Pharmacy Manual

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Pharmacy Manual

A Phase II, Open-label, Multi-centre Study to Evaluate Safety, Tolerability, Efficacy, PK, and Immunogenicity of AZD0901 as Monotherapy and in Combination with Anti-cancer Agents in Participants with Advanced Solid Tumours Expressing Claudin 18.2.

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APPROVAL

The signature on this page indicates review and approval of this document. Only one signature is required.

Approved by

	22 January 2025
Maud Fromaget Director Study Leader	**Date**

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LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation or special term	Explanation
CSP	Clinical Study Protocol
CRF	Case Report Form
DOR	Site Signature and Delegation of Responsibilities Log
EDC	Electronic Data Capture
IMP	Investigational Medicinal Product
ISF	Investigator Site File
N/A	Not applicable
NIMP	Non-investigational Medicinal Product
PI	Principal Investigator
RTSM	Randomization and Trial Supply Management
Study Intervention	Study interventions are all pre-specified, IMPs and NIMPs, medical devices and other interventions (e.g., surgical and behavioral) intended to be administered to the study participants during the study conduct.

1. PURPOSE

Pharmacy Manual is used in conjunction with the Clinical Study Protocol (CSP). This document applies to all products centrally supplied by AstraZeneca.

The manual provides instructions to the pharmacist or personnel responsible for the ordering, receipt, storage, preparation, labelling, administration and distribution of AZD0901. It also provides instruction on the ordering, receipt and storage of Chemotherapy treatments, if supplied by AstraZeneca. This manual also describes responsibilities for compounding and dispensing preparations of proper identity, strength, purity and quality.

For locally sourced chemotherapy agents, local procedures as per local policy should be followed.

2. SITE RESPONSIBILITIES

2.1 Site Personnel Responsibilities

Assignment of responsibility for the performance of study related procedures must be documented on the Site Signature and Delegation of Responsibilities (DOR) Log. The Principal Investigator (PI) for the study site is responsible for ensuring that only appropriately trained, licensed and/or certified medical healthcare professionals are assigned (delegated) to prepare and administer AZD0901/Chemo in accordance with local

regulations, protocol specifications and international regulations/guidelines and as detailed in this Pharmacy Manual if the PI will not be performing these tasks personally.

Additional site responsibilities:

1. The RTSM (Randomization and Trial Supply Management) system will calculate weight based doses consistent with the approved Clinical Study Protocol. The pharmacy team at the investigator site will have oversight of the RTSM system and will consult the identical dosing schema/instructions when verifying the dispensed dose is appropriate for the given patient.

2. As the dose calculations are based on approved instructions contained in the protocol, the RTSM system is only a convenience/adjunct to assist qualified pharmacy staff, and the pharmacy staff are expected to verify calculations are correct, the additional RTSM system function is considered as unlikely to be a medical device.

2.2 Personnel Documentation

The Responsible Person for AZD0901/Chemo management at the site and any person working with them, such as a technician or other assistant, must be licensed and certified according to local and international laws for the preparation and dispensing of AZD0901/Chemo in accordance with the CSP. In addition, each person must also be listed on the DOR. Any change of the site's Responsible Person must be reported as soon as possible to the Site Monitor. The DOR record must be updated and filed according to Investigator Site File (ISF) Index.

2.3 Accountability

Accountability is the process of documenting all aspects of AZD0901/Chemo receipt, storage, dispensation/use, return and destruction (so that a full accounting of each unit can be made).

Accountability checks are to be performed and documented, so the documentation related to AZD0901/Chemo is complete and accurate and any discrepancies explained and documented, and appropriate action taken.

The level of accountability must be at least on participant kit level or as defined in the study's Monitoring Plan. An overall final accountability check on site level is performed, when a particular study is closed at a site.

Accountability has to be documented from the moment of receipt through dispensation and the final disposal allowing traceability of AZD0901/Chemo at any moment. Dispensation can begin after site is ready to enrol and all relevant procedures were followed in order to ensure AZD0901/Chemo is approved for use.

Furthermore, documentation must be clear as to who made the entries (for example for dispensing, for return etc.) by evidence of signature and date. For accountability details site can use a paper log, for e.g. 'Study Drug Dispensing Log' or equivalent form used locally (by the Investigative Site, Local Study Team, CRO). Inventory records of received and dispensed Study Drug must be kept at the Investigative Site. The record may be electronic, in the RTSM, if applicable. If the record is electronic, it must be saved electronically for electronic ISF, or printed and filed in the ISF, if paper-based, on an ongoing basis.

