Statutory Approvals Committee - minutes

Centre 0044 (The Centre for Reproductive and Genetic Health)

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) – application to perform PGT-M for Heimler Syndrome Type 2, OMIM #616617

Date:	4 October 2021
Venue:	HFEA, 2nd Floor, 2 Redman Place, London E20 1JQ via Microsoft Teams
Committee Members:	Margaret Gilmore (Chair) Anne Lampe Ruth Wilde Jason Kasraie
Specialist Adviser:	Dr. Alison Male
Legal Adviser:	Gerard Hanratty – Browne Jacobson LLP
Members of the Executive:	Moya Berry - Committee Officer Catherine Burwood - Licensing Manager
Observers:	Jonathan Herring - Authority Member (HFEA)
Apologies:	No apologies were received for the meeting
Declarations of Interest:	Members of the committee declared that they had no conflicts of interest in relation to this item

The Committee had before it:

- HFEA Code of Practice 9th edition
- Standard Licensing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGT-M Application Form
- Redacted Peer Review
- Genetic Alliance (UK) Statement
- Supporting paper - Expanding the clinical and genetic spectrum of Heimler syndrome, Feng-Juan et al, 2019
- Supporting paper - Heimler Syndrome is caused by hypomorphic mutations in the peroxisome- biogenesis genes PEX1 and PEX6, Ratbi et al, 2015
- 2011-09-29 Licence Committee Minutes, PGD for Peroxisome Biogenesis Disorders (PBD) (Zellweger Syndrome Spectrum (ZSS))

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Alison Male, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGT-M application for Heimler Syndrome Type 2, OMIM #616617, is consistent with the peer review.

1.3. The committee noted that the condition is known on the OMIM website as Heimler Syndrome 2, OMIM #616617. To ensure consistency the condition will be known as Heimler Syndrome 2, OMIM #616617.

1.4. The committee noted that the condition being applied for is not on the list of approved PGT-M conditions.

1.5. The committee noted that the Genetic Alliance (UK) statement provided a perspective on the impact of the condition on patients, their families, and carers.

1.6. The committee had regard to its decision tree. The committee noted that the centre is licensed to carry out PGT-M. The committee was also satisfied that the centre has experience of carrying out PGT-M and that generic patient information about its PGT-M programme and associated consent forms had previously been received by the HFEA.

1.7. The committee noted that the proposed purpose of testing the embryos was as set out in paragraph 1ZA(1)(b) of Schedule 2 of the Act, i.e., 'where there is a particular risk that the embryo may have any gene, chromosome or mitochondrion abnormality, establishing whether it has that abnormality or any other gene, chromosome or mitochondrion abnormality'.

1.8. The committee noted that Heimler Syndrome 2, OMIM #616617 is inherited in an autosomal recessive manner, which means there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation.

1.9. The committee noted that the penetrance of the condition is 100%.

1.10. Heimler Syndrome 2, OMIM #616617, is characterised by sensorineural hearing loss in early childhood. Hearing impairment is severe and is usually pre-lingual and so may affect speech development. Children may also have abnormalities in the shape, growth, and development of teeth with poor enamel development. Other characteristics include broad thumbs with harmless

white marks on nails (leukonychia), in-turned feet (club feet) and pes planus (fallen arches) which can lead to problems with tendons in lower legs. Some children also have progressive retinal changes leading to progressive visual impairment, tunnel vision and night blindness.

1.11. There is no cure for the condition. Treatment is supportive and children may require hearing aids or cochlea implantation for deafness. Treatment may also involve dental restorative treatment including crowns and implants, veneers, and dentures. Low vision aids may also be required if there is a retinal dystrophy.

1.12. The committee noted the executive's request to consider Heimler Syndrome 2, OMIM #616617, for inclusion on the list of conditions approved for PGT-M. The committee agreed to consider the application on this basis.

1.13. The committee also noted the peer reviewer's recommendation to consider Heimler Syndrome 1, OMIM #234580 for inclusion on the list for which PGT-M can be applied and agreed to consider the application on this basis.

1.14. Heimler Syndrome 1, OMIM #234580, is inherited in an autosomal recessive manner meaning there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation. The condition presents with sensorineural hearing loss in early childhood and abnormalities in the shape, growth, and development of teeth with poor enamel development. Some children have progressive retinal changes leading to visual impairment and night blindness.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Heimler Syndrome 2, OMIM #616617, is a rare, serious, and painful condition which can present from birth and lead to profound deafness, and progressive visual impairment, tunnel vision and night blindness. Affected individuals may also suffer with serious painful dental abnormalities requiring significant dental interventions. Some, due to skeletal abnormalities, may also have difficulty with walking. The committee considered the possible serious physical, psychological and emotional impact on those with the condition, particularly where hearing loss may also affect speech and language development if the condition manifests early in life.

2.2. The committee also considered the condition Heimler Syndrome 1, OMIM #234580, which presents from early childhood and is indistinguishable in its presentation to Heimler Syndrome 2, OMIM #616617. In the worst-case scenario those affected suffer profound sensorineural hearing loss, progressive retinal changes which may lead to visual impairment, and painful dental abnormalities requiring significant dental interventions.

2.3. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormalities in question and that there is a significant risk that a person with such abnormalities will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness, or any other serious medical condition.

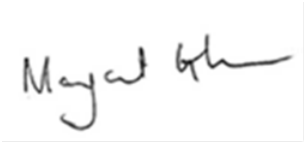
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Heimler Syndrome 1, OMIM #234580
- Heimler Syndrome 2, OMIM #616617

3. Chair's signature

3.1. I confirm this is a true and accurate record of the meeting.

Signature



Name

Margaret Gilmore

Date

27 October 2021