Odronextamab (REGN1979) Phase 3 OLYMPIA Pooled Supply Program

Pharmacy Manual Pooled Supply

Version 4.0

R1979-HM-2298 OLYMPIA-1
R1979-ONC-2075 OLYMPIA-2
R1979-ONC-2105 OLYMPIA-3
R1979-HM-2299 OLYMPIA-4
R1979-ONC-22102 OLYMPIA-5
R1979-ONC-2336 OLYMPIA-6

REVIEWERS & APPROVERS

This Pharmacy Manual is signed electronically in Regeneron's eTMF and is effective as of the last signature date. The signature page is added to the last page of the approved version.

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1. PURPOSE

The purpose of the Pooled Supply Pharmacy Manual is to describe to site personnel the procedures applicable to investigational product (IP) management including: receipt, storage, preparation, handling, administration, accountability, reconciliation, returns and/or destruction for odronextamab (REGN1979) in the OLYMPIA Pooled Supply program.

Responsibilities may be delegated to a qualified individual; however, the assigned role remains accountable.

Refer to the current version of the following documents for guidance and additional study specific information:

- Study specific Protocol
- Investigator Brochure

1.1. Trial and IP Summary

Always refer to the study protocol for the most current information.	
Study Design	☒ Open label
IP Label Design	☒ Open label
Pharmacy Status	☒ UNBLINDED
Route of Administration (ROA)	☒ Intravenous (IV)

1.2. Interactive Response Technology (IRT) Details and Supply Triggers

This section is intended as an IRT summary. The IRT User Guide should be referenced for complete details. Refer to Section 4 for Investigational Product Shipments.	
IP will be shipped to the site pharmacist in accordance with local regulations after all required documents and approvals are in place.	
Participants are screened via IRT:	☒ YES ☐ NO
Participants are randomized/ enrolled via IRT:	☒ YES ☐ NO
Initial IP shipment trigger to site via IRT occurs at:	☒ First participant screening
IRT will be used for accountability, reconciliation, destruction and/or returns:	☒ YES ☐ NO

1.	IP inventory is managed by IRT; resupply shipments are automatically (prediction) sent to sites when supply levels are low based on the resupply triggers and/or site level inventory monitoring by the CDSL Manager.
2.	If the site plans to enroll more participants in a short period of time and will need additional IP kits on site, the pharmacist should contact their assigned Site Monitor immediately.
3.	The Site Monitor will inform the CRO PM and/or Regeneron CSL who will discuss such situations with the Regeneron CDSL Manager.
4.	If agreed upon, either a manual shipment will be raised in IRT or the supply strategy will be changed in IRT by the CDSL Manager.

1.3. Change Requests

1.	Should any processes and/or procedures provided within this pharmacy manual conflict with written site procedures or local regulations, the Principal Investigator (PI), Site Study Coordinator, or Pharmacist must discuss the requirement with the Site Monitor and the decision needs to be documented and filed in the Trial Master File (TMF) and Investigator Site File (ISF).

1.4. Delegation and Changes in Study Staff

1.	Site staff responsibilities, will be documented on *VV-FRM-00055, Site Signature and Delegation Log* or CRO/Site Equivalent Documentation.
2.	For any issues or queries that arise during the study, the appropriate site personnel will contact the Site Monitor. The contact information for the Site Monitor can be found on the study contact list in the ISF.
3.	Any changes in the site staff must be discussed with the Site Monitor as soon as possible. • New staff must be adequately trained by either the Site Monitor or the Pharmacist, as appropriate and training must be documented. • New site staff must be listed and authorized by the PI on *VV-FRM-00055, Site Signature and Delegation Log* or CRO/Site Equivalent Documentation prior to commencing work on the study.

1.5. Pharmacy Staff Responsibilities

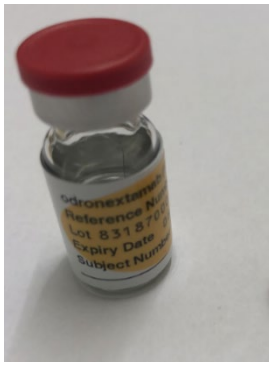
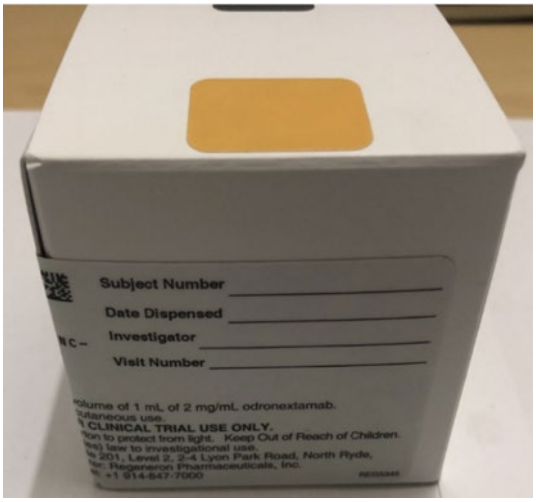
	Pharmacy Staff responsibilities:
1.	The site will identify at least two pharmacists who will be responsible for preparation and dispensation of the IP to study staff for administration
2.	Maintain the pharmacy file in a secure area with the documents for all IP shipments
3.	Receipt of IP shipments and perform accountability
4.	Ensure that all IP is stored according to clinical label for the duration of the study, all storage temperature requirements are met per Section 5.2, Temperature Controlled Storage Area, and all temperature excursions are recorded per Section 5.5, Temperature Excursion Management
5.	Prompt and accurate completion of IRT, pharmacy preparation worksheets, and other applicable documents to record IP preparation and handling. There must always be a second verification check of the dispensed IP from the IRT to ensure the right medication is provided to the correct participant for the correct visit.
6.	Communication with the Site Monitor regarding any issues
7.	Escalation of deviations to Site Monitor and Sponsor representatives
8.	Attendance during the monitoring visits

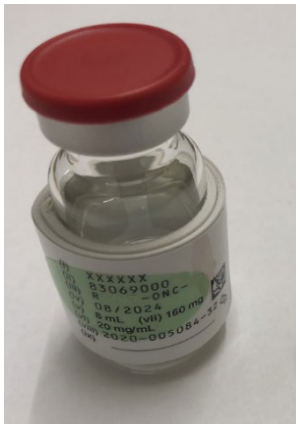
2. STUDY MEDICATION & ANCILLARY SUPPLIES

2.1. Sponsor Provided Investigational Product, Labels, and Packaging

The immediate/ primary container and outer carton are labelled with a clinical label containing drug product details, protocol information and country specific regulatory requirements.

Each kit is identified by a lot number and a unique medication number, displayed as the reference number on the clinical label. The printed text on the clinical label should not be defaced, crossed out or altered in any way without prior approval from Regeneron CDSL.

<table>
<tr><th>Unit</th><th colspan="2">Description and example</th></tr>
<tr><td>A.</td><td colspan="2">Drug description (per label): Odronextamab (REGN1979) 2 mg
Dosage Form: 2 mg/mL, 1 mL withdrawable volume in 2 mL vial, 1 vial per box
Purpose: Open label investigational product
Storage Conditions[1]: Refrigerated, Protect from Light
Carton size: 2” x 2” x 2”, with ancillary orange colored labels, one on the outer kit carton and one transparent label on the vial label</td></tr>
<tr><td></td><td>Primary:
  </td><td>Secondary: Carton
 
</td></tr>
<tr><td>B.</td><td colspan="2">Drug description (per label): Odronextamab (REGN1979) 160 mg
Dosage Form: 20 mg/mL, 8 mL withdrawable volume in 10 mL vial, 1 vial per box
Purpose: Open label investigational product
Storage Conditions[1]: Refrigerated, Protect from Light
Carton size: 2” x 2” x 2”, with ancillary green colored labels, one on the outer kit carton and one transparent label on the vial label</td></tr>
</table>

	Primary: 	**Secondary: Carton** 

[1]For definitions of the kit storage requirements see Section 5.1, Storage Requirements and Definitions. For intermediate storage conditions during preparation for dosing, see Section 3.2**,** Stability and Shelf-life During IP Preparation

2.2. Overview of the OLYMPIA *Pooled Supply* Approach

1.	Regeneron will use a single clinical site distribution vendor (PCI Clinical Services) and a single IRT system (Calyx) to support the phase 3 OLYMPIA program and enable its ***pooled supply*** approach.
2.	Regeneron will package and label odronextamab (REGN1979) investigational product at Fisher Clinical Services (FCS) with multiple protocol numbers appearing on the label to support its phase 3 OLYMPIA program: • All kits are uniquely numbered (serialized) and open-label. • Comparators and/or standard of care medications labeled by Regeneron for central provision where required will contain only the protocol number(s) they may be used in. (For example, if a SOC therapeutic is included in 3 clinical trial protocols, it would only have 3 protocols numbers on its label.)
3.	The Calyx IRT system electronically controls drug availability for distribution and will prohibit drug from erroneously shipping from PCI to the wrong site in the wrong protocol. A target quantity of kits of a given lot are manually allocated to a protocol once demand is realized. Once allocated, they may not be transferred to another study. Whereas there may be instances where a single cancer center may be actively participating in 2 or more OLYMPIA protocols, the site will receive shipments separately, maintain separate drug supplies for each protocol in their pharmacy storage, and access separate Calyx IRT system access points through their main login screen.
4.	When a drug order is generated by the IRT system for a specific protocol containing a range of kits/batches, those kits are then picked by PCI distribution staff and ***protocol-specific ancillary labels*** will be applied JIT (just in time) to each kit in a secure area located on the warehouse floor before being packed into a validated shipper and sent to a site via courier service. **The PCI packaging slip will clearly denote the single specific protocol number.**

5.	Once investigational product is shipped to a site, they may only be used for that protocol, even if a given clinical site participates in multiple OLYMPIA protocols at once. Transferring investigational product between protocols at the site is prohibited.

