Statutory Approvals Committee – minutes

Centre 0044 (The Centre for Reproductive and Genetic Health)

Pre-implantation Genetic Diagnosis (PGD) application for Lymphatic Malformation 6, OMIM #616843

Thursday, 26 November 2020

HFEA, 10 Spring Gardens, London, SW1A 2BU via Teams Meeting

Committee members	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde	
Members of the Executive	Moya Berry	Committee Officer
Specialist Adviser	Professor Mary Porteous	
Legal Adviser	Eve Piffaretti	Blake Morgan – LLP

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:

- 9th edition of the HFEA Code of Practice.
- Standard licensing and approvals pack for committee members.

The following papers were considered by the committee:

- Executive Summary
- PGD Application Form
- Genetic Alliance Statement
- Letter from Professor Sahar Mansour in response to request for public comment
- Academic Paper - , Fotiou et al 2015
- Academic Paper-, Martin-Almedina et al 2018

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Professor Mary Porteous, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for Lymphatic malformation 6 (LMPHM6), OMIM #616843, is consistent with the peer review.

1.3. The committee noted that the condition being applied for is not on the list of approved PGD conditions.

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

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

1.6. 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'.

1.7. The committee noted that Lymphatic malformation 6 (LMPHM6), OMIM #616843, 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.

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

1.9. Lymphatic malformation 6 (LMPHM6), OMIM #616843, is characterised by uniform, widespread lymphedema affecting all segments of the body from before birth, which can lead to miscarriage or neonatal death. Those surviving birth are likely to suffer long term complications of lymphedema in various organs, including the heart, lungs and gut, and other parts of the body. Many patients have multiple episodes of cellulitis in their legs, arms and face, which can be painful and disfiguring, and in some cases may lead to fatal sepsis.

1.10. There is no cure for this condition and treatment focuses on managing the symptoms.

1.11. The committee noted the executive's request to consider Lymphatic malformation 6 (LMPHM6), OMIM #616843, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.12. The committee also noted the recommendation of the peer reviewer to consider adding further types of Lymphatic malformation conditions for inclusion on the list of conditions for which PGD can be applied. The conditions Lymphatic malformation 7, OMIM #617300 and Dehydrated hereditary stomatocytosis, OMIM#194380 are both inherited in an autosomal dominant manner, which means there is 50% chance of an embryo being affected in each pregnancy if either parent has a relevant mutation. The conditions are of a similarly severe phenotype to Lymphatic malformation 6 (LMPHM6), OMIM #616843 and are characterised by generalised lymphedema before birth which can cause death in utero or in the neonatal period. In those who do survive, the conditions can cause long-term complications of lymphedema in various organs, including the heart, lungs and gut.

1.13. In addition, the peer reviewer requested that the committee also consider whether the following conditions, which are all inherited in an autosomal dominant form, should be included on the list for which PGD can be applied. The conditions Lymphatic malformation 1 (Milroy Syndrome), OMIM #153100, Lymphatic malformation 3, OMIM #613480 and Lymphatic malformation 4, OMIM #615907, are all very similar unpleasant lifelong disorders which can lead to serious infections that may be difficult to treat. Based on the advice of its specialist adviser, the committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Lymphatic malformation 6 (LMPHM6), OMIM #616843 is a severe and potentially lethal, multi-systems disorder which can cause non-immune hydrops fetalis (abnormal buildup of fluid around the heart, lungs and abdomen), which is a very serious condition in pregnancy, leading to death of the baby in utero or soon after birth. Those who do survive are likely to suffer from multiple problems and long-term complications of lymphedema around various organs and parts of the body. The committee considered the potentially devastating physical and psychological impact on the quality of life of those affected with the condition.

2.2. The committee considered in the worst-case scenario the conditions Lymphatic malformation 7, OMIM #617300 and Dehydrated hereditary stomatocytosis, OMIM #194380, are of a similar phenotype and presentation to Lymphatic malformation 6 (LMPHM6), OMIM #616843 and can result in death in utero or shortly after birth.

2.3. The committee also considered in the worst-case scenario, Lymphatic malformation 1 (Milroy Syndrome), OMIM #153100, Lymphatic malformation 3, OMIM #613480 and Lymphatic malformation 4, OMIM #615907 are very unpleasant and painful conditions, which can present at birth or in childhood and are associated with fluid overload. They may lead to life threatening infections that can be difficult to treat.

2.4. 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 abnormality in question and that there is a significant risk that a person with such an abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

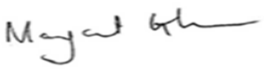
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Lymphatic malformation 1, (LMPHM1), (Milroy Syndrome) OMIM #153100
- Lymphatic malformation 3, (LMPHM3), OMIM #613480
- Lymphatic malformation 4, (LMPHM4), OMIM #615907
- Lymphatic malformation 6 (LMPHM6), OMIM #616843
- Lymphatic malformation 7, (LMPHM7), OMIM #617300
- Dehydrated hereditary stomatocytosis, OMIM #194380

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
23 December 2020