Odronextamab (REGN1979) Phase 3

OLYMPIA Pooled Supply Program

REGN1979

Pharmacy Manual Pooled Supply

Version 1.0

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

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CHANGE CONTROL

Version #	Date (DDMMMYYYY)	Revision Summary	Impact
1.0	***See appended electronic signature page***	New	N/A

SITE ACKNOWLEDGMENT AND RECEIPT OF PHARMACY MANUAL

The pharmacist and/or qualified designee(s) (see Definitions) must provide acknowledgement of receipt as well and read and understood of the pharmacy manual by completing this section. This does not need to be returned to the Sponsor, however this MUST be completed and available to the CRA. Where indicated, Regeneron forms are to be utilized including all referenced forms.

Version #	Date (DDMMMYYYY)	Pharmacist/Qualified Designee Name, Title	Initials	Monitor date/ initials
1.0				
Date of staff training on current version:				

	Storage Location of Current Version:	Pharmacy Staff date/initials	Monitor date/initials
☐ Paper copy:			
☐ Electronic copy			
Has previous version been replaced/archived? ☐ Yes ☐ No ☐ N/A Location**:**			
Comments:			

APPROVALS

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.

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ACRONYMS

AxMP	Ancillary Medicinal Product
CDSL	Clinical Drug Supply and Logistics (equivalent of CLO)
CLO	Clinical Logistics Operations (equivalent to CDSL)
CMC	Chemistry Manufacturing Control
CPD	Combination Product Development
CPRA	Combination Product Regulatory Affairs
CRA	Clinical Research Associate/Site Monitor
CRC	Clinical Review Committee
CRO	Contract Research Organization
CRT	Controlled Room Temperature
CSL	Clinical Study Lead
DEHP	Di-(2-ethylhexyl)-phthalate
eTMF	Electronic Trial Master File (at Regeneron Veeva TRACK)
EVA	Ehylene Vinyl Acetate
HSA	Human Serum Albumin
IMP	Investigational Medicinal Product
IP	Investigational Product
IRT	Interactive Response Technology, aka IVRS (Interactive Voice Response System) or IWRS (Interactive Web Response System)
PE	Polyethylene
PES	Polyether sulfone
PI	Principal Investigator
PM	Project Manager
PO	Polyolefin
PVC	Polyvinyl chloride
QML	Quality Management Lead
SDS	Safety Data Sheet
SIV	Site Initiation Visit
SMPC	Summary of Product Characteristics (equivalent to commercial product package insert)
sTMF	Site Trial Master File

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 subject). 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 and/ or qualified designee	The licensed/registered pharmacist or designee 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 hereafter as "Pharmacist".
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 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.

1. PURPOSE AND COMMUNICATION

The purpose of this Pooled Supply Pharmacy Manual is to describe the procedures applicable to the **open label** investigational product (IP) management for multiple REGN1979 studies, outline packaging and labeling of odronextamab (REGN1979) for the OLYMPIA Pooled Supply program and to clearly define the responsibilities of the study team members.

This pharmacy manual also defines the study specific forms which will be used to document, report, and verify compliance with pharmacy procedures. Refer to the current version of the following documents for guidance and additional study specific information:

- Study Specific Protocol
- Study Specific Abridged Pharmacy Manual

1.1. Deviation Requests

1.1.1. Procedural Deviations

1.	Should any processes and/or procedures provided within this pharmacy manual conflict with written site procedures or local regulations, the PI or pharmacist should discuss the requirement with the CRA and sponsor during site feasibility and qualification.

	Alternatively, should a procedural deviation review be required prior to study start or during the trial, it should be discussed, reviewed and agreed upon in writing with the sponsor as soon as it is known.
2.	Any procedural exception to the pharmacy manual must be recorded on the appropriate forms and filed at the site and in Regeneron's Veeva TMF on a site level.

1.2. IRT Details and Supply Triggers

This is intended as an IRT summary, the IRT User guide supersedes this section and should be referenced for complete details.	
IP will be shipped in accordance with local regulations to the site pharmacist after all required documents and approvals are in place.	
Study Design uses IRT vendor	**Calyx**
Medication will be provided as	☒ Open label
Patients are screened via IRT	☒ YES
Patients are enrolled via IRT	☒ YES
Initial IP shipment trigger to site via IRT occurs	☒ At first subject screening
1.	IP inventory is managed by IRT, resupply shipments are automatically sent to sites when supply levels are low.
2.	If the site plans to enroll more patients in a short time and will need more IP kits, the pharmacist should contact their assigned CRA immediately.
3.	The CRA will inform the ICON 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 from low to medium or high recruiter by CDSL Manager.

1.3. Ancillary Material Review

1.	For questions and compatibility review requests regarding ancillary materials used within the pharmacy manual refer to Section 2.4, Ancillary Materials, please complete **Form-CLO5666, Ancillary Supplies Material Compatibility Approval Form** and email the word version to **pharmacy.support@regeneron.com** for review and approval. The site will receive a return reply which shall be kept within the pharmacy binder as evidence of the request and/or approval/denial.
2.	General questions regarding the pharmacy manual should be directed to **pharmacy.support@regeneron.com.** Please include the protocol #, site # and country in the subject line of all correspondence. Copy the CRA on the message.

1.4. Blinding Requirements

This study is **OPEN LABEL**. All site staff are knowledgeable of the contents of the investigational product (IP). IP is provided to the pharmacy as open-label medication.

1.5. Safety and Handling

1.	For comprehensive information related to drug product safety and handling, please refer to the Safety Data Sheets (SDS) and Investigator Brochure: • Odronextamab REGN1979 (C2P2)_Drug_Product_100 mg/mL _Version 2.0.1_13August2020 • REGN1979 Investigator Brochure
2.	This product(s) is ☒ Biologic- Category 1.
3.	For more details on the commercial drug approved conditions and dosing details to be used in each protocol, please refer to Summary of Product Characteristics (SMPC).

1.6. Pharmacy Staff Responsibilities

All site staff (Open label)
The site will identify at least two pharmacists or designees who will be responsible for preparing the IP prior to administration.
The identification, roles and responsibilities site team members should be clearly recorded and maintained on the **Site Signature & Delegation Log** [see site binder] during the study Site Initiation Visit (SIV).
Pharmacy Staff responsibilities:
Maintain the pharmacy file in a secure area with the documents for all IP shipments
Receipt of IP shipments and accountability
Ensure that all IP is stored according to clinical label for the duration of the study, all storage temperature requirements are met per Section 4.3, Temperature Controlled Storage Area, and reporting all temperature excursions per Section 4.7, Temperature Excursion Management
Preparation and dispensation the IP to study staff for administration
Prompt and accurate completion of IRT, pharmacy worksheets, accountability logs and other applicable documents to record IP preparation and handling
Communication with the Clinical Research Associate (CRA) regarding any issues
Attendance during the monitoring visits, as needed

1.7. Communication and Changes in Study Staff

1.	The details of internal communication between team members at the site will depend on the internal organization. The details must be discussed during the SIV and documented in the SIV report, and site staff responsibilities will be documented on the **Site Signature & Delegation Log**.
2.	For any issues or queries that arise during the course of the study, the site personnel will contact the CRA.
3.	Any changes in the site staff will be discussed with the CRA as soon as possible. • New staff must be adequately trained by either the CRA or the pharmacist/ qualified person. • New site staff must be listed and authorized by the PI on the **Site Signature & Delegation Log** (see site binder) prior to commencing work on the study.

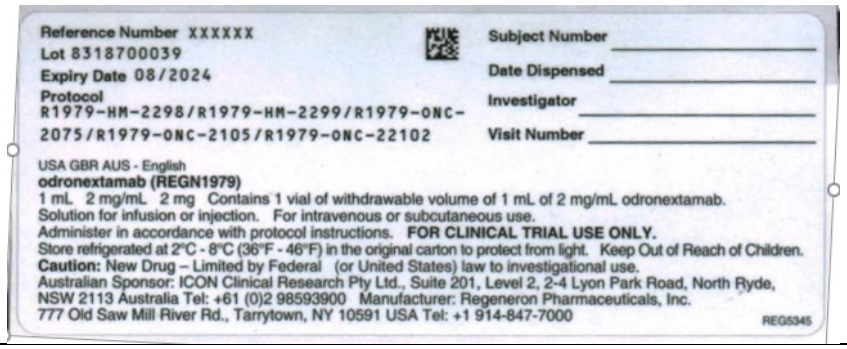
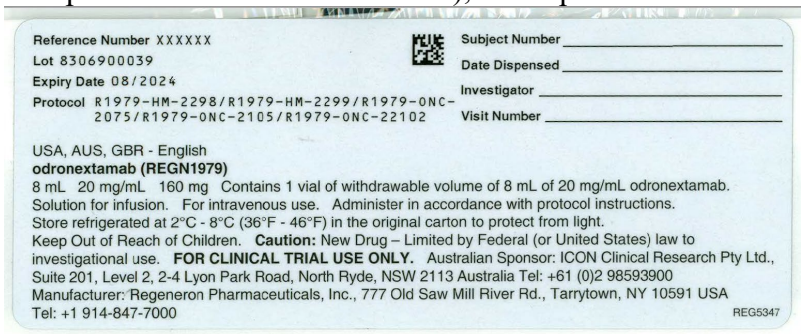
1.8. Support Contacts

Support	General Email *	Related Form	Refer to Section
Clinical Drug Supply and Logistics Manual shipment requests, intra-/inter-site transfers and/or Temperature Excursions	**Clinical.logistics@regeneron.com**	Form-CLO1174	Section 4.7 Section 5 Section 6
Product Complaints	**Product.Complaints@regeneron.com**	Form-CLO5665	Section 4.7
Pharmacy Support Services Ancillary supply materials compatibility review requests, and general procedural questions regarding the pharmacy manual content	**Pharmacy.Support@regeneron.com**	Form-CLO5666	Section 1.2 Section 2.4 Section 3
Ancillary Supply Management Request non-IP supplies provided by Regeneron	**Contact CRA**	N/A	Section 2.4
IRT: Calyx customer support, IRT data correction, IRT related questions	**Contact CRA** **Calyx Customer Service IRT help**	Data Correction Form embedded in IRT	Section 1.2
Distribution: PCI Shipment issues	**Contact Regeneron CDSL Manager**	N/A	Section 6
Returns: PCI	**Contact Regeneron CDSL Manager**	PCI Returns Form	Section 9

*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 CRA in all correspondence. See referenced sections for additional related instructions.