2.3. Safety and Handling

1	For comprehensive information related to the investigational drug product safety and handling, please refer to the Safety Data Sheets (SDS) listed in Section 10. This product is an ☒Antibody. Hazard Category: Refer to SDS.

2.4. Sponsor Centrally Supplied Marketed Drug Products (Commercially Available / Standard of Care / Rescue Medication)

Regeneron supplied drug products should **not** be dispensed, prepared, and/or administered without written confirmation of the medication reference number assigned to the participant by the IRT system for each visit. Sponsor Centrally Supplied Marketed Drug Products mentioned below referred as IP in sections 4 through 9 below and should follow outline procedures.

If marketed drug product and/or supplements are provided to the study site by the Sponsor (versus site sourced), the site must be able to provide documentation to acknowledge receipt, record accountability, reconcile usage and either destroy on-site or return products provided according to the accountability method below.

Preparation, dispensation, and administration should be documented according to site procedures and product package insert/SMPC.

When site is responsible for sourcing the marketed medication identified in the protocol. accountability, reconciliation, and destruction should be performed according to site policy.

Drug Product	**Presentation**	**Clinical Studies Supported**	**Accountability Method***
Bendamustine	100 mg/40 mL vial	R1979-HM-2298	☒ **IRT Modules**
Cyclophosphamide	500 mg powder / vial	R1979-HM-2298 R1979-ONC-2075 R1979-ONC-2105	
Doxorubicin	200 mg/100 mL vial		
Vincristine	2 mg/1 mL vial		
Prednisone	50 mg (50 tablets, 5 blisters of 10 tablets per pack)		
Ifosfamide	3 g powder / vial	R1979-HM-2299	
Carboplatin	150 mg/15 mL vial		

Etoposide	100 mg/5 mL vial		
Cytarabine	2000 mg/20 mL vial		
Dexamethasone	4 mg tablets, 50 tablets per pack		
Cisplatin	100 mg/100 mL vial		
Gemcitabine	2000 mg/20 mL vial Or 2000 mg/52.6 mL vial		
Lenalidomide	20 mg, 15 mg, 10 mg, or 5 mg hard capsules; 21 capsules per pack	R1979-ONC-22102	
Rituximab-abbs (Truxima)	100 mg/10 mL vial, 2 vials per carton	R1979-HM-2298 R1979-ONC-2075 R1979-ONC-2105 R1979-HM-2299 R1979-ONC-22102	
Rescue medication	**Presentation**	**Clinical Studies Supported**	**Accountability Method***
Tocilizumab	400 mg or 200 mg	R1979-HM-2298 R1979-ONC-2075 R1979-ONC-2105 R1979-HM-2299 R1979-ONC-22102 R1979-ONC-2336	☒ **Paper Forms/ Logs or IDS system**

2.5. Ancillary Supplies

1.	Each investigator/site is responsible for supplying the supportive medication identified in the protocol as well as the IV bag (e.g., 0.9% sodium chloride) for the dilution, preparation, and flush of study drug, as applicable, and ancillary materials required for preparation and administration. The list of suggested ancillary supplies are found in Section 2.5.1.

2.5.1. Recommended Ancillary Supplies

1.	The listed ancillary materials in this section are recommendations based on compatibility studies for the listed product composition. A list of suggested brands and product item # are available upon request.
2.	Should the site not be able to determine the compatibility of the recommended materials (based on composition and purpose), the site should contact the manufacturer to confirm the contact materials, and this should be documented in the site file.
3.	If unable to confirm compatibility, provide the type of product, manufacturer, unit reference number and any available information (i.e., specification or data sheet [in English]) to the Pharmacy Support Services Group at pharmacy.support@regeneron.com for assessment for the component along with • *VV-FRM-00172, Ancillary Supplies Material Compatibility Review Request*. THIS IS NOT A REQUIRED STEP FOR ALL MATERIALS, ONLY MATERIAL THAT CANNOT BE DETERMINED COMPATIBLE SHOULD BE REVIEWED
4.	Once reviewed, Regeneron will provide approval or a response. Correspondence with site pharmacy and Regeneron shall be retained in the ISF. **As this review may take several days depending on research required, please plan accordingly upon review of the pharmacy manual.**

Table 1: Materials for IP Preparation and/or Administration Sourced by Site

Item Name	Details
IV INFUSION	
Appropriate size Luer connections syringes	Polycarbonate or Polypropylene
21-gauge*, 1- or 1.5-inch needles	For withdrawal of liquids during preparation *Recommended gauge to minimize vial coring
IV infusion bag of 0.9% Sodium Chloride	25 mL, 50 mL or 100 mL • IV containers should be composed of polyvinyl chloride (PVC) or polyolefin (PO)
Empty containers	For preparation of 0.2 mg dose without Human Serum Albumin (HSA) • Containers should be composed of ethylene vinyl acetate (EVA), polyolefin (PO) or polyvinyl chloride (PVC).
Human Serum Albumin (HSA)	5%, 20% or 25% may be used Refer to Table 3 for volume requirements
20-22-gauge, 1-inch catheter	For administration of infusion
Calibrated Infusion Pumps for administration of drug products	• Peristaltic infusion pump • Fluid displacement infusion pump Allowed infusion rates: • 6-500 mL/hour for 0.2 mg dose without HSA • 13-500 mL/hour for 0.2 mg dose with HSA and 0.5-320 mg doses
Infusion Sets	• Infusion set with tubing made of: o PVC with DEHP – not for use in European Union

Item Name	Details
	○ PVC without DEHP ○ Polyethylene-lined PVC tubing ○ Polyurethane For **0.2 mg dose prepared with HSA and doses of 0.5 mg or greater**, the infusion set must contain an 0.2 or 5 micron in-line or add-on filter made of polyether sulfone (PES). For **0.2 mg dose prepared without HSA**, the infusion set should **NOT** contain an in-line or add-on filter. **Note**: A 15-micron polyamide drip chamber filter is acceptable for the administration of odronextamab 0.2 mg prepared without HSA.
Add-on Filters (if not included with the infusion set)	• Must be made with polyether sulfone (PES) and be 0.2 or 5 micron
MISCELLANEOUS	
Sharp Containers	For disposal of needles
Alcohol Wipes	Disinfection

3. INVESTIGATIONAL PRODUCT PREPARATION INSTRUCTIONS

3.1. General Preparation and Handling Instructions

1.	This section is covering Regeneron drug product. Regeneron supplied drug products should **not** be dispensed, prepared, and/or administered without written confirmation of the medication reference number assigned to the participant by the IRT system for each visit. Preparation of drug products locally supplied or provided centrally by Regeneron should follow the SMPC.
2.	Odronextamab (REGN1979) vials should be stored between **2-8°C (36-46°F)** as per the label prior to use.
3.	IP vials should not be shaken during transport, handling, or preparation.
	The prepared IV bags should not be transported via pneumatic tube.
4.	Ensure the investigational product has been stored at the required temperature and visually examine the vial contents to check for any damage or discoloration, or presence of particulate. If there are any of the mentioned findings, do not use the investigational product.
5.	Aseptic technique must be used during handling, preparation, and administration. Ensure you are working on a hard, clean surface. If available, work in a laminar flow hood, biosafety cabinet or segregated compounding area when required.
6.	All blank fields such as Subject Number, Date Dispensed, and Investigator Name, etc. on the IP label should be filled out prior to preparing the IP for administration. Do not deface, cross out or alter the printed label text in any way without prior approval.

7.	The pharmacist/qualified delegate will prepare and dispense odronextamab (REGN1979) to the delegated study personnel for administration.
	Please refer to **Section 6** of the Pharmacy Manual for instructions on transferring kits or prepared doses from storage locations.
8.	All IP preparations worksheets, accountability and dispensing modules must be completed. Refer to **Section 9**.

