PEG-L-ASPARAGINASE: INTRAVENOUS ADMINISTRATION - SCHN ONCOLOGY

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

This Practice Guideline is for use when administering IV PEG-L-Asparaginase (PEG-L-Asp) as part of AIEOP-BFM ALL 2009 – Study 9.

This guideline is to be used to educate Registered Nurses with FULL Cytotoxic Accreditation to allow them to administer IV PEG-L-Asp safely and following the relevant NSW Health PD and AIEOP-BFM ALL 2009 – Study 9.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st October 2016	**Review Period**: 3 years
Team Leader:	Nurse Educator	**Area/Dept**: Oncology

Date of Publishing: 15 November 2016 11:46 AM Date of Printing: 15 November 2016

CHANGE SUMMARY

1. This Practice Guideline has been instated to meet the requirements for commencement of AIEOP-BFM ALL 2009 – Study 9 protocol.
2. This is a guideline concerned with administration of IV PEG-L-Asp only.

READ ACKNOWLEDGEMENT

3. **Training/Assessment Required** –Clinical Staff administering IV PEG-L-Asp are required to have FULL Cytotoxic accreditation as per Cytotoxic and Hazardous Drugs Administration & Handling - SCH or Section 2.3 Hazardous And Cytotoxic Drugs: Administration And Handling - CHW.
4. Clinical Staff involved in the administration of IV
5. PEG-L-Asp as part of AIEOP-BFM ALL 2009 – Study 9 are required to read and acknowledge this document.

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1 Purpose / Scope

This document describes the procedure for the administration of Intravenous PEG-L-Asp by Nursing Staff for patients enrolled in the International Collaborative Treatment Protocol for Children and Adolescents with Acute Lymphoblastic Leukaemia AIEOP-BFM ALL 2009 – Study 9.

2 Expected Outcome

- Safe administration of Intravenous PEG-L-Asp.
- To ensure adequate patient assessment pre and post administration of IV PEG-L-Asp.
- Educate patient and family of signs and symptoms of a reaction and notify staff immediately

3 Responsibilities

Position	Responsibilities
Registered Nurse	Perform this procedure as described
Medical Officer	Prescribe medication as per protocol Remain on the ward for first 15minutes of infusion

4 Education and Training

Clinical Staff administering IV PEG-L-Asp are required to have FULL Cytotoxic accreditation as per Cytotoxic and Hazardous Drugs Administration & Handling - SCH or Section 2.3 Hazardous And Cytotoxic Drugs: Administration And Handling - CHW.

5 Background

L-Asparaginase is an important component of the treatment of acute lymphoblastic leukaemia (ALL) and has been shown to significantly improve long-term event-free survival in paediatric patients.[3,4] PEG-L-Asp is derived from native Escherichia coli (E. coli) enzyme, which has been covalently attached to polyethylene glycol (PEG). This has resulted in a decrease in the immunogenic potential of L-Asparaginase and has provided a longer serum half-life in comparison to native E. coli L-Asparaginase.[3,4,5,6] The use of PEG-L-Asp over the native L-Asparaginase has been associated with a decrease in ALL relapse rates in the UK and it has therefore been introduced in the Europe and US ALL protocols.[5,7] The scientific aim in AIEOP-BFM ALL 2009 – Study 9 is to determine the optimal dosing and schedule of PEG-L-Asp required for paediatric ALL patients.[6]

6 Pre-Infusion

1. IV PEG-L-Asp is used as first-line L-Asparaginase preparation in all patients enrolled on AIEOP-BFM ALL 2009 Study 9
2. Check that the patient has not had an adverse, allergic, hypersensitivity reaction to PEG-L-Asp with previous infusions. Do not administer if there has been anaphylaxis, allergic reaction or silent inactivation and inform the Medical Officer (MO)
3. Do not give premedications for PEG-L-Asp as this may mask a reaction
4. Check required evaluations and protocol requirements have been carried out prior to infusion:
    i. A current height and weight is required and must be documented in eMR within 1 week
        1. SCH – double signed height and weight
    - The required bloods as per the AIEOP-BFM ALL 2009 – Study 9 protocol must be taken, reviewed and must meet study requirements to proceed
    - Ensure that a full set of baseline observations have been taken, recorded and meet the within white or blue zones of SPOC criteria. **NOTE**: SPOC charts do not reflect the defined temperature for febrile in oncology patients, Patients within oncology are **classified as febrile at ≥ 38^{0}C**. For appropriate management of febrile patients please see the Infants and Children: Initial Management of suspected sepsis in Oncology/ Transplant patients practice guideline (NSW Health).
    - In all patients measuring of asparaginase activity and anti-asparaginase antibodies in serum and CSF is required. Refer to the asparaginase Drug monitoring request form for greater detail regarding blood and CSF sampling time points.
    - Check MO has documented the patient is ready for chemotherapy as per local guidelines.
5. Print an Emergency Drug Calculation/ Ward drug dose calculator for the patient and place at the bedside.

    CHW- http://chw.schn.health.nsw.gov.au/o/apps/picu/calculator/

    SCH- http://sch.sesahs.nsw.gov.au/clinical/wddc/
6. Ensure that emergency/resuscitation medications have been prescribed and are available at the bedside.
    - Adrenaline 1:1000 IM
    - Promethazine IV
    - Hydrocortisone IV

7. PEG-L-Asp is also referred to as **Pegaspargase** and the prepared product is labelled so from pharmacy. Ensure that PEG-L-Asp has been prescribed:
    i. CHW - on the patient powerplan :
    ii. SCH – on the Electronic Generated Chemotherapy Order Sheet

    PEG-L-Asp dose is 2 500 international units/m^2 intravenous infusion over 2 hours, with a maximal single dose of 3 750 international units.[5]

    - At CHW, see eMR oncology Powerplans document for activation information.
8. If this is the patients first dose of PEG-L-Asp, provide patient/carers with written information on the potential side effects of PEG-L-Asp Appendix 1. Ensure that patient/carers are aware of when to notify nursing staff if any reactions are observed.
9. Once the PEG-L-Asp is ready, **notify the MO that the infusion is about to commence and ensure that they will be on the ward for the first 15 minutes of the infusion.**
10. Connect the patient to a continuous oxygen saturation monitor.