2.4 Investigational Medicinal Product Administration Data Entry

After AZD0901/Chemo administration is completed, the accountability log must be updated. The updated log should be forwarded to the site personnel responsible for data entry. The following drug administration data points are required in Electronic Data Capture:

- Dose
- Date of All Study Intervention Administered
- Administration Time (Start date/Time and End date/Time of administration)
- Location Dose Administered – collected only if the Study Drug Administration or Location was Impacted by Global/Country Situation.
- Action Taken (Dose not changed, drug interrupted, Dose Reduced, Drug Withdrawn, Not applicable and Unknown)
- Main Reason for Action Taken (Adverse event, Dose administration error and Other (for Other, please specify the reason)).

2.5 HomeSupply

Not applicable

2.6 Deviations

If a deviation occurs during the preparation, dispensing and dosing of study intervention, including an error in administration, or misallocated kit event, contact the Site Monitor immediately. The deviation will be reported and documented in accordance with local procedures. A copy of the deviation may be attached to the dispensing documentation. The site must report the deviation to their IRB/EC per their IRB/EC reporting guidelines.

Any deviation from this standard must be reported to the Site Monitor immediately upon detection.

2.7 Monitoring

AZD0901/Chemo documentation, on site storage and supply will be routinely monitored by a Site Monitor soon after the first study participant is dosed and periodically thereafter by

onsite or remote monitoring visits (as per the Monitoring Plan). The site will be notified in advance by the Site Monitor as to the date and time of each monitoring visit.

2.8 Reconciliation, Return and/or Destruction of AZD0901/Chemo

After reconciliation, unused AZD0901/Chemo will be destroyed. This must be confirmed by the Sponsor before commencing any destruction of AZD0901/Chemo. The Site Monitor will arrange for all remaining AZD0901/Chemo to be destroyed at the study site according to local procedures and in accordance with all applicable local and international laws. The original Certificate of Destruction for all destroyed AZD0901/Chemo should be retained in the Pharmacy Binder.

2.9 Pharmacy Binder

All AZD0901/Chemo-related records must be kept current and on-site. The following records must be kept in an appropriate location (eg, Pharmacy file and/or Investigator site file based on local procedures). Examples of records are as follows, but not limited to:

- Current, IRB approved version of the CSP
- Current version of the Pharmacy Manual
- Shipment packing slips
- Temperature monitoring reports downloaded from Temperature Monitors received with all drug shipments
- RTSM Shipment Confirmation Notifications
- Copies of Study Site Temperature Logs
- Investigational Product Accountability Records
- Copy of Delegation of Responsibilities Log for the Study Site Team
- Temperature Excursion forms together with corresponding AZ Supply Chain documentation/reports
- Material Safety Data Sheets (MSDS). If a commercial comparator drug is used in the study, the associated MSDS must also be filed
- Study-specific correspondence regarding AZD0901/Chemo management
- Certificates of Destruction along with documentation of approval for destruction
- Information/forms documenting defects of AZD0901/Chemo

If files are kept electronically, a note to file must be kept in the Pharmacy Binder designating the electronic location of these files.

2.10 Record keeping

It is clinical site responsibility to ensure that all records are retained and available for monitoring throughout the duration of the study until study site closure procedures are performed and/or your site is notified by the Sponsor that the study has ended.

At the end of the study, the Pharmacy Binder must be incorporated into the ISF and archived according to current procedures.

3. INVESTIGATIONAL MEDICINAL PRODUCT

Intervention name	AZD0901	5-Fluorouracil	Leucovorin [a]	l-leucovorin [a]	Irinotecan	Nano-liposomal Irinotecan	Gemcitabine
Type	Antibody-drug conjugate/Biologic	Drug/chemotherapy agents	Drug/ chemotherapy agents	Drug/ chemotherapy agents	Drug/ chemotherapy agents	Drug/ chemotherapy agents	Drug/ chemotherapy agents
Dose formulation	AZD0901 is supplied as a lyophilised product for concentrate for solution for infusion.	Solution for infusion	Solution for infusion	Solution for infusion	Solution for infusion	Liposomal dispersion	Powder, Lyophilised
Use	Experimental	Experimental	Experimental	Experimental	Experimental	Experimental	Experimental
IMP or NIMP/AxMP	IMP	NIMP/IMP[b]	NIMP/IMP[b]	NIMP/IMP[b]	NIMP/IMP[b]	NIMP/IMP[b]	NIMP/IMP[b]
Sourcing	Provided centrally by the Sponsor	Provided locally by the study site, subsidiary, or designee (if required by the Sponsor)	Provided locally by the study site, subsidiary, or designee (if required by the Sponsor)	Provided locally by the study site, subsidiary, or designee (if required by the Sponsor)	Provided locally by the study site, subsidiary, or designee (if required by the Sponsor)	Provided locally by the study site, subsidiary, or designee (if required by the Sponsor)	Provided locally by the study site, subsidiary, or designee (if required by the Sponsor)

