ENZYME REPLACEMENT THERAPY (ERT) INFUSIONS IN THE HOME - CHW

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- Lysosomal storage diseases (LSD's) are a heterogeneous group of over 40 disorders. A lack of a specific enzyme leads to the accumulation of metabolites within the cells of various organs causing secondary progressive dysfunction. For some LSD's, enzyme replacement therapy (ERT) may be a treatment option.
- Children with LSD's treatable by ERT are clinically supervised by the Genetic Metabolic Disorders Service (GMDS) at CHW.
- ERT is a high cost therapy. Eligibility for treatment is based on disease specific criteria, as defined by the Federal Government's Life Saving Drugs Program (LSDP) - http://www.health.gov.au/internet/main/publishing.nsf/Content/lsdp-info
- ERT is given as an intravenous infusion either weekly or fortnightly, depending on disease, and is **lifelong**.
- ERT infusions are administered on average over 2 – 5 hours. Duration of infusion is dependent on ERT safety data, dose, size of child and immunogenicity.
- Each child will have an individualised infusion guideline.
- To be considered for home ERT therapy, the child must have had at least 12 months of in hospital ERT infusions with no or minimal, well controlled infusion associated reactions(IAR's) and stable ERT specific antibody levels.
- Infusion Associated Reactions (IAR's) are a risk of treatment, and appropriate medication to treat IAR's must be readily available with instructions in the child's home.
- Move towards empowering / educating parents to undertake Central Venous Access Device (CVAD) training and deliver ERT infusion safely, after a minimum of 3 months support, guidance and education by Community Acute/Post-Acute Care (CAPAC) team.

Approved by:	SCHN Policy, Procedure and Guideline Committee	
Date Effective:	1st May 2015	**Review Period:** 3 years
Team Leader:	CNC Mitochondrial/Lysosomal	**Area/Dept:** WSGP - CHW

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CHANGE SUMMARY

- Not applicable – New Document.

READ ACKNOWLEDGEMENT

- All clinical staff involved in the delivery of ERT in the home setting or teaching parents to carry out this role are to read and acknowledge they understand the contents of this document.

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1 Rationale

- School children, in particular, lose learning opportunities by attending hospital one day a week to receive ERT treatment during school time. The aim of this programme is to use a hospital-in-the-home system to transition care to the family's home. This programme facilitates a patient focused treatment regimen in the most convenient and safe manner for a patient and their family.
- This model of care will aim to empower families to manage their child's condition in the home environment.

2 Abbreviations

- ERT Enzyme Replacement Therapy
- LSDP Life Saving Drugs Program
- GMDS Genetic Metabolic Disorders Service
- CAPAC Community Acute/Post-Acute Care
- CVAD Central Venous Access Device
- IAR Infusion Associated Reaction
- LSD Lysosomal Storage Disorder

3 General Principles

- All children receiving ERT must have approval from the Federal Government Life Saving Drugs Program (LSDP) and be under the clinical direction of a Consultant in the Genetic Metabolic Disorders Service (GMDS) at The Children's Hospital at Westmead (CHW).
- ERT in the home for children with a variety of LSD's is common practice in Europe and the United Kingdom.
- Children assessed as being suitable for ERT in the home, will initially be supported by the Community Acute/Post-Acute Care (CAPAC) Team, with possible transition to parent administered ERT in the home, as deemed appropriate by the GMDS team.
- Children having ERT in the home will have an individual infusion guideline which must be adhered to.
- Children selected for ERT in the home will have a CVAD insitu (i.e. portacath)
- A GMDS consultant is on call 24 hours per day, 7 days a week and can be contacted via the CHW switchboard for clinical advice if required.
- ERT infusions in the home must always be administered via an infusion pump. The pump must be calibrated at 12 monthly intervals minimum.
- Infusion associated reactions (IAR's) can be a risk of treatment, but could be comparable to other therapies being administered in the home setting for children.

- Vital sign monitoring will be adapted for the home setting.
- Aim is to educate and support families to be able to deliver ERT in the home autonomously.
- A patient satisfaction evaluation questionnaire will be given to the child's carer 3 months after home infusion start to measure improvements.

Children on ERT in the home will continue to have clinical reviews at CHW as per LSDP disease specific assessment guidelines and as clinically indicated.

