GENE THERAPY - ZOLGENSMA® ADMINISTRATION AND HANDLING

PROCEDURE ©

DOCUMENT SUMMARY/KEY POINTS

- Staff involved in the handling and administration of Zolgensma® must be trained on the handling and administration and; the disposal of genetically modified organisms (GMO's) via network biosafety training.
- All administration care, including requirements for Personal Protective Equipment (PPE), should follow standard clinical care practices, unless it is nominated that additional safeguards are necessary to protect patients, staff and the environment, in accordance with the Product Information (PI) and any conditions set out in the OGTR licence.
- Zolgensma® is classified as a GMO and as such should be treated as biohazardous clinical waste in accordance with the SCHN Policy 2021-197 – Transport, Waste & Spill Management of Medicinal Products containing Genetically Modified Organisms. PPE must be worn at all times when handling Zolgensma®, including connection and disconnection of the infusion and up until disposal of all equipment and supplies that have come in contact with the agent.
- Patient and family verbal and/or written education must be delivered by the treating medical officer or delegate prior to administration of Zolgensma®.
- Parental/carer consent for treatment of the patient is required prior to administration of Zolgensma® and documented accordingly. The clinical space to be used for administration must be appropriate, with consideration of the patient's condition/care needs, risks and requirements associated with the administration of Zolgensma®.
- This guideline must be followed by all staff involved in the handling and administration of Zolgensma® gene therapy at SCHN.

Emergency Equipment and appropriate Spill Kit must be available in the clinical area.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st December 2021	**Review Period:** 3 Years
Team Leader:	Advanced Therapeutics Program Manager	**Area/Dept**: Kids Research

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CHANGE SUMMARY

- Not applicable – New Document

READ ACKNOWLEDGEMENT

Training/Assessment Required

- Staff responsible for the direct management and care of patients receiving Zolgensma® must read and acknowledge this guideline.
- Staff responsible for the administration of Zolgensma® must complete annual biosafety training for clinical staff working with GMOs and show evidence of completion.
- Staff involved in the administration or care of a patient who has received Zolgensma® must read and acknowledge the SCHN *In-vivo* gene therapy –Handling and administration procedure document.
- Staff responsible for the direct management and care of patients receiving Zolgensma® must read and acknowledge the SCHN Transport, Waste & Spill management of Medicinal Products containing GMO's procedure document.
- All medical and nursing staff working with Zolgensma® gene therapy should read SCHN 'Medication Administration' ePolicy and NSW Health Policy – Medication Handling in NSW Public Health Facilities.

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Purpose / Scope

- The purpose of this guideline is to ensure that Zolgensma® is administered in compliance with the conditions of the Office of Gene Technology Regulator (OGTR) licence issued to Novartis Australia Pty Ltd, NSW Health and SCHN policy and procedures and regulatory requirements by the Therapeutic Goods Administration (TGA) in order to ensure the safety of patients, staff and the environment.
- The requirements of this guideline are applicable to the commercial regulatory pathway Zolgensma® will be administered under.
- Procedures for pharmacy in relation to the gene therapy product receipt, storage, accountability and reconstitution of Zolgensma® are outside the scope of this document.
- Procedures for transport of Zolgensma® from the Pharmacy to the clinical area are outside the scope of this document.
- For procedures for managing waste or spill's associated with the administration of Zolgensma ® refer to the SCHN Policy – Transport, Waste & Spill Management of Medicinal Products containing GMOs.

Expected Outcome

To ensure all staff involved with the administering and handling of Zolgensma® are aware of the requirements in accordance with the OGTR licence agreement and the safety precautions required to reduce potential risk and adverse events for patients, families, staff and the organisation.