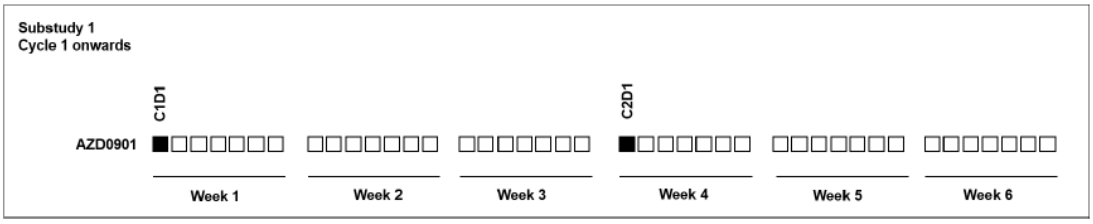
[a] Alternative salt forms of leucovorin or flat dose are permitted, per local guidance[b] These chemotherapy agents are classified as NIMP, unless local regulations (including those of the EU) require them to be designated as IMP.

AxMP = Auxiliary Medicinal Product; IMP = Investigational medicinal product; ; NIMP = non investigational medicinalproduct

In Substudy 1, Substudy 2 and Substudy 3, AZD0901 will be administered either Q3W or Q2W, as per the SoA in CSP Section 1.3.

Figure 1 shows the dosing schedule of AZD0901 in Substudy 1.

Figure 1



C = cycle; D = day.

Figures 2, 3, 4, 5 and 6 show the dosing schedules for Substudy 2.

Figure 2 (Arm 1)

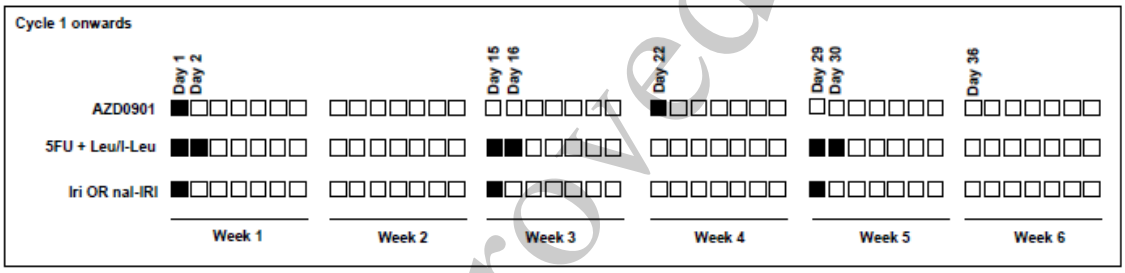


Figure 3 (Arm 1A)

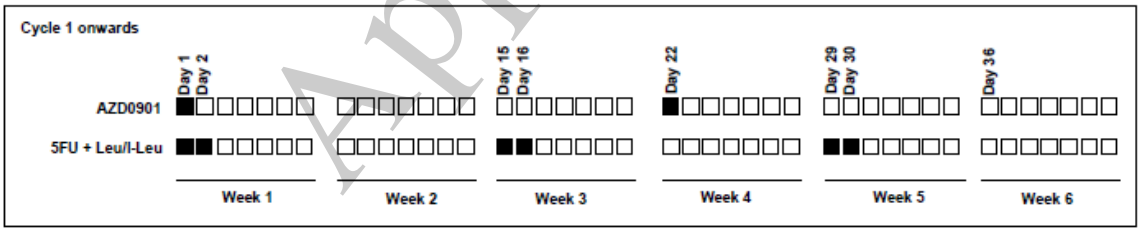


Figure 4 (Arm 1B)

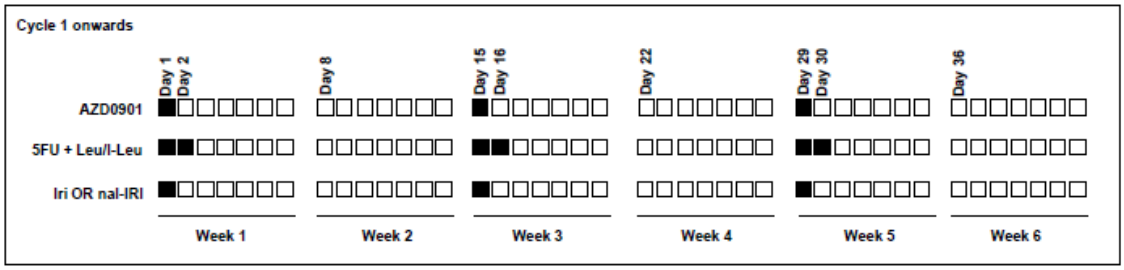


Figure 5 (Arm 1C)