3.2. Stability and Shelf-life During Investigational Product Preparation

Table 2: Odronextamab (REGN1979)

Products covered by table	Storage Conditions[1]	Acceptable Time at Stated Storage Condition	Comments/Special Instructions[2]
Original IP (Liquid in Vial) **Odronextamab (REGN1979)**	Refrigerated (2-8°C)	N/A	Maintain at original carton until ready to prepare dose
Assigned to participant in IRT and just prior to preparation start	Allow to equilibrate to room temperature	Min. 10 minutes Max. 60 minutes	May be exposed to indoor light during this time
Diluted odronextamab (REGN1979) admixture in IV bag	Room temperature, Refrigerated (2-8°C)	The prepared infusion solutions should be used immediately. If not used immediately, store the prepared infusion solution either: • Refrigerated (2-8°C): for all doses for up to **24 hours;** • Room temperature (15-25°C): - For up to **6 hours** for the 0.2 mg dose with HSA. - For up to **12 hours** for 0.2 mg dose without HSA, 0.5 mg or greater The storage time above is from the start time of IP preparation to the start of the infusion.	DO NOT SHAKE. Gently swirl to prevent foaming, Do not transport using a pneumatic tube system If it was previously refrigerated, equilibrate up to room temperature for 10 - 30 minutes before infusion.
Ready for infusion	Room temperature		
[1]Refer to Section 5.2, Temperature Controlled Storage Area for definitions of storage conditions/ranges **[2]If product is to be moved between locations within a site or off-site, refer to Section 6, Movement of IP Storage and Transfers, for further instructions**			

3.3. Dose Calculation

Table 3: Dosing Table for Odronextamab (REGN1979) IV 0.2 –320 mg

Dose (mg)	IV bag size	HSA[a] required?	No. of HSA vial(s)/bag(s) [a]	HSA vial/bag to be used[b]	Required volume of HSA (mL)	Odronextamab (REGN1979) vial to be used	Drug Product Packaging Configuration (Sticker Color)	No. of odronextamab (REGN1979) vials	Volume of odronextamab (REGN1979) (mL)
0.2	100 mL	**Yes**	1	5%	0.8	2 mg	Orange	1	0.1
				20%	0.2	2 mg	Orange	1	0.1
				25%	0.16	2 mg	Orange	1	0.1
	25 mL	**No[c]**	N/A	N/A	N/A	2 mg	Orange	1	0.1
0.5	50 mL	No	N/A	N/A	N/A	2 mg	Orange	1	0.25
1	50 mL or 100 mL	No	N/A	N/A	N/A	2 mg	Orange	1	0.5
2		No	N/A	N/A	N/A	2 mg	Orange	1	1
3		No	N/A	N/A	N/A	2 mg	Orange	2	1.5
4		No	N/A	N/A	N/A	2 mg	Orange	2	2
5		No	N/A	N/A	N/A	2 mg	Orange	3	2.5
8		No	N/A	N/A	N/A	2 mg	Orange	4	4
10		No	N/A	N/A	N/A	2 mg	Orange	5	5
10		No	N/A	N/A	N/A	160 mg	Green	1	0.5
40		No	N/A	N/A	N/A	160 mg	Green	1	2
80		No	N/A	N/A	N/A	160 mg	Green	1	4
160		No	N/A	N/A	N/A	160 mg	Green	1	8
320		No	N/A	N/A	N/A	160 mg	Green	2	16

[a] Alternatively, 0.2 mg dose can be prepared by diluting IP in a 25 mL IV bag **without** HSA and administer through an IV infusion set **without** an IV filter. **Note**: It is acceptable for the infusion set used for the administration of 0.2 mg dose without HSA to contain a 15 micron polyamide drip chamber filter. If a 25 mL IV bag is used, the overfill volume needs to be removed before adding IP to the IV bag. If a 25 mL IV bag is not available at the clinical site, a 50 mL IV bag can be used by withdrawing enough diluent to bring the final volume in the IV bag to 25 mL or adding 25 mL 0.9% sodium chloride injection to an empty IV bag. **The employment of this alternative option requires Notification to Regeneron.**

[b] Only one concentration (either 5%, 20% or 25%) of Human Serum Albumin (HSA) is required to be purchased by site (procurement options are provided).

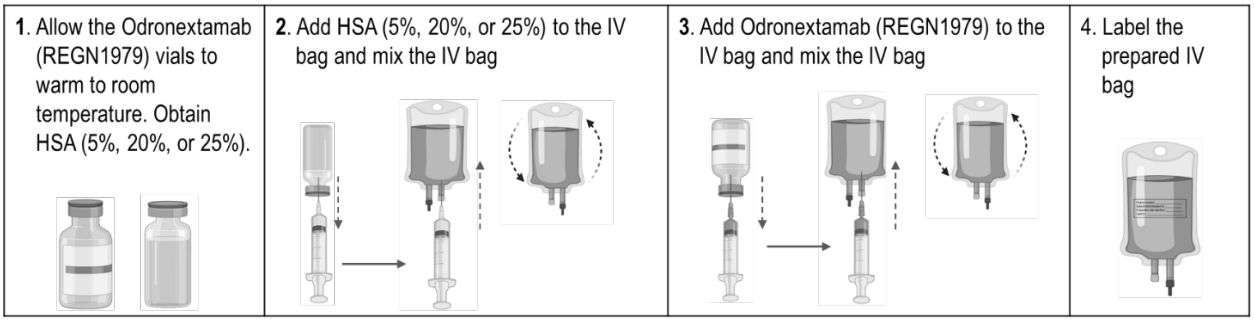
[c] A 0.2 or 5 micron filter is used to remove adventitious bacteria, endotoxins, and foreign particles from IV infusion. For sites selecting to prepare and administer 0.2 mg dose without HSA and not using filter, extra diligence for aseptic preparation is warranted to mitigate risk.

Note: The final concentration of odronextamab (REGN1979) in the IV bag must be: 1) within 0.008 – 0.5 mg/mL when diluted from 2 mg/mL odronextamab (REGN1979) in 0.9% sodium chloride injection to prepare 0.5-10 mg dose and 0.2 mg dose without HSA; 2) within 0.08 – 5 mg/mL when diluted from 20 mg/mL odronextamab (REGN1979) in 0.9% sodium chloride injection to prepare 10-320 mg dose; 3) within 0.0018 - 0.0035 mg/mL when diluted from 2 mg/mL odronextamab (REGN1979) in 0.9% sodium chloride injection supplemented with HSA to prepare the 0.2 mg dose with HSA.

3.4. Preparation of 0.2 mg Odronextamab (REGN1979) in IV Bags

3.4.1. Preparation of 0.2 mg Odronextamab (REGN1979) with HSA

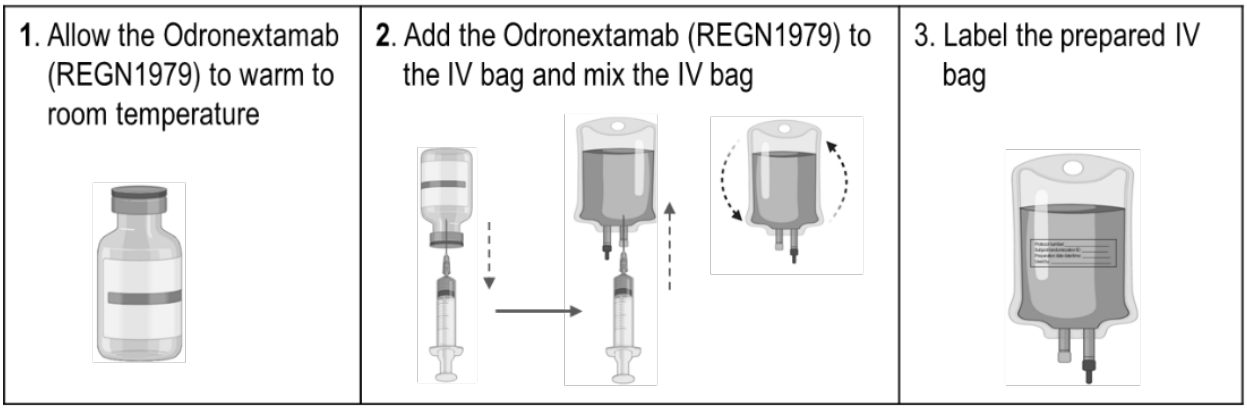
Figure 1: Procedure for Preparing 0.2 mg Odronextamab (REGN1979) with HSA



1.	Obtain the IRT assigned odronextamab (REGN1979) vial from refrigerated storage and let the vial sit at room temperature for 10-60 minutes to warm up. Additionally, obtain a vial or bag of HSA
	Obtain one IV bag (100 mL) of 0.9% sodium chloride
2.	Use a new 1 mL syringe and 21-gauge needle, withdraw a volume of HSA as specified in Table 3. Make sure there are no air bubbles in the syringe.
	Inject the withdrawn HSA solution slowly into the 0.9% sodium chloride infusion bag through the injection port and invert the IV bag 10 times to obtain a uniform mixture.
3.	Use a new 1 mL syringe and 21-gauge needle, withdraw 0.1 mL odronextamab (REGN1979) as specified in Table 3**.** Make sure there are no air bubbles in the syringe.
	Inject the withdrawn odronextamab (REGN1979) solution slowly into the 0.9% sodium chloride infusion bag through the injection port and invert the IV bag 10 times to obtain a uniform mixture.
4.	Appropriately label the infusion bag containing odronextamab (REGN1979) for infusion following the standard institutional requirements. At a minimum, the label is to include protocol number, participant ID, odronextamab (REGN1979) 0.2 mg in 0.9% sodium chloride and 0.04% HSA, directions to infuse intravenously the entire contents of the infusion bag over the required time specified in Section 3.6 plus flush, use by date/time, and the investigator's name.
The prepared infusion bag should be kept for no more than **24 hours** between 2°C and 8°C or no more than **6 hours** if it is left at controlled room temperature (15 - 25ºC) from the start time of IP preparation to the start of the infusion. If refrigerated, the diluted solution must be warmed up to room temperature prior to administration.	

