INFUSION REACTIONS

→ Rituximab can cause severe, including fatal, infusion reactions including: Urticaria, hypotension, angioedema, hypoxia, bronchospasm, pulmonary infiltrates, acute respiratory distress syndrome, myocardial infarction, ventricular fibrillation, cardiogenic shock, anaphylactoid events, or death.

→ Severe reactions typically occurr during the first infusion with time to **onset of 30–120 minutes**.

→ Premedicate patients with an **antihistamine** and **acetaminophen** prior to dosing.

→ Depending on the severity of the infusion reaction and the required interventions, temporarily or permanently **discontinue Rituximab**.

→ Obtain vital signs (patient temperature, blood pressure and pulse) upon arrival, after start of medication, every 15 minutes for the first hour of the infusion, every 30 minutes thereafter, upon discontinuing infusion and before the patient departs the facility. If prior history of an acute infusion reaction is present, monitor vitals every 10 minutes for 30 minutes then every 30 minutes and for 30 minutes after infusion.[1]

If patient reports **mild to moderate** reactions such as; flushing, chills, and rigors

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Stop temporarily and assess patient for symptoms resolution.

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Premedicate with acetaminophen, antihistamine and methylprednisolone.

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Resume infusion at a **minimum 50% reduction in rate after symptoms have resolved**.

If patient **reports more severe reaction** such as hives, difficulty breathing, chest pain, high or low blood pressure, swelling of face and hands, fever, chills or anaphylaxis, **or where mild reactions persist**

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Stop the infusion and institute medical management (e.g. glucocorticoids, epinephrine, bronchodilators, or oxygen) for infusion reactions as needed.

Desensitization protocol of Rituximab in transplantation[2]

Premedicate with with diphenhydramine (25 mg IV) and famotidine (20 mg IV) 20 minutes before starting infusion.

Target dose (mg)	600
Standard volume per bag (mL)	250
Final rate of infusion (mL/hour)	75
Calculated target concentration (mg/mL)	2.4
Standard time of infusion (minutes)	200

				Total mg per bag	Amount of bag infused (mL)
Solution 1	250	mL of	0.024 mg/mL	6.000	8.67
Solution 2	250	mL of	0.240 mg/mL	60.000	17.58
Solution 3	250	mL of	**2.382 mg/mL**	595.573	250.00

PLEASE NOTE: The total volume and dose dispensed are more than the final dose given to patient because the initial solutions are *not completely infused*

Step	Solution	Rate (mL/hour)	Time (minutes)	Volume infused per step (mL)	Dose administered with this step (mg)	Cumulative dose (mg)	Fold increase per step
1	1	1.9	15	0.47	0.0113	0.0113	-
2	1	4.7	15	1.17	0.0281	0.0394	2.5
3	1	9.4	15	2.34	0.0563	0.0956	2
4	1	18.8	15	4.69	0.1125	0.2081	2
5	2	4.7	15	1.17	0.2813	0.4894	2.5
6	2	9.4	15	2.34	0.5625	1.0519	2
7	2	18.8	15	4.69	1.1250	2.1769	2
8	2	37.5	15	9.38	2.2500	4.4269	2
9	3	9.4	15	2.34	5.5835	10.0104	2.481554688
10	3	18.8	15	4.69	11.1670	21.1774	2
11	3	37.5	15	9.38	22.3340	43.5114	2
12	3	**75.0**	186.875	233.59	556.4886	600.0000	2
Total time: 351.875 minutes = 5.86 hours							

Monitoring and charting during desensitization:

Please clearly document any reaction, including:

a. Patient's symptoms, vital signs, and physical findings;

b. Exactly when the reaction occurred (ie, what step, how many minutes into that step);

c. Treatment administered, how and when the reaction resolved, and when the protocol was restarted.

Treatment of allergic reactions:

1. **For mild reactions:** In case of isolated itching, flushing, hives, mild chest tightness, nausea, abdominal pain, or back pain, with normal vital signs, stop the infusion and treat with IV diphenhydramine. Observe patient until the reaction subsides, then resume the protocol at the point where the infusion was stopped.

2. **For severe reactions:** In case of hypotension, throat swelling, wheezing/respiratory distress, or decreased oxygen saturation, stop the infusion and treat with epinephrine 0.3 mg IM × 1, diphenhydramine methylprednisolone IV, oxygen, nebulized albuterol for bronchospasm, and IV fluids (normal saline), per AHA guidelines. Place patient in a recumbent position if hypotensive. Consider glucagon 1 to 2 mg IV bolus if patient has taken beta blockers, followed by infusion at 1 to 5 mg/hour. **Immediately alert the housestaff and supervising physician.** When the patient is stable, the protocol will be resumed as instructed by the supervising physician. *Patient should be discharged with prescription for an epinephrine autoinjector.*

(1) Selewski, David T., G. V. Shah, R. J. Mody, P. A. Rajdev, and S. K. Mukherji. 2010. "Rituximab (Rituxan)." AJNR. American Journal of Neuroradiology 31 (7): 1178–80.

(2) Brennan PJ, Rodriguez Bouza T, Hsu FI, et al. Hypersensitivity reactions to mAbs: 105 desensitizations in 23 patients, from evaluation to treatment. J Allergy Clin Immunol 2009; 124:1259.