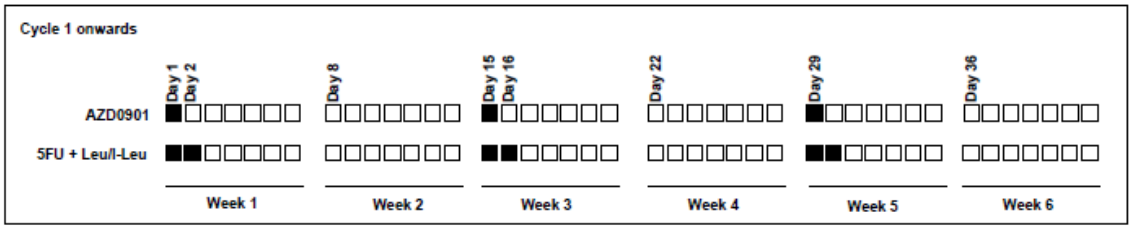


Figure 6 (Arm 2)

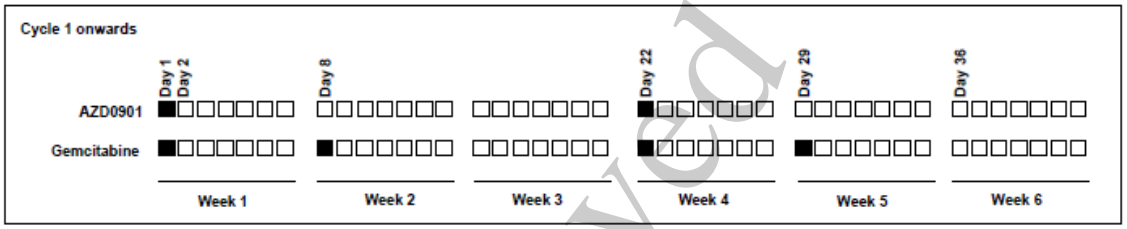
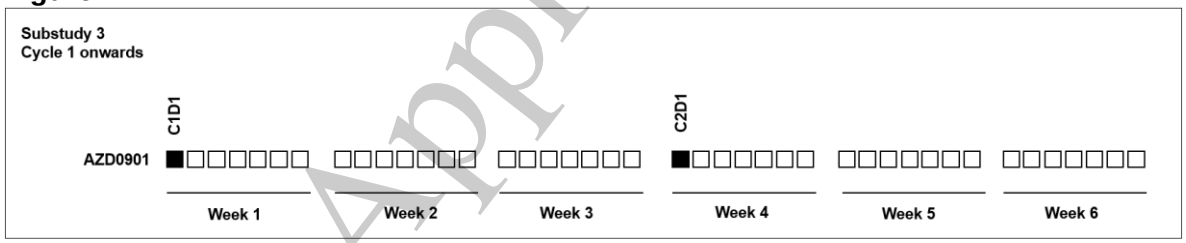


Figure 7 shows the dosing schedule of AZD0901 in Substudy 3.

Figure 7



On days when AZD0901 and chemotherapy are given, AZD0901 must be administered before other chemotherapy agents. Other chemotherapy agents should be administrated at least 60 minutes after end of AZD0901 infusion in the first 2 cycles for close observation of possible drug reactions. Thereafter, other chemotherapy agents will be given per the Investigator's discretion after end of AZD0901 infusion.

In Arm 1, the sequence of 5FU and leucovorin and irinotecan/nanoliposomal irinotecan administration after AZD0901 administration should follow local guidance.

3.1 Kit Description

AZD0901 supplies will consist of:

- single vial kits of AZD0901 (50 mg) which must be stored at site between 2°C to 8°C and protected from light.

Each kit will be labeled with a unique number. This number will be identical to the number on the vial contained inside.

All instructions related to AZD0901 preparation and administration are included in the protocol.

Please note, this section, and any future sections detailing Chemotherapy Therapies (Chemo) only applies to the Chemo supplied by AstraZeneca. All locally sourced material should be stored and prepared by local procedures as per local policy.

Chemo supplies will consist of:

- Single vial kits of Gemcitabine, Leucovorin, 5-FU (5-Fluorouracil), Nanoliposomal Irinotecan and Irinotecan. These must be stored at the following conditions;
    - Gemcitabine
      2°C to 8°C and protected from light
    - Leucovorin
      2°C to 8°C and protected from light
    - 5-FU
      15°C to 25°C and protected from light
    - Nanoliposomal Irinotecan
      2°C to 8°C and protected from light
    - Irinotecan
      15°C to 25°C and protected from light

Each kit will be labeled with a unique number. This number will be identical to the number on the vial contained inside.

4. SHIPMENTS

AZD0901 and the Chemo will be shipped via an appropriate courier and under appropriate storage conditions. All shipments should be inspected and processed immediately upon receipt and placed in the appropriate storage conditions.

4.1 Initial Shipments (Site Seeding)

Initial shipments will automatically be sent to each site at the time the site is approved by AstraZeneca to begin the study.

4.2 Re-Supply Shipments

The Randomization and Trial Supply Management (RTSM) system will automatically initiate resupply shipments to the site based on predetermined site inventory levels programmed into the system. The RTSM system will send the shipment request to the depot for processing. IMP will not be available for dosing until the site confirms receipt of the shipment with the RTSM system. The Site Monitor will follow-up with the site regarding shipments not confirmed as received.

