Summary of changes to draft Review Protocol for Pompe disease medicines on the Life Saving Drugs Program (LSDP)

Background

On June 28 2019, the LSDP Expert Panel discussed the draft Review Protocol for Pompe disease including the outcomes from the Pompe disease Stakeholder Forum (held in Sydney on 14 June 2019).

Note that a Stakeholder Forum was also held for Paroxysmal Nocturnal Hemoglobinuria (PNH) and Mucopolysaccharidosis type II (MPS II) disease medicines. If changes suggested at those forums were considered relevant to the Review Protocol for Pompe disease medicines, the changes would be included (and vice versa).

General discussion

1. The Panel noted that three Panel members attended the Pompe stakeholder forum. The Panel acknowledged that the feedback from the Stakeholder Forum was informative to the Review.

2. The Panel noted there were no significant changes recommended to the Review Protocol for Pompe.

3. The Panel noted that any changes that had been made to the Review Protocols for the Tranche 1 medicines had been included in the draft Review Protocol for Pompe.
**Individual Terms of Reference (ToRs)**

**ToR 1 – Review the prevalence of Pompe disease within Australia.**

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<tr>
<th>Suggested change to research questions</th>
<th>Expert Panel recommendation</th>
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<tr>
<td>Specification added to research question 1 'onset types (infantile, juvenile-late and adult-late)'</td>
<td>No change required to draft research questions.</td>
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<td>An additional diagnostic laboratory, PathWest, was added to the data source list.</td>
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General discussion noted:
- Pompe Association estimates that the prevalence of Pompe disease in Australia is between 58-61 patients.
- Mutations can define whether the disease is early- or late-onset.
- Australia is the only country that differentiates between infantile and juvenile onset. Other countries just use early- and late-onset.
- The specification of the three subtypes in the question regarding prevalence.
- Statistically 2.2 babies born with Pompe each year, but they do not show up on treatment. Could be death prior to diagnosis.

**ToR 2 - Review evidence for the management of Pompe disease and compare to the LSDP treatment guidelines, patient eligibility and testing requirements for the use of these medicines on the program (including the validity of the tests).**

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General discussion noted:
- Clinical utility of testing protocol by onset type needs investigation. There are 52 different tests for infantile population, 16 for juvenile population and 14 for adult population.
- Once a patient is accepted as having infantile onset, should they continue on the same testing regime for life?
- Consider anniversary testing instead of annual 1 May re-application for all patients.
- In Taiwan, patients start treatment within five days of diagnosis, which can be as soon as five
days post birth.

- Cost and time of Myozyme preparation results in some hospital pharmacies not supportive of Pompe patients being treated in their facility.

- ToR 2 needs to consider the consequences of failing to treat a baby or juvenile or treating too late as damage done cannot be reversed.

- Pseudo-deficiency allele is normal and seen in newborn screening where the sample size is very small. The current guidelines require two of three tests which rule out pseudo-deficiency as Pompe disease. This is the reason why at least two tests are required to confirm diagnosis.

- Best case scenario at present is 3 months to get from diagnosis to treatment. Double if outside a metropolitan area. Simplification of the application process is needed.

**ToR 3 - Review clinical effectiveness and safety of medicines and evaluate the evidence of comparative effectiveness of LSDP Pompe disease medicines. This will include analysis of LSDP patient data and international literature to provide evidence of life extension.**

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**General discussion noted:**

- Severity at time starting LSDP needs to be considered/assessed at time of doing the analysis.

- Untreated cohort studies pre 2012 will be needed to assess against natural history.

- Qualitative data will be critical to put ToR 3 into perspective.

- Analysis of data will be problematic due to heterogeneous population and low numbers.

- Quality and quantity of data pre 2006 (before treatment started in Australia) is very limited.

- Patients were on compassionate treatment from 2006, with a total of about 22 patients. This could distort the data as their disease likely to be severe or progressed as no enzyme replacement therapy (ERT) was available.

- Be cautious with analysis in late onset Pompe as it’s a small population and heterogeneous.
ToR 4 - Review relevant patient based outcomes that are most important or clinically relevant to patients with Pompe disease.

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<td>No change required to draft research questions, however a small clarification was added to the data sources to specify authoritative social media sites would be included in the systematic literature review.</td>
<td>No change required to draft research questions.</td>
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General discussion noted:

- A concern regarding social media inclusion as a data source was raised. This has been clarified to include authoritative social media publications such as the Australian Pompe Association.
- International Pompe Association social media has been recommended as a good avenue for patient perspectives.
- Patients experience anxiety about the required tests.
- Sequence of testing can negatively impact results (e.g. respiratory tests post 6 minute walk tests).

ToR 5 - Conduct an analysis of the value for money of LSDP Pompe disease medicines under the current funding arrangements.

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General discussion noted:

- Patient anxiety of the analysis for this ToR as the quality of life gained is considered high by patients.
- Important that the cost of individual tests and sensitivity analyses on the most applicable tests is included in value for money estimations.
- Ensure findings of ToR 2 are reflected in ToR 5.
- Ensure that the pricing analysis (commercial/committee in confidence) and patient identification is appropriately redacted.
### ToR 6 - Review the utilisation of LSDP Pompe disease medicines, including the way they are stored and dispensed, and evidence of patient compliance to treatment.

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| **General discussion noted:**<br>• Increasing weight in juvenile patients can cause dosing issues.  
• Noted there is often a lag if dosage is increased  
• Compliance is not an issue.  
• Therapy takes time to prepare. It is difficult to get infusions on Mondays or weekends. | |

### ToR 7 - Investigate developing technologies that may impact future funded access.

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<td><strong>General discussion noted:</strong>&lt;br&gt;• There are developing technologies of 2nd generation ERT and gene therapy.</td>
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