3.4.2. Alternative preparation of 0.2 mg Odronextamab (REGN1979) dose without HSA in IV Bag (Notification to Regeneron must be completed prior to preparation without HSA)

Figure 2: Procedure for Preparing 0.2 mg Odronextamab (REGN1979) without HSA*

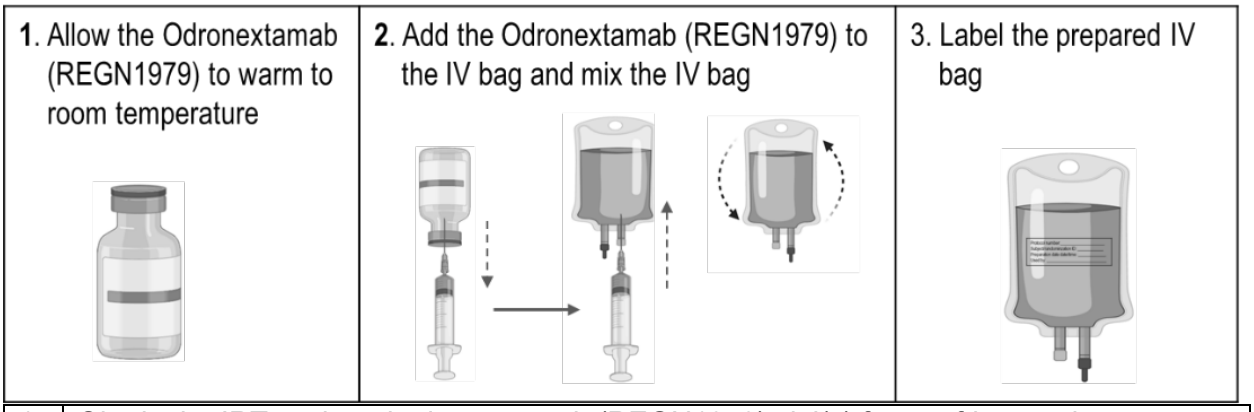


1.	Obtain the IRT assigned odronextamab (REGN1979) vial from refrigerated storage and let the odronextamab (REGN1979) vial sit at room temperature for 10 - 60 minutes to warm up.
	Obtain one IV bag (**25 mL**) of 0.9% sodium chloride. **Note:** If a 25 mL IV bag is not available at the clinical site, a 50 mL IV bag can be used by withdrawing enough 0.9% sodium chloride to bring the final volume in the IV bag to 25 mL or adding 25 mL of 0.9% sodium chloride injection to an empty bag.
2.	Use a new appropriate-sized syringe and 21-gauge needle, withdraw enough 0.9% sodium chloride from the IV bag to bring the final volume in the IV bag to 25 mL (remove overfill).
	Use a new 1 mL syringe and 21-gauge needle, withdraw 0.1 mL odronextamab (REGN1979) as specified in Table 3**.** Make sure there are no air bubbles in the syringe.
	Inject the withdrawn odronextamab (REGN1979) solution slowly into the 0.9% sodium chloride infusion bag through the injection port and invert the IV bag 10 times to obtain a uniform mixture.
3.	Appropriately label the infusion bag containing odronextamab (REGN1979) for infusion following the standard institutional requirements. At a minimum, the label is to include protocol number, participant ID, odronextamab (REGN1979) 0.2 mg in 0.9% sodium chloride, directions to infuse intravenously the entire contents of the infusion bag over the required time specified in Section 3.6 plus flush, use by date/time, and the investigator's name. **Note: the 0.2 mg dose prepared without HSA should be administered through an IV infusion set without in-line or add-on filter** .**
The prepared infusion bag should be kept for no more than **24 hours** between 2°C and 8°C or no more than **12 hours** if it is left at controlled room temperature (15 - 25ºC) from the start time of IP preparation to the start of the infusion. If refrigerated, the diluted solution must be warmed up to room temperature prior to administration.	

*0.2 or 5 micron filter is used to remove adventitious bacteria, endotoxins, and foreign particles from IV infusion. For sites selecting to prepare 0.2 mg dose without HSA and not using filter, extra diligence for aseptic preparation is warranted to mitigate risk.
** : A 15-micron polyamide drip chamber filter is acceptable for the administration of odronextamab 0.2 mg prepared without HSA.

3.5 Preparation of 0.5-320 mg of Odronextamab (REGN1979) in IV Bags

Figure 4: Procedure for Preparing 0.5-320 mg Odronextamab (REGN1979) for IV Administration



1.	Obtain the IRT assigned odronextamab (REGN1979) vial(s) from refrigerated storage and let it sit at room temperature for 10 - 60 minutes to warm up.
	Obtain one IV bag (**50 mL**) of 0.9% sodium chloride for **0.5 mg odronextamab (REGN1979)** dose or Obtain one IV bag (**50 mL or 100 mL**) of 0.9% sodium chloride for doses between **1 to 320 mg** odronextamab (REGN1979).
2.	Use a new appropriately-sized syringe and 21-gauge needle, withdraw a volume of odronextamab (REGN1979) as specified in Table 3. Make sure there are no air bubbles in the syringe.
	Inject the withdrawn odronextamab (REGN1979) solution slowly into the 0.9% sodium chloride infusion bag through the injection port and invert the IV bag 10 times to obtain a uniform mixture.
3.	Appropriately label the infusion bag containing odronextamab (REGN1979) for infusion following the standard institutional requirements. At a minimum, the label is to include protocol number, participant ID, odronextamab (REGN1979) in 0.9% sodium chloride, directions to infuse intravenously the entire contents of the infusion bag over the required time specified in Section 3.6 plus flush, use by date/time, and the investigator's name.
The prepared infusion bag should be kept for no more than **24 hours** between 2°C and 8°C or no more than **12 hours** if it is left at controlled room temperature (15 - 25ºC) from the start time of IP preparation to the start of the infusion. If refrigerated, the diluted solution must be warmed up to room temperature prior to administration.	

3.6 IV Administration of Odronextamab (REGN1979)

Dose (mg)	Infusion **D**uration*
0.2 – 320	1 hour to 4 hours
*Infuse over a minimum of 1 to 4 hours including flush. Infusion time will vary based on dose and tolerability, see protocol for additional details. Up to an additional 30 minutes may be needed to complete the infusion due to manufacturer overage in the IV bag. Please consult with your study medical team for infusions continuing beyond 4 hours.	
1.	Gather the recommended materials for infusion from **Section 2.5.1**.

2.	Attach the infusion set to the intravenous bag.
3.	Prime the infusion set with prepared intravenous bag or 0.9% Sodium Chloride Injection per site policy.
4.	• 0.2 mg dose (prepared with HSA) and 0.5-320 mg doses: administer the entire infusion solution in the bag via IV pump through an intravenous line containing a sterile, in-line/ add on 0.2 micron or 5 micron polyethersulfone (PES) filter. • 0.2 mg dose (prepared without HSA): administer the entire infusion solution in the bag via IV pump through an intravenous line **without** an IV filter. Note: : A 15-micron polyamide drip chamber filter is acceptable for the administration of odronextamab 0.2 mg prepared without HSA
5.	At the end of infusion, flush the tubing with 0.9% Sodium Chloride Injection (delivering remaining IP volume from IV line to participant) to ensure complete dose administration. Minimal flush volume should equal the tubing volume dead space (up to 50 mL) to avoid underdosing. Flush rate should equal IP infusion rate. **Note: The time required to flush the remaining IP in tubing dead space should be included in the total infusion time.**
6.	If an interruption to the infusion occurs due to an AE, please see protocol for instructions.

4. IP/DP SHIPMENTS

4.1. General Shipment Information

1.	Regeneron will be responsible for shipping kits listed in Section 2, Study Medication & Ancillary Supplies, to the sites, via a contracted distribution vendor. IP products will be released according to local regulatory requirements prior to shipment.
2.	Kits will be transported under the storage conditions specified on the clinical label. Refer to Section 5.5, Temperature Excursion Management when kits are stored outside the acceptable temperature range. An excursion should be reported to Regeneron.
3.	Depot/site shipments and inventory will be controlled and monitored via IRT. Please refer to the IRT user manual for more details.
4.	In circumstances where shipments are routed through a pass-through pharmacy or another central location, logistical details must be forwarded to Regeneron for agreement prior to execution.
5.	Shipment tracking inquiries and issue escalation should be directed to the Regeneron CDSL Manager with the Site Monitor copied on the email. List of issues to report may include but is not limited to the following: • Shipment delivery delays • Missing kits at sites after delivery is confirmed • Unable to receive shipments due to a site closure • Defective temperature monitoring device in the shipment • Mismatched batch numbers or kit discrepancy If necessary, Regeneron CDSL will arrange for a replacement shipment to be sent to the site.