5. RECEIVING SHIPMENTS

Each shipment will include:

- a packing slip,
- a Shipment Temperature Verification Form,
- a temperature monitor,
- an instruction sheet.

These documents should be retained with the site's study records. If any of the shipment documentation is missing, immediately contact your Site Monitor.

5.1 Shipment Temperature Verification

Follow the instructions for downloading the temperature data that are received with the shipment. Review the data on the enclosed temperature monitoring device to verify the transit temperature was maintained within labeled storage conditions. Check that the shipment contents match the packing list and that there is no physical damage.

If the temperature monitoring device is faulty, damaged or missing and the temperature cannot be displayed or downloaded, contact the Site Monitor immediately and await further instructions (e.g. return/ retrieval of the temperature monitoring device or next steps). Place the material in QUARANTINE according to the labeled storage conditions, segregated from other material until further notice.

The Shipment Temperature Verification Form must be completed and temperature monitor data downloaded; both items should be retained with site records. Each shipment received MUST be confirmed within the RTSM system prior to use. Please see RTSM Site User Instruction Manual for detailed instructions on how to confirm receipt of the IMP in the system.

The form must be returned to the Sponsor in the case of temperature excursions, discrepancies or defects (described in the following sections) for Sponsor review and assessment.

5.1.1 Acceptable Temperature

If the transit temperature was maintained within acceptable limits per label, and there were no shipment discrepancies or defects, then the AZD0901/Chemo is considered acceptable for use and should be stored according to the labeled storage conditions.

5.1.2 Unacceptable Temperature

If the transit temperature was not maintained within acceptable limits during transit, a temperature variation has occurred.

Complete the Shipment Temperature Verification Form and return this form and a copy of the printout of the temperature readings to the Sponsor via the contact information listed on the form. Section 2 of the Shipment Temperature Verification Form will be completed by the Sponsor, indicating whether AZD0901/Chemo is acceptable for use or rejected, and will be returned to the site contact person.

QUARANTINE all affected AZD0901/Chemo according to the labeled storage conditions, segregated from all other AZD0901/Chemo for the study, until further instruction is provided. Do not use the supply until the Shipment Temperature Verification Form is received back confirming that AZD0901/Chemo is acceptable for use in the study. If AZD0901/Chemo is not acceptable for use, a new shipment request will be processed for your site automatically.

As long as an AZD0901/Chemo kit is classified as quarantined in RTSM, the system will not allocate that kit to a subject.

5.1.3 Damage or Discrepancies

If the product received does not match the packing slip, there was damage in some of the AZD0901/Chemo or there is a discrepancy in the appearance of the material (e.g. flocculation, turbidity, volume or discoloration), then QUARANTINE all affected AZD0901/Chemo according to the labeled storage conditions segregated from all other AZD0901/Chemo for the study. Report shipment defects to the Sponsor by entering the details in the Comments section of the Shipment Temperature Verification Form. Return the form to the Sponsor via the contact information listed on the form. Note the defective kits within the RTSM system during the shipment receipt process.

Confirm shipment arrival in the shipment receipt module of the RTSM system, indicating the defective items during receipt. You may be contacted by the Sponsor if further information is needed.

A replacement shipment will be generated as required.

5.1.4 Reporting Product Complaints

Any defects with AZD0901/Chemo must be reported immediately to the AstraZeneca Product Complaint Department by the site with further notification to the site monitor. All defects will be communicated to AstraZeneca via Product Complaint Intake Form or equivalent and investigated further by the Product Complaint Department. During the investigation of the product complaint, all AZD0901/Chemo must be stored at labeled conditions and placed in QUARANTINE status in the RTSM system, unless otherwise instructed.

Contact information for reporting product complaints only:

Email contact: productcomplaints3@astrazeneca.com
Phone: +1-301-398-2105
Mail: Medimmune
Attn: Product Complaint Department
One MedImmune Way
Gaithersburg, MD USA 20878

Please note that the above contact is not for temperature excursions.

6. AZD0901 STORAGE AND TEMPERATURE MONITORING

AZD0901 and chemo must be stored at the conditions per the original outer package, as detailed in Section 3.1. All AZD0901/Chemo should be stored in a secure location with limited access.

6.1 Temperature Excursions

It is preferable that the refrigerator has an electronic temperature monitoring system or chart recorder and be on an electrical system that has an alternate power source in the event of power outages. While an electronic temperature monitoring system is preferable, the use of a min/max thermometer is acceptable. At a minimum, the on-site refrigerator must have daily (Monday through Friday) temperature monitoring of the min/max temperatures and documented in a log. For all manual log entries, appropriate GxP data entry (i.e. contemporaneous, initials and date) must be made. Holiday and weekends that do not allow for daily temperature recording should be documented indicating the reason why a temperature reading was not taken. Empty entries are not acceptable and will be returned to the site for further clarification.

