

# Preparation and administration of REGN-EB3 for Ebola virus disease (EVD)



## 1. CALCULATE DOSE 2. DILUTE 3. ADMINISTER 4. MONITOR

### 1. CALCULATE DOSE

- Weigh the patient.
- Calculate the dose as per Table 2.

**TABLE 2. Dose, number of vials, total diluted infusion volume and infusion time of REGN-EB3**

Body weight (kg)	Dose of REGN-EB3 (mg)	Volume of dose REGN-EB3 (mL)	Number of vials	Total diluted infusion solution (REGN-EB3 and dilution solution) (mL)	Infusion time of diluted infusion solution
1	50	3	1	15	4 hours
2	100	6	1	25	4 hours
3	150	9	1	25	3 hours
4	200	12	1	50	3 hours
5	250	15	2	50	3 hours
6	300	18	2	50	3 hours
7	350	21	2	50	3 hours
8	400	24	2	100	3 hours
9	450	27	2	100	3 hours
10	500	30	3	100	3 hours
11	550	33	3	100	3 hours
12	600	36	3	100	3 hours
13	650	39	3	100	3 hours
14	700	42	3	100	3 hours
15	750	45	4	100	3 hours
16	800	48	4	250	2 hours
17	850	51	4	250	2 hours
18	900	54	4	250	2 hours
19	950	57	4	250	2 hours
20	1000	60	5	250	2 hours
21	1050	63	5	250	2 hours
22	1100	66	5	250	2 hours
23	1150	69	5	250	2 hours
24	1200	72	5	250	2 hours
25	1250	75	6	250	2 hours
26	1300	78	6	250	2 hours
27	1350	81	6	250	2 hours
28	1400	84	6	250	2 hours
29	1450	87	6	250	2 hours
30	1500	90	7	250	2 hours
31	1550	93	7	250	2 hours
32	1600	96	7	250	2 hours
33	1650	99	7	250	2 hours
34	1700	102	8	250	2 hours
35	1750	105	8	250	2 hours
36	1800	108	8	250	2 hours
37	1850	111	8	250	2 hours
38	1900	114	8	250	2 hours
39	1950	117	9	500	2 hours
40	2000	120	9	500	2 hours
41	2050	123	9	500	2 hours
42	2100	126	9	500	2 hours
43	2150	129	9	500	2 hours
44	2200	132	10	500	2 hours
45	2250	135	10	500	2 hours
46	2300	138	10	500	2 hours
47	2350	141	10	500	2 hours
48	2400	144	10	500	2 hours
49	2450	147	11	500	2 hours
50	2500	150	11	500	2 hours
51	2550	153	11	500	2 hours
52	2600	156	11	500	2 hours
53	2650	159	11	500	2 hours
54	2700	162	12	500	2 hours
55	2750	165	12	500	2 hours
56	2800	168	12	500	2 hours
57	2850	171	12	500	2 hours
58	2900	174	12	500	2 hours
59	2950	177	13	500	2 hours
60	3000	180	13	500	2 hours
61	3050	183	13	500	2 hours
62	3100	186	13	500	2 hours
63	3150	189	14	500	2 hours
64	3200	192	14	500	2 hours
65	3250	195	14	500	2 hours
66	3300	198	14	500	2 hours
67	3350	201	14	500	2 hours
68	3400	204	15	500	2 hours
69	3450	207	15	500	2 hours
70	3500	210	15	500	2 hours
71	3550	213	15	500	2 hours
72	3600	216	15	500	2 hours
73	3650	219	16	500	2 hours
74	3700	222	16	500	2 hours
75	3750	225	16	500	2 hours
76	3800	228	16	500	2 hours
77	3850	231	16	500	2 hours
78	3900	234	17	500	2 hours
79	3950	237	17	500	2 hours
80	4000	240	17	1000	2 hours
81	4050	243	17	1000	2 hours
82	4100	246	17	1000	2 hours
83	4150	249	18	1000	2 hours
84	4200	252	18	1000	2 hours
85	4250	255	18	1000	2 hours
86	4300	258	18	1000	2 hours
87	4350	261	18	1000	2 hours
88	4400	264	19	1000	2 hours
89	4450	267	19	1000	2 hours
90	4500	270	19	1000	2 hours
91	4550	273	19	1000	2 hours
92	4600	276	20	1000	2 hours
93	4650	279	20	1000	2 hours
94	4700	282	20	1000	2 hours
95	4750	285	20	1000	2 hours
96	4800	288	20	1000	2 hours
97	4850	291	21	1000	2 hours
98	4900	294	21	1000	2 hours
99	4950	297	21	1000	2 hours
100	5000	300	21	1000	2 hours

**Note:** The recommended infusion volume ensures the final concentration of the diluted solution is between 9.5 mg/mL to 23.7 mg/mL