4 Patient Selection

- Currently only patients with Mucopolysaccharidoses Types I, II VI and Gaucher are being considered for ERT in the home. Children must be aged 5 years or over.
- Children selected for ERT in the home will have a 12 month history of stable infusions in the hospital setting.
- If infusion reactions have occurred, these must be under control with oral pre-medication and not have occurred for 4 ERT administrations prior to making a decision in favour of home therapy.
- If the child has clinical evidence of serious obstructive airway disease, suitability for ERT in the home will be assessed on an individual basis. Patients may be deemed eligible for home treatment if their respiratory disease remains stable and they are judged otherwise "medically fit" by the prescribing consultant at CHW.
- CAPAC to assess suitability of the home environment for the delivery of ERT in the home.
- The CAPAC criteria for admission to the service are met.
- Parents/ guardians of these children must have consented to home treatment.
- Parents/guardians must be willing to undergo education to prepare them to be able to deliver ERT autonomously once competent and confident. Parental education to include:
  - Accessing/de-accessing CVADs
  - Preparing infusion
  - Setting up of infusions via an infusion pump
  - Safe handling of ERT
  - Observation and monitoring of their child during the infusion process
  - Managing an IAR in the home
- Parents/guardians must be available at an agreed time with CAPAC for ERT infusions.
- Parents/guardians of children receiving ERT in the home must agree to sign a parental agreement form – see Appendix 1.

5 Treatment Protocol

Treatment infusion protocols for individual patients are developed in consultation with the Genetic Metabolic Disorders Service (GMDS) and Life Saving Drugs Program (LSDP). The protocols are in line with the national LSDP disease specific guidelines and individual drug product information (See Appendix 2 for list of ERT's).

5.1 Treatment under CAPAC Supervision

1. CAPAC to contact the family the morning of the infusion to check the child is well with no recent history of a temperature. The infusion is not to proceed if the child is assessed unwell.
2. Each child will have an individual infusion guideline written and adjusted by the Clinical Nurse Consultant for Mitochondrial/Lysosomal Storage Disorders.
3. Infusion guidelines will be adjusted, if required, under the direction of the LSDP and GMDS.
4. GMDS Registrar is responsible for writing/updating the medication chart as per individual patients' infusion guideline.
5. CAPAC should have a named patient kit for infusion adverse reactions (IAR) that may occur in the home.
    - The IAR kit contents should be as per each individual patient infusion guideline.
    - IAR kits will be maintained by CAPAC and subsequently the GMDS once family become infusion independent.
6. Patients are to have an infusion record completed at each infusion by either CAPAC or the parent delivering the ERT. Included on the record will be the checking of the expiry date on the IAR kit.

5.2 Treatment under Parental Care

Suitable identified parents will undergo a competency to safely and confidently administer the ERT at home. Once deemed competent, CAPAC will not supervise ERT infusion in the home but will continue to provide the following service:

1. CAPAC will call the patients home in the morning of the infusion to ensure the patient is well.
2. CAPAC will supply all medical ancillaries for the treatment and admit/discharge on day of infusion.
3. CAPAC will collect the packaged ERT (including the temperature data logger) from Pharmacy and then deliver the medication to the patient's home. Prior to the cool-box opening, CAPAC will assess the patient's clinical status. The infusion is not to proceed if the child is assessed unwell.
4. The parent will access the CVAD, prepare and run the infusion, observe the patient during the infusion and de-access the CVAD on completion.

5. CAPAC will sign the log provided by Pharmacy (including date and time the ERT was taken out of the cool-box).
6. CAPAC to return the log, temperature logger and remaining contents of the cool-box to pharmacy immediately upon return to the hospital. The information on the temperature logger will be downloaded by Pharmacy and kept on record.
7. Parent is responsible to contact CAPAC on completion of infusion and associated procedures.

5.3 Transport of ERT to the Home

ERT is a high cost drug and must be handled according to product information

1. LSDP will organise transport of ERT to CHW pharmacy. ERT is stored between 2 - 8ºC.
2. CAPAC must supply pharmacy with an up to date medication chart the day prior to the scheduled home ERT infusion.
3. The required vials of ERT will be dispensed and remain in the pharmacy fridge until collection is required.
4. On the day of infusion and if the child is well, CAPAC should collect the ERT vials as packed by pharmacy in a cool-box immediately prior to leaving for the patients' home. The cool-box will contain the specific ERT vials and a temperature data-logger.

   If on arriving at the child's home, CAPAC find the child unwell and clinically unsuitable to receive ERT, **do not open the cool-box.** Return un-opened cool-box to pharmacy immediately on returning to CHW.

5. All equipment used for packaging and safe transport of ERT vials to the home should be returned to the Pharmacy Department when arriving back at CHW.
6. Pharmacy Department are responsible for downloading the temperature data from the Data logger. This is to occur as soon as possible after the cool-box is returned.

5.4 Preparation and Administration of ERT

Please refer to individual child infusion guidelines and drug company safety guidance.

6 Nursing Principles

- Strict adherence to individual child infusion guidelines is essential.
- CNC for Mitochondrial/Lysosomal Storage Disorders to ensure individual patients infusion guidelines remain up to date.
- Infusion guidelines to be accessible to CAPAC via shared network drive and emailed to Pharmacy.
- Up to date medication charts will be prescribed by the GMDS Registrar.