4.1.1. Missing Shipments

If the kits are missing from a shipment or the shipment is lost while in transit from the depot to the site, follow the instructions below:	
1.	Clinical site, upon review of physical inventory and records, detects missing/lost kit(s) and denotes kit number(s) as “Missing” in IRT.
2.	Site contacts local Site Monitor to alert them of the kit(s) not found.
3.	Site Monitor raises issue with Regeneron CDSL Manager and provides copies of shipping documents as supporting documentation.
4.	Regeneron CDSL reviews site receipt documentation as well as depot shipment documentation.
5.	As required, Regeneron CDSL contacts depot to request investigation.
6.	Depot reviews physical inventory and records (including courier contact, if necessary) and raises investigation. Depending on situation, depot may notify local authorities and open a criminal investigation along with an internal event.
7.	If material is not found, Regeneron CDSL confirms material status as “Missing” in IRT.
8.	Regeneron CDSL assesses site/participant need and if required, generates a replacement drug order.
9.	IRT to raise a replacement order as needed and notify Regeneron CDSL within 1 business day.
10.	Regeneron CDSL, in collaboration with site/Site Monitor performs investigation to determine root cause and determine Corrective and Preventive Action.
11.	As necessary for the incident, escalation by Regeneron CDSL to Regulatory and/or Legal may be considered and should be done within 3 (three) business days of completion of the Regeneron CDSL/depot investigation.

4.2. Receipt of Drug Products

The pharmacist/qualified site personnel will perform the steps below:	
1.	Open the shipper boxes immediately upon receipt. A shipment consists of: • IP kits • packing list • operational instructions for temperature monitoring device, and temperature monitoring device to monitor shipment temperature during transit. • Eco Shipper Instructions (if material is shipped in a reusable shipper, instructions on how to return the shipper will be included).
2.	Verify the contents are in good condition (no damage, contents complete, etc.). If product defects (e.g. damaged product, empty packaging, leakage, discoloration) are identified. Refer to Section 5.6, Damaged/Defective Stock and Product Complaint Handling, to report a product complaint.

3.	Compare the packing list to the batch numbers, expiry dates, reference numbers (if applicable), quantity and dosage. For shipment issues or discrepancies, email the Regeneron CDSL Manager and include full study #, site # and country in the subject line. Email should include details of the issue and the urgency. Ensure a copy is sent to the Site Monitor. Wait for further instruction.
4.	Immediately store per storage conditions specified on the clinical label. Refer to Section 5.1, Storage Requirements and Definitions.
5.	Complete any questions asked regarding the shipment receipt on the packaging list and initial, date and time the packing list. Retain in the site file.
6.	Follow the temperature monitoring device instructions included in the shipment to identify an alarm, stop recording, and retrieve/download temperature readout report. If the IP shipment was outside the required temperature range per the clinical label, refer to Section 5.5, Temperature Excursion Management. Retain the temperature monitoring device until investigation is complete.
7.	Discard the temperature monitoring device after the temperature readout report has been downloaded and no issues are identified. If you are unable to download the temperature readout report from the temperature monitoring device, save the device and report the issue to Regeneron CDSL Manager, copying the Site Monitor. Wait for further instruction.
8.	Acknowledge receipt of the shipment promptly in IRT, answering any prompted questions. Failure to acknowledge a shipment will result in IP being unavailable for allocation to participants.
9.	File completed packing list, temperature readout from temperature monitoring device, and IRT confirmation of IP receipt in the ISF.
10.	The Site may use their own accountability logs, an IDS system (if approved for use by Regeneron) or CRO or site equivalent form in addition to the IRT. **IRT must always be used. Refer to Section 9, Accountability, Reconciliation, Returns and Destruction (ARRD).**

5. STORAGE REQUIREMENTS AND HANDLING OF IP

5.1. Storage Requirements and Definitions

The acceptable storage condition is specified on the clinical label. The designated area(s) for IP/DP storage must be maintained at the appropriate setting to preserve the integrity, stability, and effectiveness of IPs for the protocol.

5.1.1. General Requirements for Storage Area

Secure, locked storage area dedicated to IP storage only
Kept clean and in sanitary condition
Adequate size with enough space and shelving for IP/DP storage **NOTE:** Please ensure Regeneron CDSL Manager is made aware of maximum capacity for initial and resupplies to site, especially if space is limited.
Storage area capable of maintaining the temperature specified on the clinical label Refer to Section 5.2, Temperature Controlled Storage Area
Uninterrupted, continuous monitoring and recording of temperatures either manually, or via a data logger for each area where IP is stored Refer to Section 5.3, Temperature Monitoring Device Requirements

5.2. Temperature Controlled Storage Area

Controlled Room Temperature (CRT)	Appropriate system to maintain the temperature between 20ºC to 25ºC (68ºF to 77ºF), and allows for excursions between 15ºC and 30ºC (59ºF and 86ºF) that may be experienced during storage, shipping, and distribution
Refrigerator	Temperature maintained between 2ºC and 8ºC (36ºF and 46ºF)
Protect from Light during Storage	Maintain immediate container of IP in its original carton to minimize exposure to light during storage

5.3. Temperature Monitoring Device Requirements

1.	Monitor and record/document the temperatures. Refer to Section 5.4, Examples of Acceptable Temperature Monitoring Devices.
2.	Calibrate annually (or according to the manufacturer's recommendation). File calibration certificate in site files. At a minimum, calibration certificate must include: • Model/Device Name or Number • Serial Number • Date of Calibration (Report or Issue Date) • Instruments Passed Testing (Instrument is within tolerance) • Calibration normal range (in degrees Celsius) • Calibration data
3.	Maintain a copy and follow manufacturer's instructions such as maintenance, setting and resetting, and calibration.

4.	Must have an audible or visible alarm on the display to alert site personnel of a temperature excursion so action can be taken, preventing loss of IP. Refer to Section 5.5, Temperature Excursion Management.
5.	Monitor temperatures daily during normal business hours for any alarms signalling a temperature excursion.
6.	Site must have a secondary calibrated device available in case the primary device is removed from the storage area for calibration. The temperature readings are downloaded plus or minus 24 hours from the secondary device as evidence that the storage area was maintained at the appropriate storage conditions when the primary device is not in use.
7.	It is recommended that a secondary calibrated device and back-up power source for storage unit (i.e., refrigerator or freezer) is used in case the primary temperature monitoring device fails.

5.4. Examples of Acceptable Temperature Monitoring Devices

Min-Max Thermometers	• Accuracy to ±0.5°C • Manually record temperatures daily using *VV-FRM-00065, Temperature Log*, or a CRO or site equivalent form, during normal business hours. (Site Monitor to evaluate if non-Regeneron form is acceptable for use)
Chart Recorder	• Records temperatures continuously without interruptions. • Replace chart paper at the appropriate interval, depending upon the model. • Review and file previous paper record in the site file when replacing.
Electronic Temperature Data Logger	• Records temperatures at programmed time intervals, ideally at a minimum of every 30 minutes. • Download and save raw data as a computer file or print as a hard copy for the ISF.

5.5. Temperature Excursion Management

The acceptable storage condition is specified on the clinical label. Any temperature deviations/excursions must be reported within 1 business day. Temperature deviations/excursions occurring on a weekend, holiday or 'off hours' should be reported to Regeneron as soon as the site re-opens the next business day.	
1.	Site pharmacist (or appropriate personnel- if study does not have/need a site pharmacist to handle the IP) rounds the temperature to the nearest whole number. For example, if the acceptable temperature range for storage is 2 to 8ºC, then: • Round 1.5, 1.6, 1.7, 1.8, and 1.9 up to 2ºC • Round 8.1, 8.2, 8.3, and 8.4 down to 8ºC If rounded temperature is within the acceptable temperature range a temperature excursion does not need to be reported.

2.	Brief temperature excursions will sometimes be recorded for various reasons (e.g., opening refrigerator door). For odronextamab (REGN1979) these deviations from the labeled storage conditions will be deemed acceptable under the following conditions: • Labeled storage conditions of IP is 2-8°C • Excursion reported is between 8-15°C • Duration of excursion is less than 30 minutes (per occurrence) • There are fewer than 5 brief excursions in any given 24-hour period Recorded excursions meeting **all** the above criteria for Regeneron products are deemed as not being true temperature excursions and do not need to be reported to Regeneron for evaluation.
3.	Site pharmacist fills out *VV-FRM-00435, Potential Temperature Excursion Documentation and Evaluation form,* if IP is stored outside the acceptable range.
4.	Site pharmacist emails required documents as listed below to the site monitor, who will review for completeness. In urgent cases, send directly to CDSL at **Clinical.logistics@regeneron.com** and copy in the site monitor. Follow instructions in step 5.

Type of Temperature Excursion	Required Docs for Regeneron CDSL Assessment
Shipment	• **VV-FRM-00435** filled out by site • Packing List • Temperature Monitoring Report • Any Supporting Docs
Site Storage	• **VV-FRM-00435** filled out by site • Site Temperature Monitoring Logs • List of Impacted Kits (if not able to record all on form) • Any Supporting Docs

5.	Site monitor emails documents to **Clinical.logistics@regeneron.com** for IP disposition. As your email is reviewed by study specific team members through a generic mailbox, please include **Protocol #, site # and country in subject line** in addition to **temperature excursion** to ensure correct person is reviewing your correspondence and responding in a timely manner. Mark “urgent” if it will affect the sites’ ability to dose a participant within the next 48 hours.
6.	Site pharmacist physically quarantines the affected kits in a separate storage area while maintaining the temperature specified in the clinical label per Section 5.7, Quarantined Medication
7.	Site pharmacist changes the status of the kits in IRT to quarantine. Failure to do so will allow IRT to allocate the potentially impacted kits to a participant.
8.	Site pharmacist waits for a response from the Site monitor and/or Regeneron CDSL with instructions on how to proceed. Depending on the IP assessment, Regeneron CDSL will release or reject the kits in IRT accordingly.