Background

- Patients with SMA have mutations in both copies of the survival motor neuron 1 gene (*SMN1).* This causes a deficiency in survival motor neurone (SMN) protein, which is required for the development and maintenance of a healthy motor neuron in the spinal cord. People with untreated SMA experience muscle weakness and atrophy and related comorbidities, including disability in motor function, musculoskeletal deformities (scoliosis and contractures) and respiratory impairment.
- Zolgensma® (onasemnogene abeparvovec), is a prescription gene therapy used to treat children with Spinal Muscular Atrophy (SMA). It consists of adeno-associated virus type 9 (AAV9) capsids (the vector or delivery vehicle), each containing a working copy of human SMN gene. Zolgensma® is a one-time only intravenous dose (used with at least two months of oral prednisolone) and does not change or become a part of the child's DNA.
- When Zolgensma® was trialled and given to pre-symptomatic infants with a genetic diagnosis of SMA, normal motor development was seen.

- Zolgensma® has been approved in Australia by the TGA for treatment of children with genetically confirmed SMA under nine (9) months of age.
- *In vivo* gene therapies are rapidly developing and may introduce new risks to patients, staff and the environment. Due diligence must be applied in ensuring that the treating medical officer and patient care team are aware of the unique profile of Zolgensma®, including any additional safeguards necessary to protect patients, staff and the environment.

Patient and Family Education

- Patient and family verbal and/or written education must be delivered by the treating medical officer or delegate prior to administration of Zolgensma®.
- Any education provided to the patient and family must be clearly documented, along with the consent process, in the patient's electronic medical record (eMR).
- Education should include:
  - Specific Zolgensma® parent information brochure
  - The use of corticosteroids, before and after treatment including the reading of the Emergency steroid letter provided
  - Treatment plan and follow-up requirements
  - Potential side effects, adverse reactions and symptom management (acute and chronic) and the reading of the Emergency Sick Day letter provided
  - Potential environmental risks related to Zolgensma® (e.g. vector shedding) including the reading of the Post gene care letter.
  - Waste management (handling and disposal) at home post thirty (30) days of infusion as included on the post gene care letter for parents
  - Scheduled immunisations should be withheld until corticosteroids have been ceased for a minimum of one month (30 days). – see post gene care letter
  - Who and when to contact on discharge if symptoms/concerns arise – see Emergency care letter

Please ensure the following documents are given to parents/carers as they contain important information. They can be found attached to this policy as tabs.

- Medical Zolgensma® treatment letter, which includes details of product administration, and contact details of the treating medical officer should the patient receiving the therapy need care in a facility unfamiliar to their medical history.
- The instructions for corticosteroids and the 'Sick day' letter for emergencies and presentation to a health facility.
- Post care instruction letter which includes such items as follow up requirements, use of oral corticosteroids, surveillance of blood values and waste management.

Pre-dosing Preparations

- Ensure communication between treating medical officer/delegate and the appropriate ward Nurse Unit Manager (NUM) has taken place, ***and*** appropriate bed space is booked and nursing staff are made aware of patient's treatment date.
- Ensure treating medical officer/delegate has alerted neurology team of date of treatment and need for intravenous (IV) access to take place on patients arrival for planning.

It is important to alert the Paediatric anaesthetic team as IV access is difficult in this cohort.

- Ensure parents/carer are aware of treatment date, location and arrival time.
- Ensure equipment has been sourced and allocated to patient the day before infusion. Refer to checklist (Appendix 2).
- Ensure no immunisations have been given 30 days prior to dosing.
- Check child has been given the first dose of oral corticosteroid as prescribed the day before admission.
- Medical team will consider the need for fasting the child from food and fluids (NBM) prior to arrival in case an anaesthetic agent is required for IV access on an individual basis.

It is important that the treating medical officer/delegate has alerted pharmacy of treatment date, dosage required and location for delivery of therapy.

Clinical Space

- The clinical space to be used for administration must be confirmed as appropriate as below;
    - There should be a designated room/area for Zolgensma® administration with PPE/GMO signage clearly displayed alerting staff that a GMO product is being administered.
    - PPE should be readily available at the entrance outside the room/area.
    - The clinical space should allow for a single isolated bed space for the entirety of the infusion and access to equipment/supplies.
- Collect equipment, prime infusion syringe pumps with 50 mL sodium chloride 0.9% for infusion x two.
- There should also be access to a space for the insertion of the IV cannula's such as a treatment room if not using the same bed space where infusion takes place.
- Consideration should be given to the patient's condition/care needs, any risks associated with the use of the Zolgensma® (including the management of adverse events and/or containment).