Documentation of refrigerator temperature monitoring must be available for your Site Monitor. All short-term temperature variations from the acceptable storage temperature range for stored AZD0901/Chemo must be reported immediately to your Site Monitor. Once a short-term temperature variation has been identified at your site, no subjects

should be dosed with the material in question until a decision has been made by AstraZeneca and communicated to your site.

Site personnel will immediately notify the site monitor and provide the monitor with a completed Notification of IMP Temperature Variation at Clinical Site Form and a copy of the site's AZD0901/Chemo Storage Temperature Logs. AstraZeneca Logistics and Clinical Supply (LCS) will respond to the site monitor with a completed form stating the status of the affected product and will initiate a re-supply of AZD0901/Chemo, if required. AstraZeneca, Logistics and Clinical Supply (LCS) reviews all temperature excursions within one business day from receipt of fully completed paperwork (GMT -4/5, EDT/EST).

6.2 Expiration Date Management

AstraZeneca is responsible for overall management of expiry date of AZD0901/Chemo, and is based on continued stability studies. Prior to AZD0901/Chemo reaching its expiry date, a new supply of AZD0901/Chemo will be provided to your site or an expiration date extension will be established to preclude interruption of subject dosing.

Additionally, the RTSM system is programmed with several constraints to manage expiry dates. These constraints will not allow the RTSM system to dispense any AZD0901/Chemo once the expiry date has been reached. The expiry dates for AZD0901/Chemo will be maintained in the RTSM system by AstraZeneca. In the case that there is not a printed expiry date on the AZD0901/Chemo supply at your site, refer to the RTSM system for the most current expiry date for that product.

7. REVISION HISTORY

The Pharmacy Manual is a living document and updates may be required during the life of the study.

The table below indicates any changes made to the first approved version of the Pharmacy Manual.

Version	Description of Change	Date
1.0	Original Document	30 November 2023
2.0	Section 3 – changes in content Section 7 – changes in content	20 February 2024
3.0	Section 1, 2, 3, 4, 5, 6, 7 and 8 – changes in content	08 October 2024
4.0	Section 2.8 – changes in content Section 3 – changes in content; addition of Substudy 3	13 January 2025

8. APPENDICES

8.1 Drug Handling Instructions

AZD0901

Details of AZD0901 are listed below. All products must be used within the individually assigned expiry date on the label.

AZD0901

Type: Biologic

Dose Form: Sterile lyophilised product for concentrate for solution for infusion

Unit Dose Strength: 50 mg

Formulation: 10 mM L-histidine/L-histidine-HCl, 88 mM sucrose, 0.03% weight/volume (w/v) polysorbate 80, pH 5.5

Density: 1.014 g/mL

Storage: 2°C to 8°C (36°F to 46°F)

Dosing: Refer to the CSP for dosing details

Route of Administration; Infusion Time: IV infusion; 90 minutes

Preparation of AZD0901

The dose of AZD0901 for administration must be prepared by the pharmacy staff members (or an appropriate designee trained in study drug preparation), using aseptic technique in compliance with local regulations and site requirements.

Special Handling of AZD0901

AZD0901 must be kept in original packaging until time of preparation to prevent prolonged light exposure.

AZD0901 must not be frozen.

The use of Closed System Transfer Devices (CSTDs) and pneumatic tube transport with AZD0901 have not been studied, contact AstraZeneca before using.

AZD0901 should be handled in accordance with practices required for preparation and administration of a hazardous drug.

Dose Calculation(s)

The dose volume will be calculated using the following formula:

$$Dose\ volume\ (mL) = \frac{Subject\ weight\ (kg)\ x\ Dose\ level\ (mg/kg)}{Drug\ concentration\ (mg/mL)}$$

(For the measurement of subject weight(kg), use one decimal point).

The corresponding volume of AZD0901 should be rounded to the nearest tenth of a mL (i.e., 0.1 mL).

The number of AZD0901 vials needed to supply the dose is calculated by dividing the total dose volume by the label-claim volume per vial (5.0 mL), rounded up to the unit vial.

$$Number\ of\ vials = \frac{Calc.total\ dose\ volume\ (mL)}{Label\ claim\ volume\ (mL)}$$

AZD0901 Compatibility

Components of the following materials of construction have been demonstrated to be compatible with AZD0901 at 0.2 to 3.0 mg/mL in 0.9% sodium chloride for injection:

- Appropriately sized polypropylene (PP) syringes
- Stainless steel needles
- Polypropylene (PP) IV bags
- Polyethersulfone (PES) filters
- Polypropylene (PP) or polyethylene (PE) lines

Dose Preparation Procedure

Vials of AZD0901 should reach room temperature and be kept inside the original packaging prior to dose preparation.

AZD0901 Visual Inspection

Each vial selected for dose preparation should be inspected.