5.6. Damaged/Defective Stock and Product Complaint Handling

1.	Review **Table 4, Kit Conditions,** below for examples of what to report as damaged/defective sponsor provided drug products. The list is not all inclusive and you should report anything unusual pertaining to the primary unit or a prepared dosage form.

2.	If IP/device is found to be damaged or the integrity of the contents of the immediate container (e.g., vial) has been compromised, deviating from the drug description in Section 4, Investigational Product Shipments, IP should NOT be used for participant dosing.
3.	The pharmacist will contact the Site Monitor. Refer to Section 1.4, Delegation and Changes in Study Staff.
4.	The pharmacist will immediately quarantine the impacted IP at temperature specified on the clinical label in a separate storage area per Section 5.7, Quarantined Medication, until it can be determined if it will need to be returned to Regeneron for evaluation. **Do NOT discard the immediate container and/or carton.**
5.	The pharmacist will change status of the impacted kit to 'quarantine' in IRT (if it has not yet been allocated to a participant). A replacement kit can be requested in IRT (if the kit has been assigned to a participant).
6.	The pharmacist, along with the reporter, will fill out *VV-FRM-00171, Investigational Product Complaint Form* and email details of the event to the site monitor. Report product complaints as soon as possible and not later than 24 hours of becoming aware of the issue. Please include **Protocol #, site # and country** in subject line in addition to **Product Complaint- urgent.**
7.	The Site Monitor will notify Regeneron QA by forwarding the email to a dedicated mailbox: **Product.Complaints@regeneron.com** and copying Regeneron CDSL Manager within 24 hours of being made aware of the issue. If not unblinding the CSL may be included.
8.	The pharmacist waits for further instructions from site monitor, Regeneron QA, and/or Regeneron CDSL.

Table 4: Kit Conditions

Summary of Kit Conditions	
Condition	**Vial (s) in carton**
Unused Defective Kit	Text is illegible or missing from the clinical label on the carton and/or immediate container
	Carton/ Vial is missing components
	Vial is exhibiting cracks, glass breakage, leakage
	Dosing solution shows evidence of turbidity, particulates, cloudiness, discoloration, or visual foreign matters on any components
	Cap of the vial cannot be removed from the unused vial to perform participant dosing or cap is missing
Prepared	Dosing solution shows evidence of turbidity, particulates, cloudiness, discoloration, or visual foreign matters on any components, including those obtained from non-Regeneron sources
	An odor is permeating from the dosing solution

5.7. Quarantined Medications

IP with the following statuses should be physically quarantined per the handling instructions below.
NOTE: If the quarantined IP is kept in a separate storage unit different from the original storage unit, a temperature log must be filled out while in storage at this alternate location.

	IP Kit Status	Handing Instructions
1.	QUARANTINED due to a temperature excursion if IP disposition is pending or as instructed by Regeneron CDSL	• Segregate IP in a bag or box labelled “Quarantined. Do Not Administer to Participant.” • Store the IP at the temperature specified on the clinical label.
2.	DAMAGED	• Place in a separate bag or box labelled as “Damaged. Do Not Administer to Participant.” • Store IP at room temperature and document the removal in the appropriate logs.
3.	EXPIRED	• Place it in a separate bag or box labelled with “Expired. Do Not Administer to Participant.” • Store IP at the temperature specified on the clinical label until confirmation is received from Regeneron to move IP to room temperature. • After the transfer, document the removal from the original location in the appropriate logs.

6. MOVEMENT OF IP STORAGE AND TRANSFERS

6.1. IP Storage Location

GENERAL REQUIREMENTS
Store unused IP, and/ or prepared dose according to Section 3.2, Stability and Shelf-life During IP Preparation. Marketed drug products follow the SMPC.
Transfers must be monitored with a temperature monitoring device if: o The IP is allocated to participants, and the prepared dose is exposed to the outside environment during transport. o All transfers of unused IP (not allocated to participant) Refer to Section 5.1, Storage Requirements and Definitions.
Notify the Site Monitor if the site address will change to a new location. IP can only be transferred after written approval from the Regeneron CSL and CDSL Manager is received.

6.2. Inter-Site Transfers (between sites)

Should transfer of unused IP from one site to another participating site be required or requested, IP transfer will be coordinated by Regeneron CDSL ONLY. Instructions and forms will be forwarded to the site monitor and site should a transfer occur.

6.3. Intra-Site Transfer of IP (Participant Allocated IP)

Transfer of **participant allocated, ready for use kits, or prepared dose** from one storage location to another at a given site or change in site address (same PI) during the study.	
1.	Record IP hand-off to site staff on *VV-FRM-00067, Dispensing and Administration Log*, CRO or Site equivalent form.
2.	Transfer must comply with the allowable duration and storage conditions in Section 3.2, Stability and Shelf-life During IP Preparation. Transfer study medication as per the following requirements:
	If at controlled room temperature (e.g., enclosed building or structure **NOT** exposed to outside environment), Temperature monitoring is not required.
	If at uncontrolled temperatures (e.g., any areas exposed to outside environment), • Fill out *VV-FRM-00173, Investigational Product Intra-Site Transfer Form (Participant Allocated)* to record details of the move. Transport IP in a validated transfer container (to ensure maintenance at appropriate temperatures) • Transports ≤ 60 minutes do not require temperature monitoring IF they are transported in a validated temperature stabilizing container that is covered in a Regeneron reviewed Site Policy, otherwise temperature monitoring is required. • Transports > 60 minutes require temperature monitoring.
3.	Do NOT use the kit if the following occurs during the transfer: • Damage to investigational product • Temperature excursion Request replacement kit(s) in the IRT, refer to IRT user guides
4.	*VV-FRM-00173, Investigational Product Intra-Site Transfer Form (Participant Allocated)* must be filed in the ISF.

6.4. Intra-Site Transfer of IP (Unused IP, not allocated to participant)

Transfer of **unused IP (unprepared not allocated to participant, i.e., bulk supplies)** from one storage location to another at a given site or change site address during the study.	
1	**New storage location**: Confirm temperature specified on the clinical label is stabilized for a minimum period of 24 hours prior to move.
2.	Remove IP from the original storage area.
3.	Record IP removal in the current logs: ○ *VV-FRM-00065, Temperature Log*, CRO or Site equivalent (if using paper log) ○ *VV-FRM-00174, Investigational Product Intra-Site Transfer Form (Non-Allocated)*
4.	Transfer IP in a validated transfer container (maintained at the temperature specified on the clinical label) monitored with a calibrated temperature monitoring device.
5.	Store IP in the new storage location.

6.	Create or update *VV-FRM-00065, Temperature Log* (if one at this location already exist) for the new storage location.
7.	Quarantine IP if the following occurs and notify Regeneron CDSL. • Damaged investigational product • Temperature excursion (Follow Section 5.5, Temperature Excursion Management)
8.	*VV-FRM-00174, Investigational Product Intra-Site Transfer Form (Non-Allocated)* must be filed in the ISF.

7. MONITORING

1.	Monitoring of the site pharmacy will be conducted according to the Clinical Monitoring Plan.
	• An assigned Site Monitor will monitor site drug accountability on a regular basis and perform reconciliation
	• Regeneron personnel (e.g., Quality Assurance Auditor, CDSL, etc.) may also visit the pharmacy and require access to pharmacy records.
2.	Monitoring will include (at a minimum): • Ensuring the most current version of this pharmacy manual is available and in use, and that pertinent site staff is trained on the current version of this pharmacy manual • Reviewing and verifying accountability logs, pharmacy worksheets and dispensing records • Ensuring shipments have been received and documentation is complete • Checking study supplies and ensuring that the storage conditions have been adequately maintained • Verifying that the blind has been maintained, if applicable • Perform IP reconciliation • Review destruction records and/or prepare IP returns. • Follow-up of any issues identified

8. EXPIRY OF INVESTIGATIONAL PRODUCT AND RE-LABELING

Regeneron CSL will notify sites in advance via “Site Notification of Investigational Product Expiration” if the retest date will be extended per new stability data. Otherwise follow the label or IRT expiry date.	
Follow the instructions outlined below. Consult with Site Monitor if there are any questions.	
1.	**Expired IP**: Quarantine kits in accordance with Section 5.7, Quarantined Medication, until the site monitor has completed reconciliation.
2.	**IP Date Extension:** ○ If retest date is printed on the clinical label, IP should be treated in the same manner as expired IP. An IP lot with suitable dating will be shipped to the site to replace the current inventory or instructions will be provided on how to relabel. ○ If dating is NOT printed on the clinical label, kits should be maintained at the storage condition specified on the clinical label; extension will occur via IRT update.
3.	**Replacement kits**: IP will be resupplied to sites per the process in Section 4, Investigational Product Shipments when an extension will not occur.