2. STUDY MEDICATION

2.1. Investigational Product Description (Sponsor provided*)

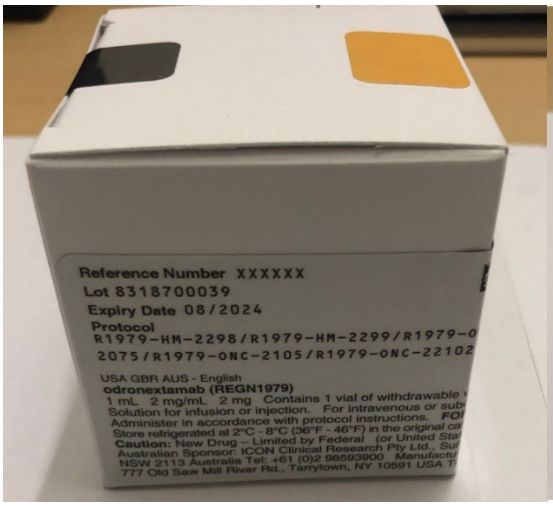
Unit	Formulation	Usage	Storage conditions[1]
A[2].	Odronextamab (REGN1979) Solution for Infusion, 2.0 mg/mL, 1.0 mL withdrawable volume in 2 mL vial, orange stickers (2 stickers applied to the 2mg kit. One on the outer kit carton, one transparent sticker on the vial label), 1 vial per box 	IP	2-8°C Protect from light.
B.	Odronextamab (REGN1979) Solution for Infusion, 20.0 mg/mL, 8.0 mL withdrawable volume in 10 mL vial, green stickers (2 stickers applied to the 160 mg kit. One on the outer kit carton, one transparent sticker on the vial label), 1 vial per box 	IP	2-8°C Protect from light.

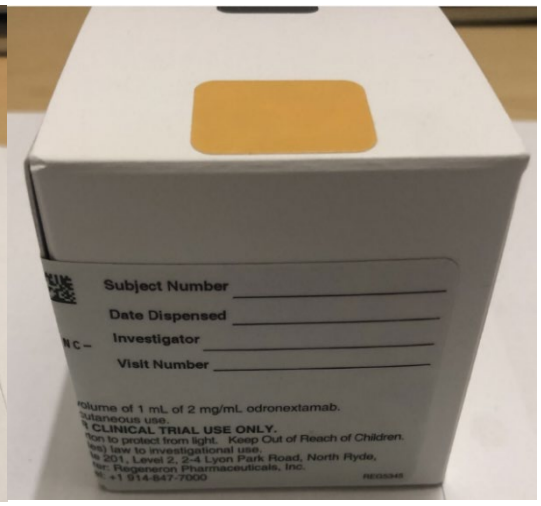
[1]For definitions of the kit storage requirements see Section 4.1, Storage Requirements and Definitions. (For intermediate storage conditions during preparation for dosing, see Section **3.2,** Stability and Shelf-life During IP Preparation.)
[2] All doses of REGN1979 will be administered IV ONLY per study protocol.

*Odronextamab (REGN1979) for the OLYMPIA Pooled Supply program incorporates multiple protocols. For every study included in the program a protocol specific -Abridged Pharmacy Manual will be provided to be used with Pooled Supply Pharmacy Manual.

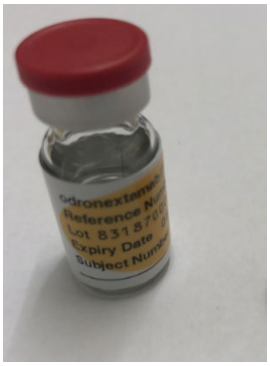
2.2. Labels and Packaging Visual Description

Odronextamab 2mg/1mL Exterior Carton:



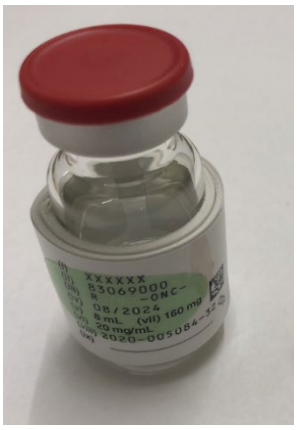


Odronextamab 2mg/1mL Vial:



Odronextamab 20mg/1mL (8mL/vial) Exterior Carton:

Odronextamab 20mg/1mL (8mL/vial) vial:



2.3. Overview of the OLYMPIA *Pooled Supply* Approach

1.	Regeneron will use one clinical site distribution vendor (PCI Clinical Services) and one 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 logon screen.
3.	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.**
4.	Once investigational product 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. Any transfers between protocols of investigational product being stored at a site is prohibited.

2.4. Site Sourced Ancillary Supplies

1.	Each investigator/site is responsible for supplying the supportive medication identified in the protocol and ancillary materials required for preparation.
2.	The listed ancillary materials in this section are recommendations based on compatibility studies in regards to the composition of the materials and listed brands are examples only.
3.	Should the site not be able to locally supply the recommended materials, or the site has procured something other than what is listed, the site should contact the manufacturer to confirm the substance/materials coming in contact with IP are equivalent, and this should be documented in the site file.
4.	**If unable to confirm**, provide the manufacturer, unit reference number and any available information (i.e., specification or data sheet [in English]) to the Pharmacy Support Service Group at **pharmacy.support@regeneron.com** for assessment and approval along with **Form-CLO5666, Ancillary Material Compatibility Approval Form,** Copy CRA on the message. Refer to Section 1.3, Ancillary Material Review. Once reviewed, Regeneron will provide approval or another suggestion. The approved form will be returned to the pharmacy with signature and shall be retained in the site file.

Table 1: Materials for Preparation and/or Dosing

Item Name	Details	Sourcing Strategy
Odronextamab (REGN1979) IV INFUSION		
Syringes with Luer Lok connection	• 1 mL, 3 mL, 5 mL, 10 mL, 20 mL, 30 mL Polypropylene or polycarbonate • BD Luer Lok or equivalent • For preparing doses	Site
21 gauge 1- or 1.5-inch needles	• For preparing dose	Site
IV infusion bag of 0.9% Sodium Chloride	• 50 mL or 100 mL • IV bags should be composed of polyvinyl chloride (PVC) or polyolefin (PO)	Site
Human Serum Albumin (HSA)	• 5%, 20% or 25 % may be used. Refer to Section 3.3.1 Table 5 for dosing requirements. • Approved for therapeutic use will only be used when preparing odronextamab 0.2 mg dose solution for IV infusion, which will always include the first split infusion of the initial dose administered. • Used as a supplemental stabilizer that is required to be on-site prior to subject dosing. • Single use only, any extra volume remaining in the vial/bag should be discarded.	Site or REGN
20-22-gauge 1-inch catheter	• B Braun Introcan catheter or equivalent	Site
Infusion Pumps	• Outlined below in **Table 2**	Site
Infusion Sets	• Outlined below in **Table 3**	Site
0.2 or 5 micron Add-on Filters	• If not included with infusion set • Must be made from polyether sulfone (PES)	Site

MISCELLANEOUS AT SITE		
Sharp Containers	• Disposal of needles	Site
Alcohol Wipes	• Disinfection	Site

Table 2: Recommended Infusion Pumps Based on Compatibility Studies

Recommended Infusion Pumps	Examples	
	Manufacturer	**Model**
Peristaltic infusion pumps	Alaris/BD Carefusion	Gemini PC-1 or similar
	Baxter	Flo-Gard 6201 or similar
	B Braun	Infusomat® Space or similar
Fluid displacement infusion pump	Hospira	Lifecare 5000 or similar

Table 3: Recommended IV Infusion Sets for Odronextamab Based on Compatibility Studies

Recommended Infusion Set Composition	Examples
Infusion set with PVC tubing containing DEHP with 0.2 or 5 µm PES inline filter (Not for use in the European Union)	• Alaris #2430-0500 or similar • Baxter #2C6571 or similar
Infusion set made from PVC tubing not containing DEHP with 0.2 or 5 µm PES In-line filter	• Baxter #2H6480 or similar • Hospira #12336-05 or similar
Infusion set with polyethylene-lined PVC tubing with 0.2 or 5 µm PES inline filter	• Alaris #11532269 or similar
A PVC-free infusion set made from polyurethane with 0.2 or 5 µm PES filter	• B Braun # 8700095SP or similar

DEHP, di-(2-ethylhexyl)-phthalate; PES, polyether Sulfone; PVC, polyvinyl chloride

3. IP PREPARATION INSTRUCTIONS

3.1. General IP Preparation Instructions

1.	Investigational Product (IP) should **not** be prepared and/or administered without written confirmation of the medication reference number assigned to the patient by the IRT system for each visit. **Only vials dispensed from IRT are to be used. Ensure verification of the kit Ref. # used versus the IRT dispensing reports.** Record all kit Ref # on the **Form-CTM1881, Pharmacy Intravenous (IV) worksheet or** Sponsor approved equivalent form/method.
2.	**Odronextamab (REGN1979)** vials should be stored between **2-8°C (36-46°F)** prior to use.
3.	Ensure the investigational product has been stored at the required temperature and visually examine the vial contents to check for any damage or discoloration. If there are any of the mentioned findings, do not use the investigational product.
4.	Aseptic technique should be used during handling, preparation, and administration. Ensure you are working on a hard, clean surface. If available, work in a laminar flow hood/segregated compounding area when required and available.

5.	All blank fields such as Subject Number, Date Dispensed, and Investigator Name, etc. on the clinical 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. Contact Regeneron Clinical Logistics to request authorization.
6.	The pharmacist/qualified person will prepare and dispense Odronextamab (REGN1979) to the delegated study personnel for administration.
7.	All IP preparations details, IRT and accountability and dispensing logs must be completed.