AZD0901 is a lyophilized white to off-white solid. Following reconstitution, AZD0901 is a clear to slightly opalescent, colorless to pale yellow solution, free from visible particles.

If there are any defects noted with the AZD0901, the investigator and site monitor should be notified immediately. Refer to the Product Complaint section for further instructions.

AZD0901 Reconstitution

To reconstitute, slowly add 5.2 mL of Sterile Water for Injection (SWFI) by tilting the vial to one side such that the liquid stream is directed along the vial wall and not directly onto the lyophilized product. Gently swirl the solution until all the solids are dissolved. Gently invert the vial to dissolve any solids that may be present at the neck of the vial or on the stopper. DO NOT SHAKE OR VIGOROUSLY AGITATE THE VIAL. Visually inspect the solution to ensure that the entire content of the lyophilized product is completely reconstituted. A thin layer of bubbles on the surface of the reconstituted liquid is normal.

Following reconstitution, the solution concentration is 10 mg/mL and the label-claim volume is 5.0 mL.

IV Bag Preparation

Doses of AZD0901 will be prepared using an IV bag containing 0.9% sodium chloride for injection. Remove the equivalent calculated volume of diluent from the IV bag prior to addition of IMP. Add the calculated volume of AZD0901 to the IV bag. The IV bag size must be selected such that the final concentration of AZD0901 in the IV bag is within 0.2 to 3.0 mg/mL, additionally, the selected IV bag size must not be > 250 mL. Mix the bag by gently inverting to ensure homogeneity of the dose in the bag. Do not shake the prepared IV bag.

Prepared Dose Stability

The total time from needle puncture of the AZD0901 vial to the start of administration must not exceed 4 hours. Otherwise, a new dose must be prepared from new vials.

AZD0901 infusion time is 90 minutes (± 10 minutes); however, if there are interruptions, the total allowable time from needle puncture of the AZD0901 vial to the completion of infusion must not exceed 6 hours with the IV bag maintained at room temperature, otherwise a new dose must be prepared from new vials.

AZD0901 does not contain preservatives; any unused portion of the vial must be discarded immediately after use.

Administration of AZD0901

Refer to the clinical study protocol for detailed administration instructions.

8.2 Notification of IMP Temperature Excursion at Clinical Site

Notification of IMP Temperature Excursion at a Clinical Site					
Protocol #:		Product:		Site #:	
Site Contact & email address:		Phone #:		Fax #:	
Section 1: Temperature Excursion Summary Provide a brief (but detailed) summary of the investigational medicinal product storage issue including how, when and by whom you were notified					
Section 2: Temperature Excursion Data Provide the following specific information and attach a copy of the site temperature log for verification (Required)					
Date(s) and time(s) of temperature excursion:			Duration of excursion:		
IMP temperature excursion range (min/max):			Number of vials/ kits affected:		
Section 3: Quality Detail Provide the following information to aid in assessing the impact of this temperature excursion on the study.					
Were subjects dosed with IMP during or after this temperature excursion? If yes, please include dates.				☐ Yes ☐ No	
If Yes, list those subject numbers:					
If Yes, list the kit/vial/ lot #s utilized (as appropriate):					
How many kits/vials remain on site:					
What kit/vial lot #'s remain on site?					
Additional comments or information: (e.g., Upcoming dosing dates etc.)					
Does this site require immediate resupply?: (If Yes, request shipment # per normal protocol procedures)		☐ Yes		☐ No	
Completed By		Signature		Date	
Section 4: Site Monitor/Unblinded Site Monitor or designee Review the form for completeness. Sign and date this form and send to Clinical_Supply_Operations@astrazeneca.com for issue resolution. **IMP must not be used until section 5 of this form has been completed and returned by LCS.**					
Print/Sign _____ Date_____					

Attach temperature log

Section 5: IMP Assessment (LCS USE ONLY)	**Receipt Date:**

5.1	Temperature excursion Memo/ Source document reference:	
5.2	Is temperature excursion within source document parameters?	Yes ☐ **IMP acceptable for use**-Skip to Section 5.4 No ☐ **IMP Not acceptable for use**-Continue to Section 5.3 if NC is applicable.
5.3	Investigation required to support excursion.	NC#: _____ N/A ☐
5.4	Date of Disposition	
5.5	LCS Reference Number	

5.6

IMP assessment completed by:

Name:

Signature/Date:

Assessment verified by:

Name:

Signature/Date:

8.3 Product Complaint Intake Form

Product Complaint Intake Form

Please ensure ALL pages of this form are filled out

Defect awareness date (dd/mm/yyyy):		**Are photos available?** *If yes, please provide photos on page 2*	☐ Yes ☐ No
Site number:		**Impacted Kit ID(s):**	
E-code (patient code):		**Lot number(s):**	
Study number:		**Batch(es):**	
Study name:		**Number of defective units:**	
Blinding status of study:		**Kit type (vial/kit/device/tablet/capsule):**	
Product name:		**Expiry date of product:**	
Product available for return?	☐ Yes ☐ No	**Reported strength of product:**	
Number of samples available for return:		**Unit of measure of product (mL, mg):**	
Was the product administered?	☐ Yes ☐ No	**SaMD version number:**	
Date product administered (dd/mm/yyyy):		**Was sample stored as per recommended storage conditions?** *If not, please detail storage conditions*	
Replacement Needed/Administered	☐ Yes ☐ No	**Did the complaint cause any SAE/AE in subject/patient?** *If yes, please detail in the description section on page 2*	☐ Yes ☐ No
How was the product/device administered? ☐ N/A ☐ Self-administered ☐ Health Care Professional administered		**Did the complaint cause any SAE/AE in anyone else?** *If yes, please detail in the description section on page 2*	☐ Yes ☐ No

Reporter Details	**Site Details**
Reporter Name (including salutation):	**Site Name:**
Reporter Address: Street: City: Country: Postal Code:	**Site Mailing Address:** Street: City: Country: Postal Code:
Reporter Email:	**1st Contact at site:** Name:

Please ensure ALL pages of this form are filled out

Reporter Phone:	Email: Phone:
Reporter Occupation:	**2nd Contact at site:** Name:
Reporter Organisation:	Email: Phone :

Mandatory for Japan/Optional for Rest of World (ROW):
Did the device malfunction likely cause a serious adverse event (SAE) in the subject/patient? ☐ Yes ☐ No Did the device malfunction cause a serious adverse event (SAE) in anyone else (e.g., investigator, nurse, distributor) besides the subject/patient? ☐ Yes ☐ No *If yes to any of the above: please provide more details in the Description section on page 2.*

Report Type: Check the appropriate box that defines the reported event	
☐ Device (includes combination product) malfunction	☐ Device (includes combination products) malfunction – with **AE/SAE** in Subject
☐ Shipment – *please specify shipment details, courier, site/depot shipped from and site/depot shipped to below*	
☐ Other (bottling, labelling, etc., specify on next page):	

Please ensure ALL pages of this form are filled out

Description: Please describe the issue – What happened? How has it happened? Were there immediate actions to contain the issue? Include timelines for the different events in the issue. Where there any adverse events / serious adverse events? *Please also fill out the table below on page 2 of this form to categorize the issue*

Photos – *please provide clear photos of the defect below or attach to the email when reporting the complaint*

Check the appropriate product defect malfunction(s) that best described the event. Complete the DESCRIPTION section above with a detailed description of the defect.			
☐ **Drug Delivery Failure**	☐ **Breakage**	☐ **Product**	☐ **Design Failure**
☐ Unable to remove needle shield/cap	☐ Broken/Malformed/Damaged	☐ Appearance e.g., discolouration, cloudy, spots	☐ Difficult to use product e.g., turning, twisting, confusing, blister difficult to open)
☐ Needle guard / safety feature did not activate	☐ Broken /Bent/ Damaged /Clogged Needle	☐ Foreign matter/particulate matter	☐ Unable to check contents
☐ Incorrect dosing-Early/Late	☐ Attachment/Detachment Issue (e.g., needle guard, syringe, plunger rod, cap, mouthpiece, canister, actuator)	☐ Volume-underfill/overfill or empty (specify)	☐ Indicator malfunction (e.g., dose knob/selection window/wheel)

Please ensure ALL pages of this form are filled out

☐ Safety Shield Activate or deployed-Early/Late	☐ Leakage (before, during or after use)	☐ Incomplete consistency/solubility	☐ Not working
☐ Medication not dispensed or dispersed (reconstituted)	☐ Misplaced Item (e.g., plunger movement, inhaler parts)	☐ Odour/taste	☐ Pen button jammed or broken (e.g., no click)
☐ Partial Dose delivered or no dose delivered	☐ Other, please specify	☐ Broken/Damaged e.g., chipped/split tablets, capsule defects, etc	☐ Instructions for use is unclear, incorrect or is causing the improper use of the product
☐ Other, please specify		☐ Other, please specify	☐ Plunger rod or autoinjector difficult to depress
			☐ Other, please specify
☐ **Medical**	☐ **Packaging/Labelling**	☐ **Missing**	☐ **Product Security**
☐ Lack of Effect	☐ Broken/ Malformed/ Damaged	☐ Part of the device/ product/ instructions for use is missing	☐ Product is an illegal representation and is counterfeit suspected
☐ Medication Error	☐ Printing (missing, illegible, or incorrect)	☐ Other, please specify	☐ Product has signs of intrusion and suspected of tampering
☐ Off-Label Use/Misuse	☐ Missing item		☐ Missing shipment
☐ Other, please specify	☐ Other, please specify		☐ Other, please specify

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Reason for signing: Document Reviewed and Approved	Name: Maud Fromaget Date of signature: 23-Jan-2025 21:56:15 GMT+0000

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