9. ACCOUNTABILITY, RECONCILIATION, RETURNS AND DESTRUCTION (ARRD)

When the site is responsible for sourcing the marketed medications identified in the protocol. accountability, reconciliation, and destruction should be performed according to site policy.

9.1. Accountability

This study will utilize the IRT to capture IP accountability site must use the IRT for shipment receipt, randomization/enrolment, and dispensing of medication kits. In addition, the IRT will be utilized for accountability, reconciliation, and returns/destruction. **IRT MUST BE USED FOR ALL TRANSACTIONS**	
The Site may use the listed Regeneron forms, their own accountability logs, an IDS system (if approved for use by Regeneron), CRO or site equivalent forms in addition to the IRT. • *VV-FRM-00067, Dispensing and Administration Log* • *VV-FRM-00068, Investigational Product Accountability and Dispensing Log* • *VV-FRM-00069, Individual Participant Investigational Product Accountability Log*	
The site must use: • *VV-TMP-00181, Odronextamab (REGN1979) Infusion Preparation Worksheet* or Sponsor approved equivalent documentation, to capture steps of the infusion preparation of the IRT assigned medication kit (IP Ref. #).	
1.	Follow Section 4.2 Receipt of Investigational Product Upon receipt of a shipment, mark the shipment as received in the IRT using the date of arrival at the site. If there are any damaged, missing kit or temperature excursion during transit, note this when prompted. • Report a temperature excursion following instructions in Section 5.5 Temperature Excursion Management. • If a kit is damaged, follow instructions in Section 5.6, Damaged/Defective Stock and Product Complaint Handling, to report a product complaint. • In addition, if any kits are missing contact the Site Monitor and the CDSL manager.
2.	The site may choose to use paper IP Product and Individual Participant Accountability forms (or equivalent method, i.e., IDS system) **in addition to the IRT** for any of the investigational products tracked in the IRT Site must use the following forms for any study medication and/or ancillary drugs or supplements, **NOT captured in the IRT** and provided by the Sponsor, if applicable. • *VV-FRM-00068, Investigational Product Accountability and Dispensing Log,* or CRO/Site equivalent • *VV-FRM-00069, Individual Participant Investigational Product Accountability Log* or CRO/Site equivalent

3.	Preparation of the participant dose must be captured on the *VV-TMP-00181, Odronextamab (REGN1979) Infusion Preparation Worksheet* or Sponsor reviewed site equivalent. Form must minimally include medication kit # (Reference #), specific dose prepared for the participant, time and date of preparation, who prepared the dose and a second person verification, and prepared IP use by date/ expiry date and time. This form may be used for accountability purposes when site policy dictates destruction of IP after preparation. When performing reconciliation, cross-check the medication kit Ref. # in the IRT to the form to ensure correct participant IP dispensing.
4.	Any discrepancy with the IRT must be corrected promptly using the IRT specific data correction form (DCF) and provided to IRT support /helpdesk for update. Refer to IRT training guides for more information (User guides are embedded in the IRT). Retain a copy of the submitted DCF and email confirmations in the site file.

9.2. Reconciliation

Reconciliation of study medication will be performed by the Site Monitor in the IRT and Accountability logs. Retain the following until the Site Monitor has reviewed IP usage and performed reconciliation in the IRT:

- Unused or damaged study medication in the original carton.
- Used medication (preferably in original carton)
- Carton of the used IP, if primary unit must be disposed of immediately after use according to site policy.

If site policy prohibits retention of the IP and carton, then reconciliation is reviewed against the IRT assigned kit # in the *VV-TMP-00181, Odronextamab (REGN1979) Infusion Preparation Worksheet* or approved equivalent.

1.	In addition to any required Accountability logs and /or preparation forms, record dispensing of IP in the IRT. When prompted, indicate if the IP was disposed of following preparation or if retained for reconciliation. Follow instructions provided by the IRT.
2.	Site monitor performs reconciliation step in the IRT at monitoring visits for each assigned kit, replacement kit, damaged kit and/or missing kit. Include any comments when warranted. All missing IP must be investigated, and all damaged IP reconciled. For non-IRT tracked ancillary medication (rescue medication and commercial product) provided by the Sponsor ensure all Accountability logs are reviewed and all IP is reconciled.
3.	If not already done, any discrepancy with the IRT must be corrected promptly using the IRT specific data correction form (DCF) and provided to IRT support /helpdesk for update. Refer to IRT training guides for more information. Retain copies of the DCF request and email confirmation of updates.
4.	Site monitor performs reconciliation step in the IRT at monitoring visits and when IP has expired. If IP is missing, mark as such in the IRT and record reason after investigation.

5.	Site monitor performs reconciliation step in the IRT at close out visits of any remaining used or unused IP on site. If an IP is missing, mark as such in the IRT and add reason after investigation. For non-IRT Study medication provided by the sponsor ensure all accountability logs are reviewed and all IP is reconciled.

9.3. Returns to Depot

Used IP should be disposed of on-site after reconciliation by the site monitor. On-site destruction of **unused** IP requires review by site monitor and CSL approval (see Section 9.4). IP may be returned to the depot for destruction for reasons which may include, but are not limited to, the following: • IP expiration • Temperature excursion/improper storage at site • IP recall • Study close-out or termination when the site is not permitted or approved for on-site destruction. • Site is unable or not willing to destroy IP	
1.	Obtain permission from the CDSL Manager to return IP to the depot for destruction. When possible, utilize on-site destruction.
2.	Site Monitor (or site pharmacist if delegated) will schedule the return pick-up date and request shipment components (i.e., shipper, tamper tape, etc) from the depot as per Distribution Vendor's IP Return Instructions that will be provided by CDSL, see Section 10. Allow a minimum lead time of 2 weeks prior to the anticipated need by date. When returning IP to the depot please keep, please package in original carton.
3.	**After reconciliation is complete and it is determined that study medication should be returned to the depot,** the site monitor or site pharmacist **may** initiate the return of medication using the Returns modules in the IRT
4.	After completing the return form, the Site should retain a copy until the final signed documents are received. Site Monitor (or site pharmacist if delegated) will pack the IP for return shipment to the depot and include the signed return form ensuring returned IP is accounted. Tamper seal the box and initiate return shipment.
5.	Site Monitor receives completed return forms from the depot, provides a copy to the site to file in the ISF, and uploads a copy to the Sponsor TMF.

9.4. Destruction On-Site

1.	Used IP may be destroyed as per site's policy/ procedure after Site Monitor has completed reconciliation (Section 9.2). Indicate in the IRT modules if destruction occurred at time preparation/administration (reconciliation can be performed by the Site Monitor using the medication kit Ref # from the vial, the carton and/or the preparation worksheet, or IDS system versus the IRT). Unused or damaged IP: *VV-FRM-00184 Checklist for Approval for On-Site Destruction of Unused Investigational Product* must be completed by the Site Monitor and signed by CSL. The completed form is uploaded to the Regeneron TMF prior to performing destruction on site.
2.	For unused material destroyed on site, provide either a site generated (IDS system) or third party generated Certificate of Destruction (CoD), *VV-FRM-00044, Documentation for On-Site Destruction* or CRO/site equivalent documentation of destruction to the Site Monitor for filing in TMF.
3.	Follow the IRT user guide to complete the destruction modules in the IRT. The IRT study accountability report will be printed and retained by Regeneron at the end of the study and added to the TMF.

10. FORMS & SUPPLEMENTAL INSTRUCTIONS

Refer to applicable sections above for instructions to complete forms, where applicable. Request the most up to date forms from the Site monitor. Templates (TMP) are customized forms (version controlled for the study) and linked to the Pharmacy Manual in TMF. All Forms (FRM) are available in Regeneron GD EDMS (Quality Docs (accessed via QMOD [Veeva Vault Quality]) and cannot be altered.