3.2. Stability and Shelf-life During IP Preparation

Table 4: Odronextamab (REGN1979)

Products covered by table	**Odronextamab (REGN1979)**		
	Storage Conditions	**Acceptable Time at Stated Storage Condition**	**Comments/Special Instructions**
Original IP (vial) Odronextamab (REGN1979)	Refrigerated 2-8°C	N/A	Maintain at labelled conditions until ready to prepare dose
Assigned to patient 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 DO NOT SHAKE. Gently mix to prevent foaming. **The room temperature storage includes the time from preparation to the end of infusion.**
Diluted Odronextamab (REGN1979) admixture in IV bag	Room temperature or Refrigerated @ 2-8°C	**Up to 24 hours at 2-8°C or up to 6 hours at room temperature including infusion**	
The prepared infusion bag should be kept for no more than **24 hours** between 2°C and 8°C from the time of IP preparation to the end of the infusion, or no more than **6 hours** if it is left at controlled room temperature (15 - 25ºC) from the time of IP preparation to the end of the infusion. If refrigerated, the diluted solution must be warmed up to room temperature prior to administration			

3.3. Preparation Instructions for Odronextamab (REGN1979)

3.3.1. Dosing Calculations for Odronextamab (REGN1979)

Table 5: Dosing table for Odronextamab (REGN1979) IV 0.2 –320 mg

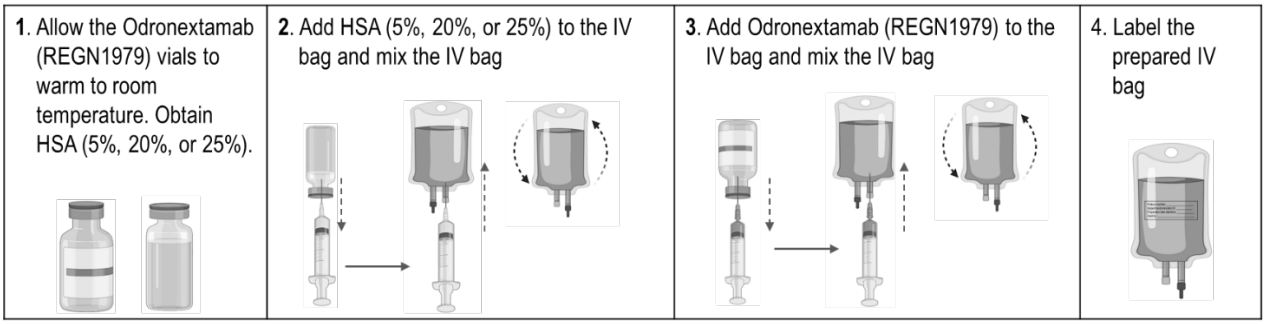
Dose (mg)	IV bag size	HSA[a] required?	No. of HSA vial(s)/bag(s)	HSA vial/bag to be used[a]	Required volume of HSA(mL)	Odronextamab (REGN1979) vial to be used	Drug Product Packaging Configuration (Sticker Color)	No. of odronextamab (REGN1979) vials	Volume of odronextamab (REGN1979) (mL)
0.2	100 mL	**Yes**	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

Dose (mg)	IV bag size	HSA[a] required?	No. of HSA vial(s)/bag(s)	HSA vial/bag to be used[a]	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)
0.5	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
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] Only one concentration of Human Serum Albumin (HSA) is required to be purchased by site (procurement options are provided).

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

Figure 1: Procedure for preparing 0.2 mg Odronextamab (REGN1979) for IV administration

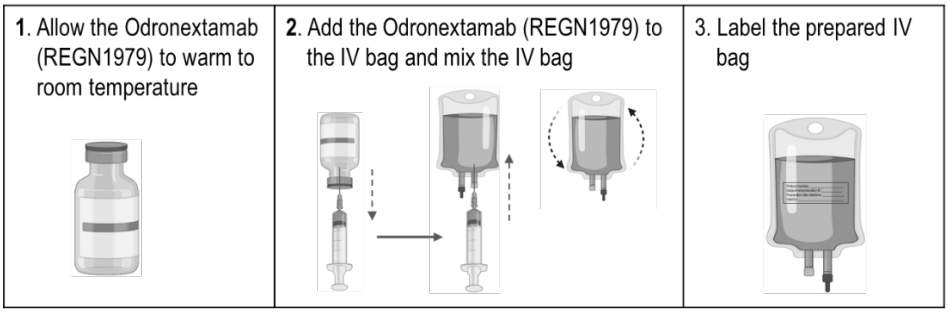


1.	Obtain the IRT assigned odronextamab (REGN1979) vial and HSA vial/bag from refrigerated storage and let the odronextamab (REGN1979) vial sit at room temperature for 10 - 60 minutes to warm up.
	Obtain one IV bag 100 mL of 0.9% sodium chloride
2.	Use a new 1 mL syringe and 21 gauge needle, withdraw a volume of HSA as specified in Table 5. 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 5**.** 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, subject ID, REGN1979 XX 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 time of IP preparation to the end of the infusion. If refrigerated, the diluted solution must be warmed up to room temperature prior to administration.	

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

Figure 2: 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 REGN1979** dose Obtain one IV bag (**50 mL or 100 mL**) of 0.9% sodium chloride for doses between **1 to 320 mg** REGN1979.
2.	Use a new appropriately-sized syringe and 21 gauge needle, withdraw a volume of odronextamab (REGN1979) as specified in Table 5 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, subject 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 **6 hours** if it is left at controlled room temperature (15 - 25ºC) from the time of IP preparation to the end of the infusion. If refrigerated, the diluted solution must be warmed up to room temperature prior to adminizstration.	

3.6 IV Administration of Odronextamab (REGN1979)

Dose (mg)	Infusion time*
0.2 – 320	1 hour (+/- 15 minutes) to 4 hours (+/- 30 minutes)
*Infusion time will vary based on doses and tolerability, please see protocol for additional details.	
1.	Gather the recommended materials for infusion from **Section 2.4**:
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.	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.
5.	At the end of infusion, flush the tubing with 0.9% Sodium Chloride Injection (delivering remaining IP volume from IV line to patient) 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.
6.	If an interruption to the infusion occurs due to an AE, please see protocol for instructions.

4. STORAGE REQUIREMENTS

4.1. Storage Requirements and Definitions

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

4.2. General Requirements for Storage Area

Secure, locked storage area
Dedicated to Investigation Product (IP) storage only
Kept clean and in sanitary condition
Adequate size with enough space and shelving for IP storage **NOTE:** If space is limited, please ensure Regeneron CDSL Manager and CRA is made aware of maximum capacity.
Storage area capable of maintaining the temperature specified on the clinical label Refer to Section 4.3, 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 4.4, Temperature Monitoring Device Requirements

4.3. Temperature Controlled Storage Area

Refrigerator	Temperature maintained between 2ºC and 8ºC (36ºF and 46ºF)

Controlled Room Temperature	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
Protect from Light during Storage	Maintain immediate container of IP in its original carton to minimize exposure to light during storage

4.4. Temperature Monitoring Device Requirements

1.	Monitor and record/document the temperatures. Refer to Section 4.5, 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 4.7, 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.

4.5. Examples of Acceptable Temperature Monitoring Devices

Min-Max Thermometers	• Accuracy to ±0.5°C • Manually record temperatures in a daily log (**Form-CTM1876, Temperature Log template**) or site equivalent form (if Regeneron approval is granted) during normal business hours.
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 site file.

4.6. Temperature Excursion Management

The acceptable storage condition is specified on the clinical label. Any 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 designee rounds the temperature to the nearest whole number. If rounded temperature is within the acceptable temperature range and a temperature excursion does not need to be reported.
   - 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
2. Brief temperature excursions will sometimes be recorded for various reasons (e.g., opening refrigerator door). 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
   - There are fewer than 5 brief excursions in any given 24-hour period

   Recorded excursions meeting all the above criteria are deemed as not being true temperature excursions and do not need to be reported to Regeneron for evaluation.
3. Site pharmacist or designee fills out **Form-CLO1174**, **Potential Temperature Excursion Documentation and Evaluation,** if IP is stored outside the acceptable range.
4. Site pharmacist or designee emails required documents as listed below to the CRA/site monitor, who will review for completeness.

Type of Temperature Excursion	Required Docs for REGN CDSL Assessment
Shipment	• **Form-CLO1174** filled out by site • Packing List • Temperature Monitoring Report • Any Supporting Docs
Site Storage	• **Form-CLO1174** filled out by site • Site Temperature Monitoring Logs • List of Impacted Kits (if not able to record all on form) • Any Supporting Docs

5. CRA/site monitor emails documents to **Clinical.logistics@regeneron.com** for IP disposition. Email must include **Protocol #, site # and country in header** to ensure prompt review of all documents.
6. Site pharmacist or designee physically quarantines in a storage area while maintaining the temperature specified in the clinical label per Section 4.9, Quarantined Medication

7.	Site pharmacist or designee 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 subject.
8.	Site pharmacist or designee waits for a response from the CRA 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.

4.7. Damaged/Defective Stock and Product Complaint Handling

1.	Review **Table 6, Kit Conditions,** below for examples of what to report as damaged/defective IP. The list is not all inclusive and site pharmacist or designee 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, IV bag, etc.) has been compromised, deviating from the drug description in Section 6, Investigational Product Logistics, IP should NOT be used for patient dosing.
3.	The site pharmacist or designee will contact the CRA.
4.	The site pharmacist or designee will immediately quarantine the impacted IP at room temperature per Section 4.9, Quarantined Medication, until it can be returned to Regeneron for evaluation. **Do NOT discard the immediate container and/or carton.**
5.	The site pharmacist or designee will change status of the impacted kit(s) to 'quarantine' in IRT (if it has not yet been allocated to a subject). A replacement kit can be requested in IRT (if the kit has been assigned to a subject).
6.	The site pharmacist or designee, along with the reporter, will fill out **Investigational Product Complaint, Form-CLO5665** and email details of the event to the CRA/site monitor. Report product complaints as soon as possible or within 24 hours of becoming aware of the issue.
7.	The CRA/site monitor will notify Regeneron QA by forwarding the email to a dedicated mailbox: **Product.Complaints@regeneron.com** and copying Regeneron CDSL Manager and CSL. Site should report to the CRA within 24 hours of becoming aware of the issue.
8.	The site pharmacist or designee should wait for further instructions from CRA/site monitor, Regeneron QA, and/or Regeneron Clinical Drug Supply and Logistics.

Table 6: 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 patient 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-REGN sources
	An odor is permeating from the dosing solution

4.8. Quarantined Medication

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 Subject.” • 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 Subject.” • 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 Subject.” • Store IP at the temperature specified on the clinical label until confirmation is received from REGN to move IP to room temperature. • After the transfer, document the removal from the original location in the appropriate logs.

5. MOVEMENT OF IP STORAGE AND TRANSFERS

5.1. IP Storage Location

GENERAL REQUIREMENTS
• Store IP, commercial drug products and/ or prepared dose according to Section 3.2, Stability and Shelf-life During IP Preparation.
• Transfers must be monitored with a temperature monitoring device if o The IP is allocated to patients, or the prepared dose is exposed to the outside environment which includes an open building or structure. o All transfers of unused IP (not allocated to patient) • Refer to Section 4.1, Storage Requirements and Definitions.
• Notify the CRA if the site address changes to a new location. IP can only be transferred after written approval from Regeneron CSL and CDSL is received.

