated	Reduce to 70 mg
Other strong CYP3A inhibitor	Contraindicated	Reduce to 100 mg
Moderate CYP3A inhibitor	Reduce by at least 50%	Reduce by at least 50% (to 200 mg or less)
P-gp inhibitor	Reduce by at least 50%	Reduce by at least 50% (to 200 mg or less)

[a]Consider alternative medications or reduce the venetoclax dose as described.
CYP3A=cytochrome P450, family 3, subfamily A; P-gp=P-glycoprotein.
Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024.

DOSE MODIFICATIONS FOR ADVERSE REACTIONS (1 of 2)

Adverse reaction	Occurrence	Venetoclax dose modification	Rituximab dose modification (Cycles 1–6)
Hematologic adverse reactions			
Grade 3 neutropenia with infection or fever OR **Grade 4 hematologic toxicities (except lymphopenia)**	1st occurrence	• Interrupt venetoclax • Upon resolution to Grade 1 or baseline level, resume venetoclax at the same dose	• Withhold rituximab • Upon resolution, resume rituximab at the same dose
	2nd and subsequent occurrences	• Interrupt venetoclax • Upon resolution, resume venetoclax at the reduced dose[a]	
	Any occurrence	• Consider G-CSF or growth factors for neutropenia as indicated	
Non-hematologic adverse reactions			
Grade 2 non-hematologic toxicities	Any occurrence	• Delay venetoclax and rituximab • Upon resolution to Grade ≤1 or baseline, resume at same doses	
Grade 3 or 4 non-hematologic toxicities	1st occurrence	• Interrupt venetoclax • Upon resolution to Grade 1 or baseline level, resume venetoclax at the same dose	• Delay rituximab • Upon resolution to Grade 1 or baseline, resume rituximab at the same dose
	2nd and subsequent occurrences	• Interrupt venetoclax • Upon resolution, resume venetoclax at the reduced dose[a]	

[a]See next slide for dose reductions. G-CSF=granulocyte-colony stimulating factor.

1. Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024. 2. Seymour JF, et al. *N Engl J Med.* 2018;378:1107–1120 (protocol).

DOSE MODIFICATIONS FOR ADVERSE REACTIONS (2 of 2)

Adverse reaction	Occurrence	Venetoclax dose modification
Tumor lysis syndrome		
Blood chemistry changes or symptoms suggestive of TLS	Any occurrence	• Withhold the next day's dose. If resolved within 24–48 hours of last dose, resume at the same dose • For any blood chemistry changes requiring more than 48 hours to resolve, resume at the reduced dose • For any events of clinical TLS,[a] resume at the reduced dose following resolution

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

Venetoclax dose at interruption, mg	Venetoclax restart dose, mg[b,c]
400	300
300	200
200	100
100	50
50	20
20	10

[a]Clinical TLS was defined as laboratory TLS with clinical consequences such as renal failure, cardiac arrhythmias, or sudden death and/or seizures. [b]During the ramp-up phase, continue the reduced dose for 1 week before increasing the dose. [c]If a dosage interruption lasts more than 1 week during the ramp-up phase or more than 2 weeks after completion of ramp-up, reassess the risk of TLS and determine whether reinitiation at a reduced dosage is necessary.

1. Venclexta (venetoclax) [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2024.