Title	**Form Number**
Safety Data Sheet (SDS) for Investigational products — Title: Odronextamab Solution SDS	
Regeneron Forms that are mandatory to be used when needed:	
Potential Temperature Excursion Documentation and Evaluation	VV-FRM-00435
Ancillary Supplies Material Compatibility Review Request Form	VV-FRM-00172
Investigational Product Complaint Form	VV-FRM-00171
Checklist for Approval for On-Site Destruction of Unused Investigational Product	VV-FRM-00184
Checklist for Use of Investigational Product Management System/ Investigational Drug System (IDS)	VV-FRM-00183
Regeneron Forms that may be substituted with either CRO or site forms/equivalent (with approval-discussed with site monitor and documented in ISF):	
Documentation for On-Site Destruction	VV-FRM-00044
Temperature Log	VV-FRM-00065
Dispensing and Administration Log	VV-FRM-00067
Investigational Product Accountability & Dispensing Form	VV-FRM-00068
Individual Participant Investigational Product Accountability Log	VV-FRM-00069
Investigational Product Intra-Site Transfer Form (Participant Allocated)	VV-FRM-00173
Investigational Product Intra-Site Transfer Form (Non-Allocated)	VV-FRM-00174
Customized Forms for Study	
Notification to Sponsor on use of alternative preparation for the REGN1979 0.2mg Dose without Human Serum Albumin (HSA) (customized & version controlled- available in TMF linked to pharmacy manual)	
Odronextamab (REGN1979) Infusion Preparation Worksheet, template VV-TMP-00181 (customized & version controlled- available in TMF linked to pharmacy manual)	
IP Returns Instructions/ Form (Vendor specific) Request from CDSL Manager (not in TMF)	

11. ACRONYMS

CDSL	Clinical Drug Supply and Logistics
CMC	Chemistry Manufacturing Control
CRC	Clinical Review Committee
CRO	Contract Research Organization
CRT	Controlled Room Temperature
CSL	Clinical Study Lead
DEHP	Di-(2-ethylhexyl)-phthalate
DP	Drug Products (refers to Sponsor Centrally Supplied Marketed)
EDMS	Electronic Document Management System
EVA	ethylene vinyl acetate
FDG	Formulation Development Group
GD	Global Development
IDMS	Investigational Drug Management System
IDS	Investigational Drug Service
IP/ IMP	Investigational Product/ Investigational Medicinal Product
IRT	Interactive Response Technology, also known as IVRS (Interactive Voice Response System) or IWRS (Interactive Web Response System)
ISF	Investigator Site File
IV	Intravenous
JIT	Just in Time
PE	Polyethylene
PES	Polyether sulfone
PI	Principal Investigator
PM	Project Manager
PO	Polyolefin
PSL	Pharmacy Support Lead
PSS	Pharmacy Support Services
PVC	Polyvinyl chloride
QML	Quality Management Lead
SDS	Safety Data Sheet
SIV	Site Initiation Visit
SMD	Study Medical Director
SMPC	Summary of Product Characteristics (equivalent to commercial product package insert)
TMF	Trial Master File (at Regeneron Veeva TRACK)

12. DEFINITIONS

Investigator or Principal Investigator (PI)	A qualified, licensed physician responsible for the conduct of a clinical study at an investigational site (i.e., under whose immediate direction the drug is administered or dispensed to a participant). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of the team. The responsible leader is often referred to as the Principal Investigator (PI).
Research Pharmacist	The licensed/registered pharmacist must be qualified to conduct the tasks delegated to them, based on appropriate experience, training, education, and licensure/registration (as applicable according to local, national laws and regulations and/or other requirements). Referred to as “Pharmacist” throughout the document. The pharmacist may also delegate tasks within the pharmacy to appropriately trained personnel according to site SOPs/ policies. In some studies, this task may be delegated to the Study Coordinator or Research Nurse, if appropriate for tasks involved (please discuss with your site monitor).
Research Pharmacy	The location for the local storage and preparation of Study products for REGENERON studies will be referred to as the research pharmacy. IP must be stored in safe, secure, and appropriate locations and at correct storage conditions based on the requirements of the manufacturer and the study protocol, blinding needs, and labeling. Referred herewith as “Pharmacy”.
Temperature Excursion	An event in which temperature-sensitive investigational product or commercial drug is exposed to temperatures outside the range prescribed for storage and/or transport as defined by the product specification and/or stability data. If a temperature excursion occurs, impacted drug should be quarantined preventing its usage and should be reported to Regeneron CDSL for its suitability to be assessed.

13. SUPPORT CONTACTS

Support	General Email *	Related Form
Clinical Drug Supply and Logistics (CDSL) Temperature Excursions or Shipment related questions	Clinical.logistics@regeneron.com Always include Protocol, Site # / PI name in subject line.	VV-FRM-00435 VV-FRM-00173 VV-FRM-00174
Product Complaints	Product.Complaints@regeneron.com Include in email Regeneron CDSL Manager/ Site Monitor	VV-FRM-00171
Pharmacy Support Services (PSS) *Ancillary supply materials compatibility review requests, and general procedural questions regarding the pharmacy manual content*	pharmacy.support@regeneron.com Include in email Regeneron CDSL Manager/ Site Monitor	VV-FRM-00172
Ancillary Supply Management Request non-IP supplies provided by Regeneron	Contact Site Monitor	N/A
IRT: IRT data correction, IRT related questions	Refer to IRT User Guide	N/A
Distribution: Shipment issues	Contact Regeneron CDSL Manager	N/A
Return of used and/or unused IP	Contact Site Monitor and Regeneron CDSL Manager	N/A

*As your email is reviewed by study specific team members through generic mailboxes, please include **Protocol #, site # and country in header** to ensure correct person is reviewing your correspondence and responding in a timely manner. Include the Site Monitor in all correspondence.

14. CHANGE CONTROL

Version #	Date (DDMMMYYYY)	Revision Summary	Impact
1.0	14Sep2023	New	N/A
2.0	06Dec2023	-Section 2.4 added EVA bags to approved ancillary supplies -Section 3.3 and 10 updated to add option to prepare REGN1979 0.2 mg dose without HSA/filter -Section 3.2 and 3.3 stability of prepared IV admixture updated to 6 hours from the start time of IP preparation to start of infusion -Removal of HSA logistics, ARRD procedures as it will not be provided sponsor.	To allow use of EVA bags for IP preparation Site will need to seek approval if unable to procure HSA using Authorization Request See Appendix 15 for details. Site can use beyond use date (BUD) of 6 hours and up to 4 hours infusion time. Site sourcing of HSA (if needed) will be managed by locally established procedures.
3.0	***02 Apr 2024***	R1979-ONC-2336 (OLYMPIA-6) added to title page	Adding protocol to pooled supply program

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Version Number 4.0
OLYMPIA Pooled Supply

Version #	Date (DDMMMYYYY)	Revision Summary	Impact
4.0	***See appended electronic signature page***	Updated to VV-TMP-00030 Version 8.0 which is the current template of the Pharmacy Manual and refence to new forms was added Updated study contacts Reference to “patient” updated to “participant” throughout Authorization Request renamed Notification to Sponsor Deviation requests now referred to as Change Requests. Table 1 updated to allow infusion set used for the administration of 0.2 mg dose without HSA to contain a 15 micron polyamide drip chamber filter. Section 2.4: OLYMPIA 1-6 studies were included with corresponding commercial comparators and rescue medications; accountability process updated Table 2: Stability and Shelf-life during Investigational Product Preparation Room temperature storage updated to up to 6 hours for the 0.2 mg dose with HSA and up to 12 hours for 0.2 mg dose without HSA, 0.5 mg or greater Table 3: added option to prepare 10 mg dose using 160 mg vial presentation; REGN1979 concentration ranges added Section 12- Removed reference to specific vendors- Site to refer to IRT User Manual	Sections have been moved around and new forms added Time to start infusion (BUD) updated

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15. SITE ACKNOWLEDGEMENT & RECEIPT OF PHARMACY MANUAL

The pharmacist(s) (see Definitions) must provide read & acknowledgement of receipt (especially updates) of the current version of the pharmacy manual by completing the table in this section. This does NOT need to be returned to the Sponsor, however this MUST be completed and available to the Site Monitor in the ISF. Staff training would be captured in site training documentation and TMF.

Version #	Date (DDMMMYYYY)	Pharmacist Name, Title	Initials	Monitor date/ initials

	Storage Location of Current Version:	Pharmacy Staff date/initials	Monitor date/initials
☐ Paper copy:			
☐ Electronic copy			
Has previous version been replaced/archived? ☐ Yes ☐ No ☐ Not applicable- Version 1 Location**:**			
Comments:			

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Reason for signing: Approved	Name: Yuan Cheng Role: Other Date of signature: 12-Aug-2025 17:58:16 GMT+0000
Reason for signing: Approved	Name: Stefani Gjoni Role: Clinical Trial Management Date of signature: 12-Aug-2025 18:01:04 GMT+0000
Reason for signing: Approved	Name: Chris Campbell Role: Clinical Drug Supply and Logistics Date of signature: 12-Aug-2025 18:18:08 GMT+0000
Reason for signing: Approved	Name: Ameet Narwal Role: Clinical Trial Management Date of signature: 12-Aug-2025 19:51:27 GMT+0000
Reason for signing: Approved	Name: Nazia Iqbal Role: Clinical Science Date of signature: 12-Aug-2025 20:59:01 GMT+0000
Reason for signing: Approved	Name: Himal Thakar Role: Clinical Science Date of signature: 13-Aug-2025 01:11:49 GMT+0000
Reason for signing: Approved	Name: Kathleen Snyder Role: Clinical Trial Management Date of signature: 13-Aug-2025 04:18:15 GMT+0000
Reason for signing: Approved	Name: Soujanya Chandrasekharan Role: Clinical Trial Management Date of signature: 13-Aug-2025 18:32:58 GMT+0000

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Reason for signing: Approved	Name: Erika Floyd Role: Clinical Trial Management Date of signature: 14-Aug-2025 18:48:03 GMT+0000

Reason for signing: Approved	Name: Ashish Risal Role: Medical Monitoring Date of signature: 15-Aug-2025 15:01:57 GMT+0000

Reason for signing: Approved	Name: Galina Bargman Role: Clinical Drug Supply and Logistics Date of signature: 15-Aug-2025 17:42:34 GMT+0000

Reason for signing: Approved	Name: Manjusha Namuduri Role: Medical Monitoring Date of signature: 25-Aug-2025 16:00:32 GMT+0000

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