5.2. Inter-Site Transfers

Transfer of unused IP from one site to another participating site.
IP transferred between two sites will be coordinated by Regeneron CDSL ONLY. Instructions and forms will be forwarded to the site should a transfer be needed.

5.3. Intra-Site Transfer of IP (Patient Allocated IP)

Transfer **patient allocated ready for use kits or prepared dose** from one storage location to another at a given site or change in site address during the study.	
1.	Record IP hand-off to site staff in **Form-CTM1878, Dispensing and Administration log**
2.	Transfer must comply with the allowable duration and storage conditions in Section 3.2, Stability and Shelf-life During IP Preparation. Transfer IP 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 **Form-CLO5668, Investigational Product Intra-Site Transfer Form (Non-Allocated)** to record details of the move. • Transfer IP in a container (maintained at refrigerated or CRT temperatures and protected from light. Refer to Table 5). • Transfer IP in a container (maintained at appropriate temperatures) o IP transports ≤ 20 minutes do not require temperature monitoring o IP transports > 20 minutes to ≤60 minutes do not require temperature monitoring IF they are transported in a validated container that has been approved by Regeneron o IP transports >60 minutes require a calibrated temperature monitoring device.
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.	**Form-CLO5668, Investigational Product Intra-Site Transfer Form (Non-Allocated)** must be filed in the pharmacy binder.

5.4. Intra-Site Transfer of IP (Unused IP not allocated to patient)

Transfer **unused IP (unprepared not allocated to patient)** 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: • **Form-CTM1876, Temperature Log Template** or Site log • **Form-CLO5667, Investigational Product Intra-Site Transfer Form (Subject Allocated)**
4.	Transfer IP in a 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 **Form-CTM1876, Temperature Log** (if ones 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 4.7, Temperature Excursion Management)
8.	**Form-CLO5667, Investigational Product Intra-Site Transfer Form (Subject Allocated) Log** must be filed in the pharmacy binder.

6. INVESTIGATIONAL PRODUCT LOGISTICS

6.1 Investigational Product Shipments

6.1.1. General Shipment Information

1.	Regeneron will be responsible for shipping kits listed in Section 2, Study Medication to the sites, via a contracted distribution vendor, **PCI Clinical Services.**
2.	Kits will be transported under the storage conditions specified on the clinical label. Refer to Section 4.7, 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 **Calyx** 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 CRA 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 scheduled 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.

6.1.2. 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 CRA to alert them of the kit(s) not found.
3.	CRA 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/patient 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/CRA, 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.

6.2 Receipt of Investigational Product

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.
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 4.7 , Damaged/Defective Stock, 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 CRA. Wait for further instruction.
4.	Immediately store per storage conditions specified on the clinical label. Refer to Section 4.1, Storage Requirements and Definitions.
5.	Initial, date and time the packing list.
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 4.7, Temperature Excursion Management. Retain the temperature monitoring device until investigation is complete.
7.	Discard the temperature monitoring device after temperature readout report has been downloaded.
	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 CRA. Wait for further instruction.
8.	Acknowledge receipt of the shipment promptly in IRT. Failure to acknowledge a shipment will result in IP being unavailable for allocation to patients. **IRT must always be used.**
9.	File completed packing list, temperature readout from temperature monitoring device, and IRT confirmation of IP receipt in the pharmacy binder.
10.	**Accountability logs must be used for non-IRT IP (any Regeneron provided rescue medication or HSA)** The Site may use their own accountability logs, an IDS system (if approved for use by Regeneron) or CRO equivalent accountability form in addition to the IRT. **IRT must always be used.**

7. MONITORING

1.	Monitoring of the site pharmacy will be conducted according to the Clinical Monitoring Plan.
	• An assigned CRA will monitor all site drug accountability on a regular basis.
	• Reconcile used, expired, and/or damaged IP on a regular visit in IRT (suggestion to perform reconciliation at each visit) and Accountability Logs (for non-IRT rescue medication and HSA provided by Sponsor)
	• Unblinded 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), refer to Monitoring Plan for complete list of tasks: • 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 • Preparing IP returns and/or review destruction records • Follow-up of any issues identified

8. EXPIRY OF INVESTIGATIONAL PRODUCT AND RE-LABELING:

Regeneron CSL or designee will notify sites via "Site Notification of Investigational Product Expiration" memo if the retest date will be extended per new stability data.	
Follow the instructions outlined below. Consult with CRA if there are any questions.	
1.	**Expired IP**: Quarantine kits in accordance with **Section 4.9**, Quarantined Medication.
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 site will be provided with instructions on how to relabel (NOTE: site relabeling is an exception and will only occur under rare circumstances).
3.	IP will be resupplied to sites per the process in **Section 6**, Investigational Product Logistics.

9. ACCOUNTABILITY, RECONCILIATION, RETURNS AND DESTRUCTION

9.1. Accountability

This study will utilize the IRT to capture IP accountability. The site must use the IRT for shipment receipt, randomization, dispensing, accountability, reconciliation, and returns/destruction. The site must **Form-CTM1881, Pharmacy Intravenous (IV) worksheet** or Sponsor approval equivalent, to capture steps of the Infusion preparation of the IRT assigned medication kit (IP Ref. #). **IRT MUST BE USED FOR ALL TRANSACTIONS**	
1.	**Follow Section 6.2 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 following instructions in Section 4.7 Temperature Excursion Management. • If a kit is damaged, follow instructions in Section 4.7, Damaged/Defective Stock, to report a product complaint. • In addition, if any kits are missing contact the CRA and the CDSL manager.
2.	The site may choose to use paper IP product and Individual Subject accountability forms (or equivalent method, i.e., IDS system) **in addition to the IRT** for any of the investigational products recorded in the IRT (optional for IP registered in the IRT), Site must use the following forms for any ancillary drugs, including HSA and tocilizumab **NOT captured in the IRT** and provided by the Sponsor, if applicable). • **Form-CTM1879 Investigational Product Inventory Log** or CRO/Site equivalent • **Form-CTM1880 Individual Subject Investigational Product Accountability Form** or CRO/Site equivalent
3.	Preparation of the patient dose must be captured on the **Form-CTM1881, Intravenous (IV) Pharmacy Worksheet** or Sponsor reviewed site equivalent. Form must minimally include medication kit #, specific amounts prepared for the patient, time & date of preparation, and who prepared with second person verification. This form may be used for accountability purposes to cross-check the IRT to ensure correct patient IP dispensing when performing reconciliation when the site policy dictate destruction of IP after preparation. • **Study Specific Form-CTM1881 Pharmacy Intravenous (IV) Worksheet**
4.	Any discrepancy with the IRT must be corrected promptly using the IRT specific data correction form (DCF) provided to IRT support /helpdesk for update. Refer to IRT training guides for more information. Retain a copy of the submitted DCF and email confirmations in the site file.

9.2. Reconciliation

Reconciliation of IP is recommended to be performed by the CRA at each visit in the IRT and Accountability logs. Retain the following until the CRA has reviewed IP usage and performed reconciliation in the IRT:

- Unused or damaged IP in carton provided
- Used IP in carton provided
- 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 **Pharmacy Intravenous (IV) worksheet** or 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.	CRA /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 ancillary medication (rescue medication and HSA) 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) 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.	CRA /site monitor performs reconciliation step in the IRT at monitoring visits when IP has expired. If IP is missing, mark as such in the IRT and add reason after investigation.
5.	CRA /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 & 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

Used IP should be disposed of on-site after reconciliation. On-site destruction of **unused** IP requires review by CRA/site monitor and CSL approval (see Section 9.4). IP may be returned to the depot 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.	
1.	Obtain permission from the CDSL Manager to return IP to the depot for destruction. When possible, utilize on-site destruction. CRA (or site pharmacist if required) 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, see Section 10**. Allow a minimum lead time of 2 weeks prior to the anticipated need by date. • Unused or damaged IP in carton provided • Used IP in carton provided.

2.	CRA (or site pharmacist if required) will initiate the return shipment of IP according to Regeneron's directed method. **After reconciliation, Initiate the Return using either the Returns modules in the IRT or the depot provided forms.**
3.	CRA (or site pharmacist if required) will pack the IP for return shipment to the depot as per **Distribution Vendor's IP Return Form Instructions, see Section 10.**
4.	CRA receives depot completed return forms. Provide copy to the site to file and upload a copy to the Sponsor TMF.

9.4. Destruction

<table>
<tr><td rowspan="5">On-site Destruction</td><td colspan="2">Destroy IP per site's procedure after CRA has completed reconciliation:
Used IP in carton provided
Unused or damaged IP in carton provided Form-CLO5783 Checklist for Approval for On-Site Destruction of Unused Investigational Product must be completed by the CRA and signed by CSL. The completed form is uploaded to the Regeneron TMF prior to performing destruction on site.
DO NOT DESTROY UNLESS PRIOR APPROVAL IS GRANTED FROM REGENERON. Contact the CRA to confirm.</td></tr>
<tr><td colspan="2">Record on-site destruction of IP as per the Regeneron directed method.</td></tr>
<tr><td>IRT Recording</td><td>For IP that is accounted for in the IRT. Record the destruction in the IRT after reconciliation has been performed.</td></tr>
<tr><td>Manual Recording</td><td>For any ancillary medication (rescue medication and HSA) not recorded in the IRT, ensure completion of Form-CTM1879, Investigational Product Inventory Log and fill out Form-CLO1051, Authorization for Destruction and forward to CRA for filing in TMF, as promptly and accurately as possible.</td></tr>
<tr><td colspan="2">For unused material destroyed on site, provide either a site generated/available Certificate of Destruction, Form-CLO1051, Authorization for Destruction or CRO/site equivalent documentation of destruction to the CRA for filing in TMF.</td></tr>
<tr><td></td><td colspan="2">If the site cannot perform on site destruction, then IP must be returned to the Sponsor's preferred depot. Refer to Section 9.3, Returns.</td></tr>
</table>

10. FORMS & SUPPLEMENTAL INSTRUCTIONS

Refer to applicable sections above for instructions to complete forms, where applicable.