- Due to the risk of acute systemic reaction including anaphylaxis it is required that appropriate resuscitation equipment is readily available in the ward area throughout the entire administration process and post-administration observation period.
- Ensure emergency drug calculations are readily available and emergency medication list is prepared and at the bedside. These are accessible via the applications window or on the intranet for –
  - ***SCH*** use the *Ward Paediatric emergency drug calculator* http://sch.schn.health.nsw.gov.au/clinical/wddc
  - ***CHW*** use the *Resus Drug Calculator* http://chw.schn.health.nsw.gov.au/o/apps/picu/calculator/
- ***Emergency Equipment*** must be available in the clinical area.
- Any preparation for administration of Zolgensma® gene therapy in the clinical care setting must occur on a medication trolley away from distractions and; maintaining an aseptic field when required and only by the trained nursing staff administering with the second checker.
- Ensure there are clinical waste bins and biohazard waste bags available in the room.

Arrival to Ward

Patient/family

- On arrival orientate patient and the family onto the ward/room/bedspace.
- Explain that IV access will be the priority of the morning procedures
- Notify neurology team of the patient's arrival
- Confirm with the medical team regarding keeping child fasted until after IV access is established
- Two IV access lines must be made available prior to infusion. As the product has a short shelf life a secondary line should be used in the event of the primary line failing. Consider running fluids to maintain access.
- Once access is gained allow patient to eat and drink as normal until administration of the therapy begins.
- Notify pharmacy to prepare infusion
- Ensure second dose of oral prednisolone is given to patient prior to infusion noting that the first dose should have been administered 24 hours prior to the infusion

Zolgensma®

- Zolgensma® must be personally accepted to the clinical space from the assigned delivery person/courier by an appropriately trained staff member who is responsible for administering the drug.
- Once Zolgensma® has been prepared for administration by pharmacy it must be kept below 25°C. Upon receipt of Zolgensma® into the clinical space, the temperature

monitoring device accompanying the product should be checked and the temperature recorded in the medical notes (the acceptable temperature reading for Zolgensma® is below 25°C)

- If a temperature incursion has occurred, notify treating medical officer immediately.
- On receipt, Zolgensma® must be checked to verify appropriate labelling and should continue to be maintained securely in the cold box, to ensure it is maintained within the required temperature range, until administration.
- Avoid prolonged storage in the clinical space at all times.

It is important to administer the dose within six (6) hours of the preparation time stated on the label. This includes administration time.

Pre-administration

- Ensure that the in vivo gene therapy is checked in accordance with the SCHN Practice Guideline 2020-043 – Medication Administration.
- Don PPE, as recommended per the SCHN Policy 2016-9029 - Personal Protective Equipment for Infection Control and the stated requirements of the therapy being administered.
- PPE must include, but is not limited to, a long-sleeved gown, gloves, protective eye wear and enclosed footwear. Long hair must be tied back at all times.
- Perform hand hygiene before donning and post-doffing PPE.
- Remove PPE prior to leaving the clinical space and discard appropriately placed clinical waste bin.

It is important that all food, drink and 'cosmetic' products are removed from the clinical space/bed area prior to the administration of Zolgensma®.

Administration

- Refer to the SCHN Policy 2021-033 – *in vivo* Gene Therapeutics Administration and Handling for the requirements of clinical spaces used to administer this therapy.
- Record baseline observations including blood pressure (BP) of the patient
- Continuously monitor pulse oximetry during infusion.
- Record observations every 15 minutes for the hour of infusion.
- Two qualified staff must check the prescribed Zolgensma® gene therapy and one appropriately trained staff member must remain present until the administration has been completed for observation of any reaction and vital sign changes.
- Treating medical officer must be present for the first 15 minutes of the infusion.
- The syringe pump settings used to administer Zolgensma® must be checked by a second person. *(Only use Zolgensma® drug profile settings as per Braun® pump)*
- Prepare trolley to connect Zolgensma®.