- CAPAC clinical concerns to be discussed with the GMDS Registrar up to 17.00hrs on the day of infusion and the GMDS Consultant on call out of hours. Both can be contacted via the CHW switchboard.
- Vital sign management in the home:
  - On arrival observe child and take baseline temperature, pulse and respirations **prior to removing ERT from cool-box**.
  - Contact GMDS team if concerned as per above.
  - Access and manage CVAD as per CHW policy.
  - Visually observe child during the infusion – follow immediate management guidelines below if IAR occurs.
  - On completion of infusion, repeat temperature, pulse and respirations.
- De-access and heplock port-a-cath and dispose of consumables per CVAD Practice Guideline.

7 Infusion Associated Reactions (IAR)

- IAR can be a risk, but for children who have been selected for ERT in the home, this risk is assessed as being minimal.
- There are two types of IAR that have been observed with ERT.
  - The reactions that occur during the infusion are usually minor and respond quickly to oral therapy and/or reduction of the infusion rate. The patients generally develop symptoms 5 – 60 mins after starting the infusion.
  - Delayed or Biphasic reactions can occur, these tend to present as a rash, pyrexia, and occasional respiratory symptoms. The second wave of symptoms usually occurs one – 8 hours after the first symptoms but this delay can be longer.
- An IAR is more common if ERT is administered when there is evidence of active infection.
- The infusion should be given with caution in children with asthma and/or eczema, or if the child has had an immediate hypersensitivity reaction previously to another drug.
- The child is at more risk of an IAR if they have had an interrupted course of ERT.

7.1 Preventing Infusion Associated Reactions

- Do not give the infusion if the child is unwell or has a temperature above 37.5°C.
- Administer the infusion at the prescribed rate for that patient, as per individualised infusion guidelines.
- See guidelines for infusion for drug specific information.

7.2 Types of IAR and their immediate management in the Home

Note: All IAR to be notified to GMDS doctor on call at the time of the event and recorded in IIMS

Symptoms	Action
Mild reaction ▪ Flushing ▪ Fever and/or shivering ▪ Nausea ▪ Irritability (especially in young children) ▪ Headache	▪ Reduce rate by 50%. ▪ Give oral anti-pyretic and/or anti-histamine. ▪ Reduce rate by a further 25% if symptoms persist. ▪ If symptoms continue despite rate reduction stop infusion ▪ Pre-treat with oral antihistamine and antipyretic prior to next infusion
Moderate reaction ▪ Chest pain ▪ Itching and/or raised urticarial rash ▪ Severe headache ▪ Gastro intestinal symptoms, vomiting, diarrhoea, abdominal cramping.	▪ Stop infusion ▪ Give oral antihistamine and consider IV corticosteroids ▪ Record all details in infusion log ▪ Next infusion to be given in hospital. ▪ Pre-treat with oral antihistamine and antipyretic prior to next infusion.
Severe Anaphylactic Reaction ▪ Respiratory Involvement. Shortness of breath, wheezing, laryngeal oedema. ▪ Respiratory Failure, ▪ Cardiac Arrhythmias ▪ Analphylactic/Anaphylatoid shock with hypotension and circulatory collapse.*	▪ **Stop Infusion** ▪ **Call Emergency Services 000** ▪ **Give Adrenaline – Use Epipen** ▪ **Give oral antihistamines and corticosteroids IV** ▪ **Maintain very close monitoring as drug dosages may need to be repeated** ▪ **Review pre-treatment and next infusion in hospital.** ▪ **Obtain bloods for IgE status 3-5 days later**

7.3 Drugs that may be used for IAR

Refer to individual Patient Infusion Guidelines and Medication Charts

Drug	Type	Age	Dose
Oral Paracetamol	Antipyrexic	1 month upward	15/mg/kg (up to max 1g) 4-6 hourly. (Max 4 doses in 24 hours)
Oral Ibuprofen	Antipyrexic	Over 3 months of age	5mg/kg (up to max 400mg)3-4 times daily.
Oral Loratadine	Antihistamine	1 -2 yrs 2 – 5 yrs 6 – 11yrs	2.5mg/dose *(not/kg)* 24 hourly 5mg/dose *(not/kg)* 24 hourly 10mg/dose *(not/kg)* 24 hourly
Oral Promethazine	Antihistamine	> 2 years	0.3mg/kg (up to max 25mg) single dose
IV/IM Hydrocortisone	Corticosteroid	6 -12yrs 12- 18yrs	100mg 200mg
Adrenaline IM – Epipen			Under 20kg: Epipen Junior 150 microgram ≥20kg: Epipen 300 micrograms

8 Related Policies and Guidelines

The following documents are to be read and observed in conjunction with this document:

1. **Home Intravenous Medication: Parent/Carer Administration – CHW Policy**: http://chw.schn.health.nsw.gov.au/o/documents/policies/policies/2006-8301.pdf
2. **Implantable Vascular Access Device (IVAD) CHW Homecare Guideline**: http://chw.schn.health.nsw.gov.au/o/documents/policies/homecare/2013-8001.pdf
3. **Central Venous Access Devices (CVAD) Practice Guideline**: http://chw.schn.health.nsw.gov.au/o/documents/policies/guidelines/2013-9037.pdf
4. **Individual Patient ERT Infusion Guidelines** (accessed via shared network drive)
5. **Genzyme – Aldurazyme: Product Information**: www.genzyme.com.au/Products/~/media/GenzymeAU/Files/aid-pi.pdf
6. **Genzyme Product Consumer Information**: www.genzyme.com.au/Products/Consumer-Medicine-Information.aspx

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Appendix 1

CHILDREN'S HOSPITAL AT WESTMEAD (CHW)
HOME ENZYME REPLACEMENT THERAPY (ERT) PROGRAM
Parental Agreement

The Home ERT Program was initiated to examine ways of improving quality of life by enabling families to deliver ERT in the home. This pilot program is supported by a grant which is reviewed annually. The success of this program depends on the close collaboration between the Genetic Metabolic Disorders Service (GMDS), the Community Acute/Post-Acute Care Team (CAPAC) and the patient's family. This Parental Agreement provides the basis for this collaboration.

1. I, _____ (parent/guardian) of _____ (child) agree to comply with the requirements, guidance and policies of the GMDS, CAPAC and CHW for the safe delivery of ERT in the home to my child.
2. A home risk assessment will be completed by CAPAC to ensure it is safe for nurses to visit.
3. Members of the CAPAC team will be rostered to deliver the home service on a weekly basis.
4. I may need to take my child to CHW for a scheduled ERT infusion if a CAPAC team member is unable to attend for a home ERT infusion.
5. The weekly infusion may be omitted in the event that drug is damaged prior to administration.
6. If my child suffers an infusion associated reaction (IAR) I will return to CHW for subsequent ERT infusions until advised by the clinician in charge that it is safe to return home.
7. My child is bound by the agreement I have signed with the Australian Government Life Saving Drugs Program (LSDP) dated _____to undergo assessments and reviews at CHW.
8. My competence in delivering ERT at home e.g. accessing/de-accessing Portacaths will be assessed on an annual basis.
9. I will inform the clinical team of any issues or extraordinary events which arise in the course of administering ERT e.g. child illnesses, planned holidays, IARs.
10. This arrangement can be terminated in writing at any time by the supervising clinical team at CHW for reasons of non-compliance with this agreement or discontinued support for ERT.
11. I have received sufficient information to proceed with Home ERT infusions for my child.

Parent name:		CAPAC NUM name:	
Signature:	_____	Signature:	_____
Date:	_____	Date:	_____

Metabolic physician name: _____

Signature: _____

Date: _____

Appendix 2

Enzyme Replacement Therapy (ERT) Dosage

Note: ERT is funded by the Federal Government and authorised by the Life Saving Drugs Program (LSDP)

Disorder	Defective Enzyme	ERT	Dosage & Frequency	Dilution (0.2µm low protein binding inline filter to be used for all ERTs)
MPS 1 : Hurler Syndrome / Hurler Scheie	α-L-iduronidase	**Aldurazyme:** (Laronidase) 2.9 mg per 5mL vial	**0.58mg/kg weekly IV**	Must be diluted with NaCl 0.9%. Patients with a body weight ≤20kg should receive a total volume of 100mL. Patients with a body weight ≥ 20kg should receive a total volume of 250 ml
MPS II : Hunter Syndrome	Iduronate Sulfatase	**Elaprase:** (Idursulfase) 6mg per 3mL vial	**0.5mg/kg weekly IV**	Dilute in 100ml of NaCl 0.9%
MPS VI: Maroteaux Lamy Syndrome	*N*-Acetylgalactosamine-4-sulfatase (arlsulfatase B)	**Naglazyme:** (Galsulfase) 5mg per 5mLvial	**1mg/kg weekly IV**	Dilute with NaCl 0.9% - volume between 100 - 250 mL dependent on dose and weight
Gaucher Disease	Glucocerebrosidase (acid β glucosidase)	**Cerezyme:** (Imiglucerase-rch) 200 or 400unit powder vials. Reconstitute with Water for Injections to yield a 40 units/mL solution	**60 units/kg fortnightly IV**	Dilute with NaCl 0.9% to as indicated
Gaucher Disease	Glucocerebrosidase (acid β glucosidase)	**VPRIV:** (Velaglucerase alfa ghu) 400 Units/vial (10mg). Powder to be reconstituted with 4.3mL Sterile Water to give extractable volume of 4.0mL - 100 Units/mL	**60 units/kg fortnightly IV**	Dilute with 100mL 0.9% Sodium Chloride