Name of Form/Document	Form, Version # and restricted status (when completed by site)	Mandatory or Optional Form
Safety Data Sheet (SDS)	Odronextamab REGN1979_(C2P2)_Drug_Product_100 mg/mL_V2.0.1_13August2020	(Mandatory) Refer to Section 1.5, Safety and Handling
Temperature Log	Form-CTM1876	Site must have a means to record temperature monitoring (Options available: use of listed Regeneron form, CRO/site generated log, or electronic monitoring device record (must be able to provide a printed read-out) To be completed by site pharmacy staff and reviewed by monitor.
Temperature Excursion Form	Form-CLO1174	(Mandatory use of listed form, if needed) Used by site pharmacist to document any temperature excursion. Email to CRA and CDSL. Refer to Section 4.7, Temperature Excursion Management, for instructions.
Ancillary Supplies Material Compatibility Approval Form	Form-CLO5666	(Mandatory use of listed form, if needed) Use if not already captured during site qualification. Document the request/approval for ancillary material evaluation. Must be maintained in the site file. Refer to Section 1.2.2, Ancillary Supply Review
Investigational Product Complaint Form	Form-CLO5665	(Mandatory use of listed form, if needed) Use by site to document any damages/complaints regarding IP. Refer to Section 4.7, Damaged/Defective Stock and Product Complaints.
Pharmacy Intravenous (IV) worksheet	Form-CTM1881 Customized for study	(Mandatory use of listed form) Use form to prepare and record allocation and preparation of IV dose for subject. Refer to Section 9.1, Accountability, for instructions.

Name of Form/Document	Form, Version # and restricted status (when completed by site)	Mandatory or Optional Form
Individual Subject Investigational Product Accountability Log	Form-CTM1880	(Mandatory use for non-IRT study medications) Used by site pharmacy to document preparation, record dispensing, and administration of IV doses. *Site may choose to use CRO or site equivalent form.* Exception: May not be required if site is approved to use an Electronic Record system (IDS) and can provide all information in case if audit- use of system must be documented for site if not used
Investigational Product Accountability Log	Form-CTM1879	(Mandatory to use for non-IRT study medications and /or HSA) Used by site pharmacist to document all receipt and subject visit specific dispensing of IP during trial; CRA reviews at pharmacy monitoring visit(s). Refer to Section 9.1, Accountability, for instructions. *Site may choose to use CRO or site equivalent form.* Exception: May not be required if site is approved to use an Electronic Record system (IDS) and can provide all information in case if audit- use of system must be documented for site if not used.
Dispensing and Administration Log	Form-CTM-1878 Customized for study	(Mandatory, if needed) Used by site pharmacy to document preparation, record dispensing, and administration of IV doses. *Site may choose to use CRO or site equivalent form* Exception: May not be required if site is approved to use an Electronic Record system (IDS) and can provide all information in case if audit- use of system must be documented for site if not used.
Investigational Product Intra-Site Transfer Form (Subject Allocated)	Form-CLO5667	(Mandatory, if needed) Used to transfer prepared IP dose, Refer to Section 5, Movement of IP Storage and Transfers *Site may choose to use CRO or site equivalent form*
Investigational Product Intra-Site Transfer Form (Non-Allocated)	Form-CLO5668	(Mandatory) Used to transfer unused IP, Refer to Section 5, Movement of IP Storage and Transfers *Site may choose to use CRO or site equivalent form*
EL Pro® Libero Temperature Monitoring Device		Provides detail on how to use the temperature monitoring device provided in the IP shipment.

Name of Form/Document	Form, Version # and restricted status (when completed by site)	Mandatory or Optional Form
Authorization for Destruction	Form-CLO1051	(Mandatory when IP is destroyed at site if a Certificate of Destruction or equivalent is not available) *Site may choose to use CRO or site equivalent form.*
Returns Form (Vendor specific)	Investigational Product Return Form Template PCI	(Mandatory for sponsor provided product not managed by IRT)
Ancillary Supply Site Order form	Form-CLO5500	Sites will use this form to request shipments of ancillary supplies like HSA or tocilizumab.

SAFETY DATA SHEET

SECTION 1 - IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND OF THE COMPANY/ UNDERTAKING

Contact information

General

REGENERON

Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Rd., Tarrytown, NY 10591
Main: +1 (914) 847-7000
Fax: +1 (914) 847-7991
E-mail: SDScoordinator@regeneron.com

Emergency telephone number

1-(914) 847-2222 (U.S. and Canada)
24-hour Availability

Product identifier	REGN1979, (C2P2), Drug Product, 100 mg/mL
Synonyms	None identified
Trade names	None assigned
Chemical family	Monoclonal antibody
Relevant identified uses of the substance or mixture and uses advised against	Active pharmaceutical ingredient for research and development purposes only; under investigation for treatment of non-Hodgkin's lymphoma (NHL), chronic lymphocytic leukemia (CLL), and other B-cell malignancies.
Note	This SDS is written to address potential worker health and safety issues associated with the handling of the active pharmaceutical ingredient. This SDS will be revisited if more data become available.

SECTION 2 - HAZARDS IDENTIFICATION

Classification of the substance or mixture

Globally Harmonized System [GHS]	Specific Target Organ Toxicity (single exposure) - Category 1.
Other/Supplemental	Substance not yet fully tested

Label elements

SECTION 2 - HAZARDS IDENTIFICATION …continued

GHS hazard pictogram

GHS signal word Danger

GHS hazard statements H370 - Causes damage to the immune system.

GHS precautionary statements P260 - Do not breathe dust/mist/vapors/spray. P264 - Wash hands thoroughly after handling. P270 - Do not eat, drink or smoke when using this product. P308 + P311 - IF exposed or concerned: Call a POISON CENTER or doctor/physician. P405 - Store locked up. P501 - Dispose of contents/container to location in accordance with local/regional/national/international regulations.

Other hazards REGN1979 is a human bispecific antibody, directed specifically at CD3 and CD20. The most commonly observed treatment-emergent adverse effects in clinical trials following intravenous (IV) administration include cytokine release syndrome (fever, chills, hypotension, nausea), fatigue, elevated hepatic enzymes, increased C-reactive protein (a marker of inflammation), leukocytosis (anemia, neutropenia, decreased lymphocyte counts, thrombocytopenia) and infusion-related reactions. Based on mechanism of action considerations, exposure to REGN1979 may result in B-cell decreases or depletion, increased risk of infection, hepatitis B reactivation, and/or progressive multifocal leukoencephalopathy.

Based on effects observed at very low doses in animal studies and the presence of B-cells in the lung, a potential to cause B-cell suppression following inhalation cannot be excluded in the absence of data.

Note This substance is classified as hazardous under GHS as implemented by Regulation EC No 1272/2008 (EU CLP), WHMIS 2015 (Health Canada), and Hazard Communication Standard No. 1910.1200 (US OSHA).

SECTION 3 - COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient	CAS #	EINECS/ ELINCS#	Amount	GHS Classification
REGN1979	N/A	N/A	10.0%	STOT-S1: H370

Note The substance listed above is considered hazardous. See Section 16 for full text of GHS classifications.

SECTION 4 - FIRST AID MEASURES

Description of first aid measures	
Immediate Medical Attention Needed	Yes
Eye Contact	If easy to do, remove contact lenses, if worn. Immediately flush eyes with copious quantities of water for at least 15 minutes. If irritation occurs or persists, notify medical personnel and supervisor.
Skin Contact	Wash exposed area with soap and water and remove contaminated clothing/shoes. If irritation occurs or persists, notify medical personnel and supervisor.
Inhalation	Immediately move exposed subject to fresh air. If not breathing, give artificial respiration. If breathing is labored, administer oxygen. Immediately notify medical personnel and supervisor.
Ingestion	If swallowed, call a physician immediately. Do not induce vomiting unless directed by medical personnel. Do not give anything to drink unless directed by medical personnel. Never give anything by mouth to an unconscious person. Notify medical personnel and supervisor.
Protection of first aid responders	See Section 8 for Exposure Controls/Personal Protection recommendations.
Most important symptoms and effects, both acute and delayed	See Sections 2 and 11
Indication of immediate medical attention and special treatment needed, if necessary	Medical conditions aggravated by exposure: None known or reported. Treat symptomatically and supportively.

SECTION 5 - FIREFIGHTING MEASURES

Extinguishing media	Use water spray (fog), foam, dry powder, or carbon dioxide, as appropriate for surrounding fire and materials.
Specific hazards arising from the substance or mixture	No information identified. May emit carbon monoxide, carbon dioxide, oxides of nitrogen, and nitrogen-containing compounds.
Flammability/ Explosivity	No explosivity or flammability data identified. As product is an aqueous solution, it is not expected to be flammable or explosive.
Advice for firefighters	In case of fire in the surroundings: use the appropriate extinguishing agent. Wear full protective clothing and an approved, positive pressure, self-contained breathing apparatus. Decontaminate all equipment after use.

SECTION 6 - ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures	If product is released or spilled, take proper precautions to minimize exposure by using appropriate personal protective equipment (see Section 8). Use only with adequate ventilation. Do not breathe mist/spray.
Environmental precautions	Do not empty into drains. Avoid release to the environment.
Methods and material for containment and cleaning up	DO NOT CAUSE MATERIAL TO BECOME AIRBORNE. For small spills, soak up material with absorbent, e.g., paper towels. For large spills, cordon off spill area and minimize the spreading of spilled material. Soak up material with absorbent. Collect spilled material, absorbent, and rinse water into suitable containers for proper disposal in accordance with applicable waste disposal regulations (see Section 13). Decontaminate the area twice.
Reference to other sections	See Sections 8 and 13 for more information.

SECTION 7 - HANDLING AND STORAGE

Precautions for safe handling	Follow recommendations for handling pharmaceutical agents (i.e., use of engineering controls and/or other personal protective equipment if needed). Use adequate ventilation. Avoid breathing dust/mist/spray.
Conditions for safe storage including any incompatibilities	Store at 5 °C (unit set point). Acceptable operating range 2°C to 8°C
Specific end use(s)	No information identified.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION

Control Parameters/ Occupational Exposure Limit Values

Compound	Issuer	Type	OEL
REGN1979	Regeneron	OEL	1 µg/m³

Exposure/Engineering controls

Control exposures to below the OEL (for the active ingredient(s) if available). Selection and use of containment devices and personal protective equipment should be based on a risk assessment of exposure potential. Utilize closed and sealed systems whenever possible. Solutions used for procedures where aerosolization may occur (e.g., spraying, pumping, open transfers,) must be handled using an engineered local exhaust ventilation (LEV) and/or enclosure or isolator system. Control the potential for spills and leaks by securing all connections. Use clean-in-place systems.