## 2. DILUTION

- **Prepare** REGN-EB3 in a clean dedicated space in the low-risk zone.
- **Wash** hands per protocol.
- **Remove** vials from the refrigerator and allow them to reach room temperature.
- **Check** there is no discolouration in the content of any vial.
- **Select** type of dilution solution and volume required (Table 2), either:
  - 0.9% sodium chloride
  - 5% dextrose (recommended solution for neonates) or
  - Ringer's lactate solution.
- **Withdraw and discard** solution from the IV bag equal to the calculated volume of REGN-EB3 in mL required, using appropriately sized syringe and 21-gauge needle following standard aseptic techniques.
- **Add** the calculated volume of REGN-EB3 required to the IV bag of dilution solution.
- **Invert** the IV bag 10 times to ensure thorough mixing. Do not shake.
- **Label** the IV bag with the patient's name, date of birth, weight in kg, dose of REGN-EB3 included and date/time of drug expiration.

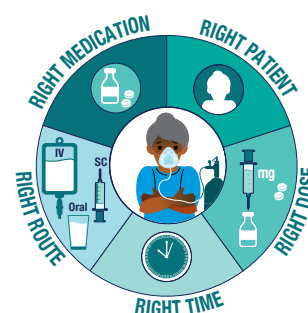
## 3. ADMINISTER

- **Introduce** yourself to the patient and explain that you are planning to administer the medication.
- **Do not mix** with or administer with other medicinal products.
- **Allow** the diluted infusion solution to reach room temperature prior to administration.
- **Administer** the diluted infusion solution via infusion pump (for paediatric patients < 20 kg it is preferable) or manually through an IV giving set containing a sterile **in-line or add-on 0.2-micron filter**.
- **Select** the appropriate infusion rate.
 

If manually:  $\text{drip rate} = (\text{total volume (mL)} / \text{minutes}) \times \text{drop factor}^*$

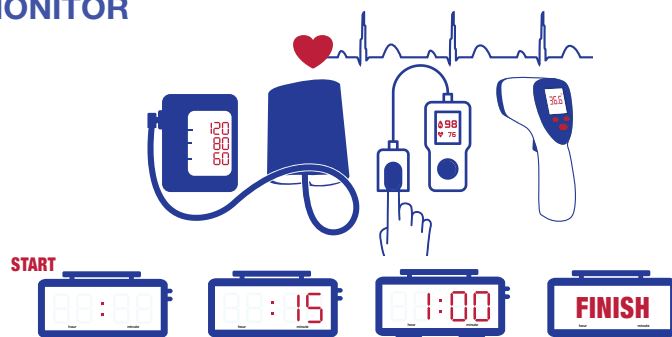
\* Check the giving set packaging!
- **Record** the time and date the infusion was started.
- **Flush the line** at the end of the infusion.
  - When the infusion bag is almost empty, hang a 250-mL 0.9% sodium chloride flush bag or inject at least an additional 50 mL of 0.9% of sodium chloride into the IV infusion bag.

**Remember the FIVE RIGHTS of drug administration:**



## 4. MONITOR

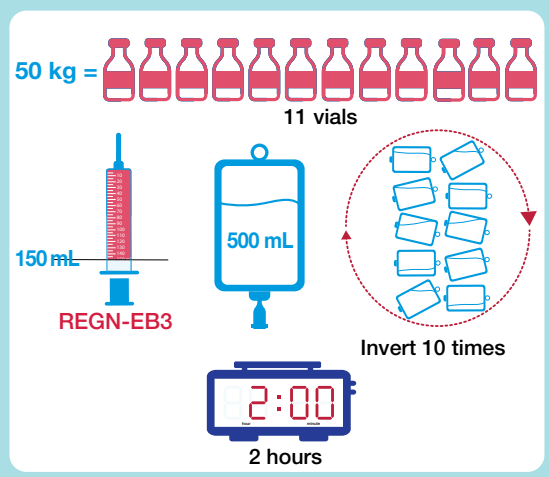
- Monitor patient symptoms and vital signs: heart rate, blood pressure, respiratory rate and oxygen saturation:
  - immediately before infusion
  - 15 minutes after starting the infusion
  - 1 hour into the infusion
  - at the end of the infusion
  - if any clinical deterioration during the infusion, take vital signs more frequently and assess the patient clinically.

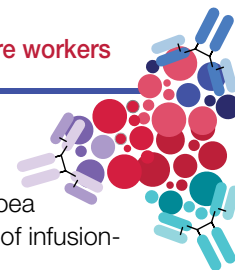


### EXAMPLE

#### Patient weighting 50 kg

- Recommended dosage is 2500 mg of atoltivimab, 2500 mg of maftivimab and 2500 mg of odesivimab OR 150 mL of REGN-EB3.
- The dosage requires 11 vials of REGN-EB3.
- Take an IV bag of 500 mL of dilution solution (0.9% sodium chloride, Ringer's lactate or 5% dextrose solution).
- Withdraw and discard 150 mL of the solution with an appropriately sized syringe and 21-gauge needle following standard aseptic techniques.
- Inject 150 mL of REGN-EB3 into the infusion solution to have a total infusion solution of 500 mL.
- Invert 10 times (do not shake).
- Infuse the 500 mL of diluted infusion solution over 2 hours.