- Don PPE, open container and remove pre-prepared Zolgensma® syringe.
- Ensure medication administration policy is followed prior to administration - SCHN Practice Guideline 2020-043 – Medication Administration.
- Ensure IV access patency by flushing prior to commencement of infusion. Maintain second cannula in case it is required during infusion time.
- All non-disposable equipment used by the bedside for administration such as oxygen saturation monitors, syringe pumps and IV poles, should be cleaned and disinfected using 0.5% sodium hypochlorite solution before they are reused.
- Disposable items should be discarded appropriately into biohazard waste bags at the end of the procedure. These biohazardous waste bags should then be placed into clinical waste bins located in the treatment administration area.
- It is the expectation that all interventions and clinical assessments are documented clearly in the patient's electronic medical record (eMR) as per SCHN policy 2016-9052 – Clinical Procedure Safety.

If parent/ carer wishes to cradle patient during the infusion they must wear PPE due to the potential for an inadvertent spill or disconnection.

Post-Administration

Zolgensma®

- Don PPE and prepare sterile field
- Disconnect Zolgensma® syringe and place on sterile field for containment
- Ensure extension tubing is flushed with 5 mL of sodium chloride 0.9% to ensure the entirety of the drug has been received by the patient. Once flushed, disconnect the extension tubing and place on sterile field for containment.
- Remove PPE.

Patient

- Continue to monitor patient for two (2) to four (4) hours post infusion or longer if directed by the treating medical officer.
- Record observations half hourly for the next two (2) hours and hourly for up to four (4) hours.
- All post-administration care should follow standard clinical care practices.
- IV cannula's/access can be removed only once patient has been reviewed by treating medical officer/delegate as stable. Don PPE for removal.
- All staff involved in post-administration care must to be aware of potential risks associated with Zolgensma®, including side effects and any notification/escalation pathways applicable.
- Patient should be reviewed by treating medical officer/delegate prior to discharge.

- Emergency letters, sick day instructions and post gene care instructions are to be discussed and given to parent/carer prior to discharge.
- Gloves are to be worn when handling the treated patients bodily fluids and strict handwashing procedures followed due to the potential for vector shedding.
- Waste precautions for bodily fluids will continue for a period of 30 days.

All disposable items used for Zolgensma ® administration, including PPE, are to be placed into a biohazard waste bag. This waste bag should then be tied and placed into the clinical waste receptacle available in the treatment area as per SCHN Policy 2021-197 – Transport, Waste & Spill Management of Medicinal Products containing GMOs.

Role Responsibilities

See Appendix 4 – SCHN Zolgensma administration and Handling Roles & Responsibilities flow chart

Related Documents - see attachment tabs

Emergency care post-gene therapy

Post dosing instructions

Emergency steroid information

Emergency 'Sick Day' steroid instructions

Equipment and supplies

Clinical waste bin, biohazard waste bags and signage

Biohazardous Spill kit appropriate for Zolgensma®

PPE trolley and signage

Pulse oximeter and patient lead, probe

2 x syringe pumps on IV pole

2 x 50 mL syringes, extension tubes, labels

100 mL bag of sodium chloride 0.9% for injection

Cannula trolley with accessories

Spill kit for containment and barrier 'Blue' sheets

Sterile dressing packs

Sterile plastic field drapes

Extra gauze, tapes for cannula removal

Waste & Spill Management

Refer to the SCHN Policy 2021-197 – Transport, Waste & Spill Management of Medicinal Products containing GMOs.

Abbreviations

°C	Degrees Celsius
AAV	Adeno-associated viruses
AE/SAE	Adverse Event/Serious Adverse Event
GMO	Genetically Modified Organism
IBC	Institutional Biosafety Committee
IMS+	Incident Management System
IV	Intravenous
NBM	Nil by Mouth
NSW	New South Wales
OGTR	Office of the Gene Technology Regulator
PBAC	Pharmaceutical Benefits Advisory Committee
PC	Physical Containment
PI	Product Information
PPE	Personal Protective Equipment
SCH	Sydney Children's Hospital
SCHN	Sydney Children's Hospitals Network
SMA	Spinal Muscular Atrophy
TGA	Therapeutic Goods Administration