SECTION 8 - EXPOSURE CONTROLS/PERSONAL PROTECTION …continued

Respiratory protection	Choice of respiratory protection should be appropriate to the task and the level of existing engineering controls. A powered air-purifying respirator (PAPR) with HEPA filters and head cover is required when performing aerosol generating operations. An airline respirator or self-contained breathing apparatus (SCBA) and disposable outerwear is required for spill cleanup.
Hand protection	Wear nitrile or other impervious gloves if skin contact is possible. Double gloves should be considered.
Skin protection	Wear disposable coveralls appropriate to the task, booties, two pairs of gloves and safety glasses with side shields. Protective garments (coveralls, disposable coveralls, lab coats) are not to be worn in common areas (e.g., cafeterias) or out-of-doors. Employees must be trained in proper gowning and degowning practices. An anteroom or transition area must be used for gowning and degowning.
Eye/face protection	Wear safety glasses with side shields, chemical splash goggles, or full face shield, if necessary. Base the choice of protection on the job activity and potential for contact with eyes or face. An emergency eye wash station should be available.
Environmental Exposure Controls	Avoid release to the environment and operate within closed systems wherever practicable. Air and liquid emissions should be directed to appropriate pollution control devices. In case of spill, do not release to drains. Implement appropriate and effective emergency response procedures to prevent release or spread of contamination and to prevent inadvertent contact by personnel.
Other protective measures	Wash hands in the event of contact with this substance, especially before eating, drinking or smoking. Protective equipment is not to be worn outside the work area (e.g., in common areas or out-of-doors).

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

Appearance	Liquid
Color	Clear, colorless
Odor	No information identified.
Odor threshold	No information identified.
pH	No information identified.
Melting point/ freezing point	No information identified.
Initial boiling point and boiling range	No information identified.
Flash point	No information identified.

SECTION 9 - PHYSICAL AND CHEMICAL PROPERTIES …continued

Evaporation rate	No information identified.
Flammability (solid, gas)	Not applicable.
Upper/lower flammability or explosive limits	No information identified.
Vapor pressure	No information identified
Vapor density	No information identified.
Relative density	No information identified.
Water solubility	No information identified.
Solvent solubility	No information identified.
Partition coefficient (*n-octanol/water*)	No information identified.
Auto-ignition temperature	No information identified.
Decomposition temperature	No information identified.
Viscosity	No information identified.
Explosive properties	No information identified.
Oxidizing properties	No information identified.

Other information

Molecular formula	Protein
Molecular weight	≥150 kDa

SECTION 10 - STABILITY AND REACTIVITY

Reactivity	No information identified.
Chemical stability	No information identified.
Possibility of hazardous reactions	No information identified.
Conditions to avoid	No information identified.
Incompatible materials	No information identified.
Hazardous decomposition products	No information identified.

SECTION 11 - TOXICOLOGICAL INFORMATION

Information on toxicological effects

Route of entry

REGN1979 is intended to be administered *via* IV injection. As a large protein, it is unlikely to be absorbed through skin contact, or ingestion. Absorption through inhalation is also likely to be limited.

Acute toxicity

Compound	Type	Route	Species	Dose
REGN1979	--	--	--	--

Irritation/Corrosion

No studies identified.

Sensitization

No studies identified.

STOT-single exposure

Single IV doses of REGN1979 in monkeys resulted in multiorgan inflammation and associated moribund condition in one animal, likely the result of an opportunistic infection. Some depletion of B-cells was also observed following single doses of 0.001 mg/kg.

STOT-repeated exposure/Repeat-dose toxicity

In a 4-week monkey study, administration of five once weekly doses of REGN1979 at 0.01 to 1 mg/kg resulted in complete depletion of B-cells in the peripheral blood and lymphoid tissues. Vomiting and inflammatory lesions in the liver occurred at 1 mg/kg, likely a consequence of the expected pharmacologic effects of REGN1979. The occupational NOAEL is considered <0.01 mg/kg/dose.

Reproductive toxicity

No studies for REGN1979 were identified.

Developmental toxicity

No studies for REGN1979 were identified. In an embryo-fetal developmental toxicity study with a mechanistically similar compound, IV administration to pregnant monkeys during early gestation did not result in any teratogenic effects, but a decrease in lymphoid tissue B-cells was observed in exposed offspring. Decreases in B-cells were also observed in the offspring of treated pregnant monkeys in a pre- and postnatal reproductive toxicity study.

Genotoxicity

No studies identified. As a large protein, REGN1979 is unlikely to be genotoxic.

Carcinogenicity

No studies identified.

Aspiration hazard

No studies identified

Human health data

See "Section 2 - Other Hazards"

Additional information

The toxicological properties of this substance have not been fully characterized.

SECTION 12 - ECOLOGICAL INFORMATION

Toxicity

Compound	Type	Species	Concentration
REGN1979	--	--	--

SECTION 12 - ECOLOGICAL INFORMATION …continued

Persistence and Degradability	Monoclonal antibodies are proteins and are likely to break down rapidly in the environment.
Bioaccumulative potential	No data available.
Mobility in soil	No data available.
Results of PBT and vPvB assessment	No data available.
Other adverse effects	No data available.
Note	The environmental characteristics of this substance have not been fully investigated. Releases to the environment should be avoided.

SECTION 13 - DISPOSAL CONSIDERATIONS

Waste treatment methods	Dispose of wastes in accordance to prescribed federal, state, and local guidelines, e.g., appropriately permitted chemical waste incinerator. Do not send down the drain or flush down the toilet. All wastes containing the material should be properly labeled. Rinse waters resulting from spill cleanups should be discharged in an environmentally safe manner, e.g., appropriately permitted municipal or on-site wastewater treatment facility.

SECTION 14 - TRANSPORT INFORMATION

Transport	Based on the available data, this substance is not regulated as a hazardous material/ dangerous good under EU ADR/RID, US DOT, Canada TDG, IATA, or IMDG.
UN number	None assigned.
UN proper shipping name	None assigned.
Transport hazard classes and packing group	None assigned.
Environmental hazards	Based on the available data, this substance is not regulated as an environmental hazard or a marine pollutant.
Special precautions for users	Due to lack of data, avoid release to the environment.
Transport in bulk according to Annex II of MARPOL73/78 and the IBC Code	Not applicable.

SECTION 15 - REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture	This SDS generally complies with the requirements listed under current guidelines in the US, EU and Canada. Consult your local or regional authorities for more information.
Chemical safety assessment	Not conducted.
TSCA status	Drugs are exempt from TSCA.
SARA section 313	Not listed.
California proposition 65	Not listed.
Additional information	No other information identified.

SECTION 16 - OTHER INFORMATION

Full text of H phrases and GHS classifications	STOT-S1 - Specific Target Organ Toxicity Following Single Exposure Category 1. H370 - Causes damage to the immune system.
Sources of data	Information from published literature and internal company data.
Abbreviations	ACGIH - American Conference of Governmental Industrial Hygienists; ADR/RID - European Agreement Concerning the International Carriage of Dangerous Goods by Road/Rail; AIHA - American Industrial Hygiene Association; CAS# - Chemical Abstract Services Number; CLP - Classification, Labelling, and Packaging of Substances and Mixtures; DNEL - Derived No Effect Level; DOT - Department of Transportation; EINECS - European Inventory of New and Existing Chemical Substances; ELINCS - European List of Notified Chemical Substances; EU - European Union; GHS - Globally Harmonized System of Classification and Labeling of Chemicals; IARC - International Agency for Research on Cancer; IDLH - Immediately Dangerous to Life or Health; IATA - International Air Transport Association; IMDG - International Maritime Dangerous Goods; LOEL - Lowest Observed Effect Level; LOAEL - Lowest Observed Adverse Effect Level; NIOSH - The National Institute for Occupational Safety and Health; NOEL - No Observed Effect Level; NOAEL - No Observed Adverse Effect Level; NTP - National Toxicology Program; OEL - Occupational Exposure Limit; OSHA - Occupational Safety and Health Administration; PBT - Persistent, Bioaccumulative, and Toxic; PNEC - Predicted No Effect Concentration; SARA - Superfund Amendments and Reauthorization Act; STOT - Specific Target Organ Toxicity; STEL - Short Term Exposure Limit; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act; TWA - Time Weighted Average; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System
Issue Date	February 21, 2020
Revisions	This is the third version of this SDS.

Disclaimer

The above information is based on data available to us and is believed to be correct. Since the information may be applied under conditions beyond our control and with which we may be unfamiliar, we do not assume any responsibility for the results of its use and all persons receiving it must make their own determination of the effects, properties and protections which pertain to their particular conditions.

No representation, warranty, or guarantee, express or implied (including a warranty of fitness or merchantability for a particular purpose), is made with respect to the materials, the accuracy of this information, the results to be obtained from the use thereof, or the hazards connected with the use of the material. Caution should be used in the handling and use of the material because it is a pharmaceutical product. The above information is offered in good faith and with the belief that it is accurate. As of the date of issuance, we are providing all information relevant to the foreseeable handling of the material. However, in the event of an adverse incident associated with this product, this Safety Data Sheet is not, and is not intended to be, a substitute for consultation with appropriately trained personnel.

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TEMPERATURE LOG

Protocol Number:

Principal Investigator:___________________ Site Number: _______

Responsible personnel:__________________ Thermometer Reference: ____________________

Specify location, where IP supply is stored: ____

The IP supplies must be stored in a secure place at controlled temperature as indicated on the IP labels:

If the storage temperature was out of range, please complete the Temperature Excursion Documentation Form CLO1174

Date	Time	Temperature Recording (please tick the applicable unit) ° Celsius ☐ ° Fahrenheit ☐			Comments (e.g. any temperature deviations)	Signature
		Current Temperature	Minimum Temperature	Maximum Temperature		

Was investigational product transferred to another storage location? ☐ **Yes** ☐ **No**
If Yes, provide documentation of transfer and temperature min/max during this transfer

REGENERON

Potential Temperature Excursion Documentation and Evaluation Form

Please store the affected Investigational Product in quarantine maintaining the appropriate temperature range until further instruction is received from Clinical Logistics to ensure that affected IP are not allocated to patients while in quarantine for evaluation.