7 Infusion

- Prepare a sideline for administration of medications in the event of an allergic/ hypersensitivity reaction.
- Administer as per the Cytotoxic and Hazardous Drugs: administration and Handling policy.
- CHW- http://chw.schn.health.nsw.gov.au/o/documents/policies/procedures/2011-8019.pdf
- SCH- http://chw.schn.health.nsw.gov.au/o/documents/policies/procedures/2013-7025.pdf
- For the first 15 minutes of the infusion monitor for signs and symptoms of an adverse/hypersensitivity reaction (see Section 8):
    - Nurse must be at the bedside
    - MO must be on the ward
- For the remainder of the infusion the patient must be supervised by a parent/guardian/carer/nurse/MO and remain on continuous oxygen saturation monitoring.
- Record observations after the first 15 minutes of infusion and then hourly unless otherwise indicated. Record any adverse reaction.

8 Post Infusion

- Prior to discharge, check urinalysis and educate the family about the signs of hyperglycaemia. Ask family to monitor the patient at home for any signs of polydipsia and polyuria. If in an outpatient area, patient must be monitored prior to discharge for:
    - 1 hour at SCH
    - 40 minutes at CHW
- Document administration procedure in the patient's medical record.

9 Adverse/Allergic/Hypersensitivity Reactions

Adverse/allergic/hypersensitive reactions with PEG-L-Asp may occur. The patient should be closely monitored for sudden onset of any of the following symptoms[5,8]:

- Urticaria
- Angioedema (face and tongue swelling)
- Pruritus
- Agitation
- Shortness of breath
- Wheezing
- Stridor
- Hypotension
- Abdominal Pain
- Chest pain
- Chills and fever
- Headache

- If the patient develops one or more of these reactions STOP the infusion, do not leave the patient, call for help, contact MO and prepare to administer emergency/resuscitation medications.
- Document any adverse events in the patients' medical records and complete an alert card.
- If the patient develops an allergic/hypersensitivity reaction during or after the administration of PEG-L-Asp, then its use should be discontinued permanently.[5] It is hypothesized that the PEG-L-Asp has been immunologically inactivated and that has therefore ceased to be effective.[5]
- If there is a reaction, switch to Erwinia Asparaginase. Order the 'ONC Erwinia Asparaginase' power plan at CHW. Seven doses of Erwinia replace each dose of PEG-L-Asp. Do not replace randomised doses.
- If the patient develops an allergy or silent inactivation to PEG-L-Asparginase, please consult AIEOP-BFM ALL 2009 – Study 9 protocol for recommendations regarding ongoing Asparaginase therapy.[5]
- In the event of an allergic reaction to PEG-L-Asp or if there is clinical suspicion of an allergy, it is recommended that Asparaginase activity and Asparaginase antibodies be measured.[5] In order to do this, **a serum blood sample should be taken from the patient immediately after the event (approximately 1 hour after the end of the Asparaginase infusion)** as well as 7 days after, provided the patient has not been given another Asparaginase preparation in the meantime.[5] Refer to the Asparaginase Drug monitoring request form for further details.

- Some patients develop abdominal pain with PEG-L-Asp infusion, which is considered an equivalent to an allergic reaction.[5] In these cases Asparaginase activity and Asparaginase antibodies should also be measured and the preparation should be changed in case of insufficient activity.[5]
- All adverse reactions must be reported to the study centre.

10 Additional Side Effects and Toxicities

Common side effects experienced with the administration of PEG-L-Asp are:

- Mild to severe nausea and vomiting.
- Loss of appetite.
- Abdominal pain.
- Lethargy.
- Drowsiness.
- Malaise.
- Hyperglycaemia (polydipsia, polyuria and polyphagia) associated with decreased insulin synthesis.
- Mild anaemia may occur.[2,5]

- **Coagulopathy and thrombosis** can occur as a result of PEG-L-Asp administration and therefore any patient with a history of clotting disorders or thrombosis should be identified to the MO prior to commencing treatment.[2,4,5] The patient should be observed for any signs or symptoms of bleeding and/or thrombosis.[9]
- Bleeding: Petechia, haematoma, bleeding gums, malaena, haematemesis, joint pain, dizziness, headache and changes in vision.
- **Thrombosis:** Usually present in the legs, and symptoms include pain, redness, and swelling. Pulmonary embolism symptoms include chest pain and shortness of breath. An arterial thrombosis is extremely dangerous and can cause a heart attack, stroke, or organ damage.[9]
- **Pancreatitis** is a common toxicity occurring from the use of L-asparginase.[2,4,5] Symptoms of pancreatitis include: Elevated serum amylase and/or lipase level, abdominal pain, radiating abdominal pain into the back, nausea, vomiting and constipation.[2] If there is confirmed pancreatitis (as defined by the protocol) asparaginase therapy should be discontinued.
- Hyperlipidaemia can occur as a result of L-asparaginase and should be closely monitored as it can increase the risk of developing pancreatitis.[2,4,5] In the case of highly elevated levels (triglycerides >2000mg/dL), closely scheduled pancreas enzyme controls are recommended.[5]

- If the patient develops a toxicity secondary to L-Asparaginase therapy, please consult AIEOP-BFM ALL 2009 – Study 9 protocol for recommendations regarding any treatment modifications

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