References

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5. SCHN Policy 1/C/14:9047-01:00 Immunisation - https://www.schn.health.nsw.gov.au/_policies/pdf/2014-9047.pdf
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11. SCHN Policy 2021-0033 V1 Procedure: In Vivo Gene Therapeutics – Administration and Handling – https://www.schn.health.nsw.gov.au/_policies/pdf/2021-033.pdf
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13. SCHN Policy 2016-9029 - Personal Protective Equipment for Infection Control - http://webapps.schn.health.nsw.gov.au/epolicy/policy/2609
14. SCHN Policy 2015-9070 – Waste Management http://webapps.schn.health.nsw.gov.au/epolicy/policy/4701
15. SCHN Practice Guideline 2013-9031 – Hand Hygiene - http://webapps.schn.health.nsw.gov.au/epolicy/policy/4806
16. SCHN Practice Guideline 2006-8324 – Incident Management - http://webapps.schn.health.nsw.gov.au/epolicy/policy/3795
17. SCHN Practice Guideline 2020-043 – Medication Administration - http://webapps.schn.health.nsw.gov.au/epolicy/policy/5024
18. TGA - The Australian Regulatory Guidelines for Biologicals (ARGB) - https://www.tga.gov.au/publication/australian-regulatory-guidelines-biologicals-argb

Appendices

Appendix 1 – SCHN In-Vivo Gene Therapy Exposure Log

Appendix 2 – Planning Checklist

Appendix 3 – Blood tests schedule for pre and post-dosing for clinicians

Appendix 4 – Roles & Responsibilities Flow Chart

Appendix 1 – Exposure Log

IN VIVO GENE THERAPY EXPOSURE LOG*									
Name				**Employee Number**					
Department									
EXPOSURE LOG								**CHECKED BY**	
Date *(DD-MMM-YY)*	**Product**	**Dosage** *(Strength/Form)*	**Route of Administration**	**Exposure Time** *XX:XX - XX:XX*	**Activity**	**PPE Used**	**Signature**	**Signature**	**Date** *(DD-MMM-YY)*

*All staff involved in the handling and administration must complete and record any occasions of handling and administration on the SCHN In-Vivo Gene Therapy Exposure Log

Appendix 2 – Planning Checklist

Zolgensma Planning Checklist		
Name: DOB:	MRN:	
At least 4 weeks prior	Date:	Sign:
Ward area and date of infusion identified		
RFA submitted		
Parents/carers aware		
Day before infusion		
Neurology Team and Paediatric anaesthetics notified		
Bed area allocated suitable to requirements		
2 x syringe pumps & IV poles allocated		
Source pulse oximeter + probe & electronic BP machine + cuff		
Ensure 1st dose of oral prednisolone is given		
Ensure GMO waste bin is ordered / available		
Day of infusion		
Emergency bedside equipment & drug calculations are checked		
Emergency trolley location identified		
Set room up with required equipment		
Clinical waste bin & extra biohazard waste bags for disposal		
IV cannula insertion area & equipment prepared plus		
- 2 x 50 mL syringes		
- 2 x extension tubing's (NO-FILTER)		
- sodium chloride 0.9% for priming lines		
- Extra tape and bandages to secure sites		
Ensure Zolgensma is ordered in eMR		
Check that 2nd dose of oral prednisolone is given		
PPE trolley placed outside of room & posters placed where required		
Spill kit placed in room (read procedure document)		
Trolley ready for preparation & administration of drug		
- dressing pack / extra gauze and tapes		