Temperature Excursion Number (Issued by Clinical Logistics):_____

Section I: To be Completed by the Clinical Study Lead (CSL), Contract Research Organization (CRO), Investigational Site, or Medical Operations Manager (MOM) **Please submit form to: clinical.logistics@regeneron.com**			
Protocol Specific Information			
Protocol Number:	Investigational Product(s) Name and dosage form (vials, syringes, capsules, etc…):		
Affected Investigational Product Kit Number(s) and associated Lot number(s) for this evaluation:			
Name and Contact information of Principal Investigator, Sponsor Investigator, as applicable:			
Reporter's Name: Date Reported (ddmmmyyy):	Principal Investigator's name:		
Telephone Number:	Address:		
Email address:	Site Number:		
Potential Temperature Excursion Information: Check "°C" or "°F" based on the unit of measure			
Date(s) Temperature Excursion Occurred			
Highest Temperature Reached	☐ °C ☐ °F		
Total time above high temperature limit	(days/hours/minutes) ☐ D ☐ H ☐ M		
Lowest Temperature	☐ °C ☐ °F		
Total time below low temperature limit	(days/hours/minutes) ☐ D ☐ H ☐ M		
☐ **Transit Excursion: Attach Packing List and Temperature Chart**			
Shipment Order/Consignment Number:	Temperature Recording Log ID Number:		
☐ **Site Storage Excursion: Attach Temperature Monitoring Logs**			
Section II: To be Completed by Regeneron Clinical Logistics			
Affected Investigational Product Kit Number(s) and associated Lot number(s) with previous evaluations:			
Kits Approved for use:			
Kits not approved for use:			

Potential Temperature Excursion Documentation and Evaluation Form

Please store the affected Investigational Product in quarantine maintaining the appropriate temperature range until further instruction is received from Clinical Logistics to ensure that affected IP are not allocated to patients while in quarantine for evaluation.

Temperature Excursion Number (Issued by Clinical Logistics):_____

Comments		
Approved By:		
Print Name and Title	Signature	Date (DDMMMYYYY)

REGENERON

Ancillary Supplies Material Compatibility Approval Form

Instructions:

- **Section I** is to be completed by the Requestor, Site pharmacist, CRA or Clinical Study Lead (CSL) for hospital/clinical sites. Please fill out section I (maintain in Word format) and forward this form to pharmacy.support@regeneron.com
- **Section II** is to be completed by the formulation development group at Regeneron Pharmaceuticals, Inc. for material approval.

Section I (A-D): To be completed by the Requestor, Clinical Study Lead (CSL) for hospital/clinical sites

A) General Information

Clinical Study Number:		Address:	
Name of hospital/site:		Email:	
Name of Principle Investigator:		Phone Number:	
Requires approval for:	☐ IV infusion materials ☐ Subcutaneous/intramuscular materials ☐ Other (Please specify)		

B) IV Infusion Materials

1. IV Container

#	Brand	Item #	IV Container Material	Diluent Type
1a			☐ PVC ☐ Glass ☐ Polyolefin (Polypropylene/polyethylene) ☐ Other _____	☐ 0.9% Sodium Chloride ☐ 5% Dextrose ☐ Other _____
1b			☐ PVC ☐ Glass ☐ Polyolefin (Polypropylene/polyethylene) ☐ Other _____	☐ 0.9% Sodium Chloride ☐ 5% Dextrose ☐ Other _____

2. IV Infusion Sets and Filter

#	Brand	Item #	Tubing Material	Filter	Filter Pore Size	Filter Material
2a			☐ PVC with DEHP ☐ PVC without DEHP ☐ PE-lined PVC ☐ Polyurethane ☐ Polybutadiene ☐ Other _____	☐ Add-On ☐ In-Line	☐ 0.2 or 0.22 µm ☐ 1.2 µm ☐ Other _____	☐ PES ☐ Nylon ☐ Other _____
2b			☐ PVC with DEHP ☐ PVC without DEHP ☐ PE-lined PVC ☐ Polyurethane ☐ Polybutadiene ☐ Other _____	☐ Add-On ☐ In-Line	☐ 0.2 or 0.22 µm ☐ 1.2 µm ☐ Other _____	☐ PES ☐ Nylon ☐ Other _____

3. IV Infusion Catheter

#	Brand	Item #	Catheter Material		
3a			☐ Polyethylene ☐ Teflon/PTFE	☐ Polyurethane ☐ FEP	☐ Silicon ☐ Other _____
3b			☐ Polyethylene ☐ Teflon/PTFE	☐ Polyurethane ☐ FEP	☐ Silicon ☐Other _____

4. Infusion Pump

#	Brand	Item #	Pumping Mechanism		
4a			☐ Peristaltic	☐ Fluid Displacement	☐ Other _____
4b			☐ Peristaltic	☐ Fluid Displacement	☐ Other _____

Ancillary Supplies Material Compatibility Approval Form

5. CSTD (Closed System Drug-Transfer Device)

#	Brand	Item #	CSTD Component Material
5a			
5b			
5c			
5d			
5e			
5f			

C) Subcutaneous/Intramuscular Materials

6. Syringe

#	Brand	Item #	Syringe Material
6a			☐ Polypropylene ☐ Polycarbonate ☐ Other _____
6b			☐ Polypropylene ☐ Polycarbonate ☐ Other _____

7. Withdrawal Needle

#	Brand	Item #	Needle Size (Gauge)	Needle Length (Inches)
7a			☐ 18 - 21G ☐ Other _____	☐ 1" ☐ 1/2" ☐ Other _____
7b			☐ 18 - 21G ☐ Other _____	☐ 1" ☐ 1/2" ☐ Other _____

8. Injection Needle

#	Brand	Item #	Needle Size (Gauge)	Needle Length (Inches)
8a			☐ 27G ☐ 25G ☐ Other _____	☐ 1/2" ☐ 5/8" ☐ Other _____
8b			☐ 27G ☐ 25G ☐ Other _____	☐ 1/2" ☐ 5/8" ☐ Other _____

D) Other materials

#	Brand	Item #	Material
9a			
9b			

E) Additional Comments

Requestor (Full Name)/title/email:	**Request Date**:

Section II: To be completed by Formulation Development Group at Regeneron Pharmaceuticals

The material(s) in **Section I** is/are:

☐ Approved

☐ Not approved

☐ Partially approved. Please see comments below.

Comments:

Approver (Full Name)/title :	**Date**: /see appended approval page

REGENERON

Investigational Product Complaint Form

Sponsor Protocol No.:	Study Investigational Product (IP) Drug Name:
Investigator Name:	Site No.:
Subject ID:	Site Country:

Please complete and email this form to Product.complaints@regeneron.com , include CRA and Regeneron Clinical Logistics Manager in cc field.

Please store the affected Investigational Product in quarantine until further instruction is received from Regeneron to ensure that these affected IP are not dispatched to patients while in quarantine.

Batch/Lot No*.:	Kit Reference No.:

Product Presentation*: ☐ Vial ☐ Pre-Filled Syringe ☐ Pre-Filled Syringe with Safety System ☐ Pre-Filled Pen ☐ Other: _____

***Note: All devices included in this study are associated with commercial product. Commercial regulatory reporting requirements (e.g. PMSR, BPDR) apply. Sponsor to evaluate all reports accordingly.** [Delete this line if not using Regeneron commercial product when adding to pharmacy manual.]

Date Defect Observed	Was the defect identified prior to administration?	Is there an SAE associated with this event?	Who was administering the product at the time of the defect?	Was the suspect product/device used to administer Drug to the patient?	Are images available? If yes, please attach	Is the product/device available to return to Sponsor?
	☐ Yes ☐ No	☐ Yes ☐ No ☐ Unknown	☐ HCP ☐ Caregiver ☐ Patient ☐ Other: _____	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No

Describe details of observed defect including how the defect was identified. Include any Action taken/further investigation and additional comments, if applicable. Additional pages may be attached if needed (ensure protocol # and kit ref # is added to additional pages).

Additional Comments:

Reported by: _____ _____ _____ _____

Date | Print Name | Signature | Functional Area

REGENERON

PHARMACY INTRAVENOUS WORKSHEET
Protocol: R1979-_____

Subject Number:		**Site Number:**	
Date (dd/mmm/yyyy):		**Investigator:**	

Drug product: REGN1979		**Total Dose:_____ mg**
REGN1979 vial (Odronextamab)	Total number of vials used:	
	REGN1979 Vial Concentration	☐ 2 mg/ 1 mL ☐ 20mg/mL (160mg/8mL)
	Lot number:	
	Vial Ref. number(s):	
	Expiry Date:	
Date/Time vial(s) removed from refrigerator:		_____/_____/_____ (dd/mmm/yyyy) _____:_____ (hh:mm)
IV Infusion Bag	Type of IV bag used ☐ 0.9% Sodium Chloride for Injection bag	
	Volume of IV bag used ☐ 50 mL bag ☐ 100 mL bag	
	Manufacturer	
	Lot number:	
	Expiry Date:	
HSA (Human Serum Albumin) required* : ***Only be used when preparing odronextamab 0.2 mg dose solution for IV infusion**		☐ **Yes, complete section below** ☐ **No**
Human Serum Albumin	Human Serum Albumin Concentration ☐ **5%** ☐ **20%** ☐ **25%**	
	Manufacturer	
	Lot number:	
	Expiry Date	
Total volume of HSA added to IV infusion Bag:		mL
Total volume of REGN1979 added to IV Infusion Bag:		_____ **mL**
Final IV Infusion Bag Expiration	**Date** (dd/mmm/yy):	
	Time (hh:mm):	_____:_____
Final IV Infusion Bag Dosing Solution is clear and essentially free of particulates:		☐ **Yes** ☐ **No**

Performed by:		**Date** (dd/mmm/yy):	
Checked by:		**Date** (dd/mmm/yy):	

REGENERON

INDIVIDUAL SUBJECT INVESTIGATIONAL PRODUCT ACCOUNTABILITY LOG

Protocol Number:	**Investigator Name:**	**Site Number:**
Investigational Product (IP):	**Site Name:**	**Storage Area:**
Dose Form and Strength:	**Subject Number:**	

Date	Kit Reference #	Lot #	Dose \Volume (mL)	Expiration Date	Dispensed by	Comments	Monitor Review (Date/Initials)

PAGE _____ of _____

REGENERON

INVESTIGATIONAL PRODUCT ACCOUNTABILITY LOG

Investigational Product (IP)	Protocol Number	Site Number	Investigator
REGN	R		

IP Receipt						IP Disposition						
Shipment		Reference Number	Lot Number	Dosage	Pharmacist (Initials)	Date IP Dispensed	Subject Screening Number	Subject ID	Quantity Dispensed	Quantity Available (Balance)	Pharmacist (Initials)	Monitor (Initials)
Date IP Received	Quantity Received											

Pharmacist Signature_____ **Date**_____

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Dispensing & Administration Log
Protocol Number: R1979_____

Subject ID:			
Date:		**Visit Number:**	

For Pharmacy:

IV Infusion Bag prepared by:		
IV Infusion Bag prepared for administration:	**Date:**	
	Time:	

IV Infusion Bag dispensed to:		
IV Infusion Bag received:	**Date:**	
	Time:	

Signed _____ **Date:** _____

Pharmacist

For Site Study Staff:

Reminder: IV Infusion must be completed within 6 hours.