## HYPERSENSITIVITY AND INFUSION REACTIONS

Hypersensitivity reactions including infusion-associated events have been reported during and post-infusion with REGN-EB3. The most common adverse events (incidence  $\geq 20\%$ ) are pyrexia, chills, tachycardia, tachypnoea and vomiting. The rate of infusion of REGN-EB3 may be slowed or interrupted if the patient develops any signs of infusion-associated events.

**IF SIGNS OR SYMPTOMS OF A CLINICALLY SIGNIFICANT HYPERSENSITIVITY REACTION OR ANAPHYLAXIS OCCUR, IMMEDIATELY DISCONTINUE THE INFUSION AND INITIATE APPROPRIATE MEDICATIONS, SUPPORTIVE THERAPY AND AIRWAY MANAGEMENT.**

### INFUSION REACTION GUIDE

**Suggestions only – not meant to replace existing clinical guidelines or alter clinical judgment.**

INFILTRATION	FEVER	HYPERTENSION	OTHER SYMPTOMS:	SEIZURES	ANAPHYLAXIS	ALLERGIC REACTION
(Watch for pain, swelling, tightness around injection site; skin cooling/blanching; leakage at insertion site) 1. STOP infusion 2. Discontinue IV site, bandage, apply heat OR cold if available 3. Insert new peripheral IV	<b>38 °C – 39 °C</b> 1. Continue infusion, monitor vital signs 2. Administer paracetamol	<b>Mild</b> 1. Continue infusion, monitor vital signs	<b>SHIVERING HYPOTENSION OEDEMA PERIPHERAL NEUROPATHY</b> <b>Mild</b> 1. Continue infusion, monitor vital signs	<b>Brief, no loss of consciousness</b> 1. Continue infusion, monitor patient		
	<b>39 °C – 40 °C</b> 1. Reduce infusion rate by 50% 2. Monitor until temperature is $< 39\text{ °C}$ , then resume regular rate increase 3. Administer paracetamol per schedule	<b>BP &gt; 140/90 (OR increase of diastolic pressure &gt; 20 mmHg)</b> 1. Reduce infusion rate by 50% 2. Monitor BP every 15 min until BP is $< 140/90$ , then resume regular infusion schedule	<b>Moderate</b> 1. Reduce infusion rate by 50% 2. Monitor until symptoms are reduced to mild 3. Resume regular infusion schedule	<b>Self limiting seizure</b> 1. STOP infusion. 2. Monitor vital signs q 15 min for 15–30 min. 3. If vital signs are stable and seizure does not recur, resume regular infusion schedule	<b>Moderate</b> 1. STOP infusion 2. Administer IV diphenhydramine 3. Notify site physician as soon as possible 4. Continue to administer regular IV fluid 5. Monitor vital signs q 15 min until reaction subsides and patient stabilizes	<b>Moderate</b> 1. Reduce infusion rate by 50% 2. Administer IV diphenhydramine 3. Administer IV fluids 4. Monitor patient q 15 minutes until symptoms are reduced to Grade 1 or below, then resume regular infusion schedule
	<b>&gt; 40 °C</b> 1. STOP infusion 2. Continue to administer regular IV fluid, paracetamol 3. External cooling measures (if available) 4. When temperature is $< 39\text{ °C}$ , resume infusion rate at 50% 5. Monitor at 50% rate for 15–30 min with vital signs q 15 min 6. If reaction does not re-occur, resume regular infusion schedule	<b>BP &gt; 160/100 (OR increase of diastolic pressure &gt; 30 mmHg)</b> 1. STOP infusion 2. Administer BP medications if available 3. When BP is reduced $< 140/90$ , resume infusion rate at 50% 4. Monitor at 50% rate for 15–30 min with vital signs q 15 min 5. If reaction does not re-occur, resume regular infusion schedule	<b>Severe</b> 1. STOP infusion 2. When symptoms are reduced to mild, resume infusion rate at 50% 3. Monitor at 50% rate for 15–30 min 4. If reaction does not re-occur, resume regular infusion schedule	<b>Persistent seizures</b> 1. STOP infusion 2. Assess and secure airway 3. Continue to administer regular IV fluid, diazepam 4. Monitor vital signs every 15 min until seizures subside and patient stabilizes 5. When stable, resume infusion at 50% previous rate 6. Monitor for 15–30 min with vital signs every 15 min 7. If seizures do not re-occur, resume regular infusion schedule	<b>Severe</b> 1. STOP infusion 2. Assess and secure airway 3. Administer IM epinephrine 4. Supplemental oxygen 5. Volume resuscitation: 1–2 L IV as needed 6. For bronchospasm resistant to IM epinephrine, give salbutamol via nebulizer, or inhaler 7. IV diphenhydramine 8. Monitor vital signs q 15 min until reaction subsides and patient stabilizes	

**REPORT:** Access the website using the QR code provided on the product.