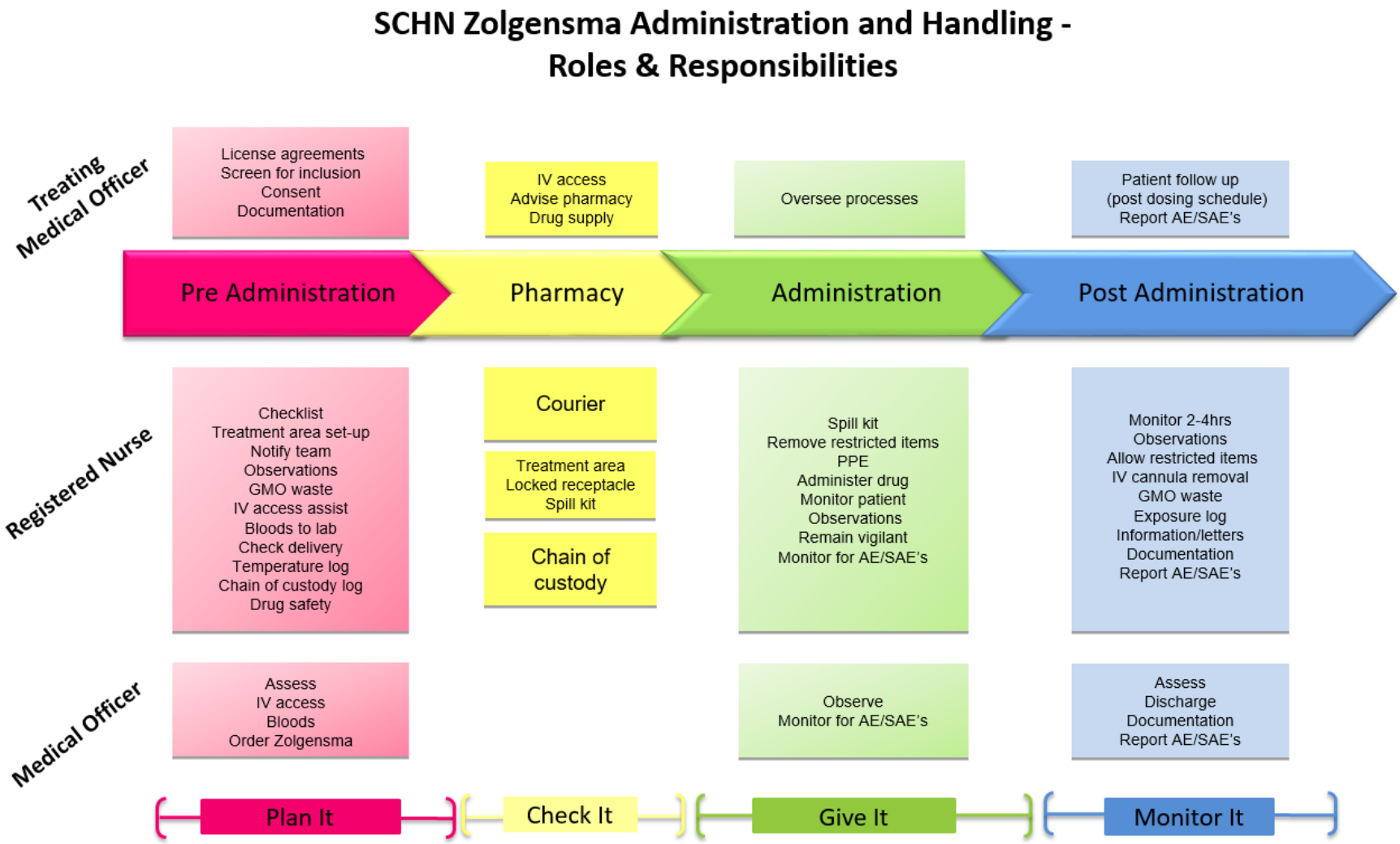
Appendix 3 – Blood test schedule

Blood tests recommended pre and post-dosing for clinicians

	Australia
Liver function	Assess liver function (clinical examination, AST, ALT, total bilirubin, prothrombin time) weekly for the first month, and every other week for the second and third months, until results are unremarkable (normal clinical examination, total bilirubin, and prothrombin results, and ALT and AST levels below 2× ULN
Platelet counts	Measure platelet counts weekly for the first month, and then every other week for the second and third months, until platelet counts return to baseline
Troponin-I	Assess troponin-I weekly for the first month, and then monthly for the second and third months, until troponin-I level returns to baseline

Surveillance recommendations from each country are shown as described in the respective product information (PI).

Appendix 4 – Roles & Responsibilities flow chart



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