IV Infusion Bag administered by:		
IV Infusion Bag commenced:	**Date:**	
	Time:	
IV Infusion Bag completed:	**Date:**	
	Time:	

☐ IV Infusion Bag was not given to a subject

Reason:

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Investigational Product Intra-Site Transfer Form (Subject Allocated)

Protocol Number		**Site Number**	
Originating Address:		**Destination Address:**	
Location Distance [e.g., km, miles]		**Performer Printed Name / Signature** [Pharmacist or Qualified Person]	

Subject # / ID	**Visit**	**Reference # (if Requested)**	**TRANSFER DETAILS (exposed to outside environment)**			
			Transfer Date (DD-MMM-YYYY) **/ Time**			
			Start	[Move from Current Storage Location to Transfer Container]	**End**	[Move from Transfer Container to New Storage Location]
			Time Duration [e.g., minutes, hours]			
			Required Storage Condition [e.g., 2-8C]			
			Temperature Monitoring Device		**Transfer Container**	
			Type [e.g., data logger]		**Type** [e.g., cooler bag, green box]	
			Model			
			Serial #			
			Calibration Date			
			Any Temperature Excursions Occur?		☐ NO	☐ YES Request replacement kit(s) as instructed in Pharmacy Manual
			Received prepared dose in good condition?		☐ YES	☐ NO Request replacement kit(s) as instructed in Pharmacy Manual

Comments: _____

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Investigational Product Intra-Site Transfer Form (Non- Allocated)

Protocol Number		**Site Number**	
Originating Address:		**Destination Address:**	
Location Distance [e.g., km, miles]		**Originator's Name** [Pharmacist or Designee]	

Label Drug Name	**IP Batch #**	**IP Reference #**	**TRANSFER DETAILS (non-allocated IP)**			
			Transfer Date (DD-MMM-YYYY) **/ Time**			
			Start	[Move from Current Storage Location to Transfer Container]	**End**	[Move from Transfer Container to New Storage Location]
			Time Duration [e.g., minutes, hours]			
			Required Storage Condition [e.g. 2-8C]			
			Temperature Monitoring Device		**Transfer Container**	
			Type [e.g., data logger]		**Type** [e.g., cooler bag, green box]	
			Model			
			Serial #			
			Calibration Date			
			Any Temperature Excursions Occur?		☐ NO	☐ YES Refer to Pharmacy Manual for next steps

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Investigational Product Intra-Site Transfer Form (Non- Allocated)

NEW STORAGE LOCATION			
Temperature Monitoring Device		**Storage Area**	
Type [e.g., data logger]		**Is temperature stable for a minimum of 24 hours?**	
Model		**Is temperature within acceptable range?**	
Serial #		If 'NO' to above, do not store in new storage location	
Calibration Date			

IP RECEIPT STATUS			
Received all kits in good condition	☐ YES	☐ NO	If 'NO', list affected reference #s and description of incident. Refer to Pharmacy Manual for next steps.
Comments			

Receiver (Pharmacist or Designee)

_____	_____	_____
Signature	**Printed Name**	**Date** (DD-MMM-YYYY

LIBERO Temperature Monitor Instructions

DRUG RECEIPT

1. Upon receipt of drug, immediately retrieve the temperature monitor.
    - The LCD screen should show RUN and either:
        i. A ✔ icon indicating that the LIBERO is active and temperature is within specification, or
        ii. A ✘ icon indicating that a temperature excursion has occurred.
2. Press down on the STOP button until the STOP appears along the bottom of the LCD screen (~ 3 seconds).
3. If ONLY STOP and ✔ icon appears on the LCD screen:
    - Shipment arrived in acceptable condition.
    - Place in appropriate storage conditions.
    - Download the temperature monitor data (see instructions for downloading).
    - Email the temperature monitor to appropriate recipient

- If the ✘ icon appears:
    - The temperature was outside of the acceptable condition during transit.
    - Place the drug in quarantine under appropriate storage conditions.
    - Download the temperature monitor data (see instructions for downloading).
    - Email the temperature monitor to appropriate recipient
    - Immediately contact your study CRA.

INSTRUCTIONS FOR DOWNLOADING THE USB TEMPERATURE MONITOR DATA:

1. Remove the clear rubber USB cover
2. Connect the monitor to a computer via the USB
3. Once inserted, PDF will appear on the LCD screen
4. Depending on the configuration of your computer, the LIBERO file folder may open automatically, if not then you should browse to the file folder the same as you would for any other USB device.
5. Double click the Adobe Acrobat PDF file (note: the file name corresponds to the LIBERO serial number).
6. Print and save the Adobe Acrobat PDF file along with the packing slip in the appropriate study file.
7. Refer to Site Manual for additional instructions as appropriate.

We recommend against the use of a PDF Editor application to save the PDF file otherwise the embedded data will be lost and no further analysis will be possible. Copy and Paste the file into the appropriate folder or email.

Please Note: After downloading the LIBERO data, the device may be disposed of according to local regulations.

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Authorization for Destruction

Date: **<<DDMMMYYYY>>**
Subject: Authorization of Destruction for **<<List the name of Investigational Product (IP) and/or Commercial Drugs>>**
Protocol **<< Protocol Number>>**, Site Number **<<Site Number>>**

Delete all instructional blue text in the finalized form

Authorization for On-Site Destruction [Delete this section if Depot Destruction will be performed]

I have authorized the destruction of the below mentioned clinical supplies.

☐	Drug Description	Enter Drug Description
☐	Batch Number	Enter Batch Number on Clinical Label
☐	Total Quantity	Enter Total Quantity to be Destroyed
	Reference Numbers	
	List Reference Numbers in the rows below OR add statement to see attached report for reference numbers then delete the rows.	
☐		
☐		
☐		
☐		
☐		
☐		

After the destruction is complete, the following evidence of destruction will be documented as per site's procedure and forwarded to the CRA for filing in TMF.

Select the applicable evidence of destruction documentation	
☐	Certificate of Destruction (CoD)
☐	Equivalent Documentation

Print Name/ Signature	**Date**
Title [Site Pharmacist or designee]	

REGENERON

Authorization for Destruction

Delete all instructional blue text in the finalized form

Authorization for Depot Destruction [Delete this section if On-site Destruction will be performed]

I authorize the destruction of the below mentioned clinical supplies. After the destruction is complete, please provide the Certificate of Destruction to Regeneron Clinical Drug Supply & Logistics.

Drug Description	Enter Drug Description
Batch Number	Enter Batch Number on Clinical Label
Total Quantity	Enter Total Quantity to be Destroyed
Reference Numbers	Refer to Attachment # <<Add Attachment #>> for reference numbers

Delete or add additional tables below, as needed

Drug Description	Enter Drug Description
Batch Number	Enter Batch Number on Clinical Label
Total Quantity	Enter Total Quantity to be Destroyed
Reference Numbers	Refer to Attachment # <<Add Attachment #>> for reference numbers

Drug Description	Enter Drug Description
Batch Number	Enter Batch Number on Clinical Label
Total Quantity	Enter Total Quantity to be Destroyed
Reference Numbers	Refer to Attachment # <<Add Attachment #>> for reference numbers

Print Name/ Signature	**Date**
Add 'Refer to Appended Signature Page' note if signed by approver in TMF	
Title [Clinical Drug Supply & Logistics Manager or designee]	

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Clinical Trial Ancillary Supply Site Item Request

Protocol / Study Information			
Protocol / Study Number:		Requested By:	
Request Submission Date:		Requestor Role:	
Requested Delivery Date:		Requestor Email:	

Site Information					
Site Name:					
Site Number:		Contact / Investigator:			
Address:					
Town / City:		State / Province / Region:		Postal Code:	
Country:		Telephone:		Contact Email:	

Item Number	Product Description	Current Inventory	Quantity Requested	Requested Product Specifics Serial #/ Lot #/ Other	Storage	Expiry

Comments/Instructions

Signature Page for VV-TMF-2716144 v1.0

Reason for signing: Approved	Name: Giovanni Dibiase Role: Clinical Trial Management Date of signature: 13-Sep-2023 16:07:31 GMT+0000

Reason for signing: Approved	Name: Erika Floyd Role: Clinical Trial Management Date of signature: 13-Sep-2023 16:08:08 GMT+0000

Reason for signing: Approved	Name: Yuan Cheng Role: Other Date of signature: 13-Sep-2023 16:14:22 GMT+0000

Reason for signing: Approved	Name: Ameet Narwal Role: Clinical Trial Management Date of signature: 13-Sep-2023 16:25:21 GMT+0000

Reason for signing: Approved	Name: Soujanya Chandrasekharan Role: Clinical Trial Management Date of signature: 13-Sep-2023 16:36:46 GMT+0000

Reason for signing: Approved	Name: Chris Campbell Role: Clinical Logistics Date of signature: 13-Sep-2023 16:53:12 GMT+0000

Reason for signing: Approved	Name: Stefani Gjoni Role: Clinical Trial Management Date of signature: 13-Sep-2023 17:10:22 GMT+0000

Reason for signing: Approved	Name: Ashish Risal Role: Medical Monitoring Date of signature: 14-Sep-2023 13:52:50 GMT+0000

Signature Page for VV-TMF-2716144 v1.0

Signature Page for VV-TMF-2716144 v1.0

Reason for signing: Approved	Name: Nazia Iqbal Role: Clinical Monitoring Date of signature: 14-Sep-2023 15:18:40 GMT+0000

Reason for signing: Approved	Name: Manjusha Namuduri Role: Medical Monitoring Date of signature: 14-Sep-2023 15:25:32 GMT+0000

Signature Page for VV-TMF-2716144 v1.0