Statutory Approvals Committee – minutes

Centre 0035 (Oxford Fertility)

Pre-implantation Genetic Diagnosis (PGD) application for

Nemaline Myopathy ACTA 1, OMIM #161800

Thursday, 26 October 2017

Church House Westminster, Dean's Yard, Westminster SW1P 3NZ

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford Bobbie Farsides	
Members of the Executive	Dee Knoyle Bernice Ash Susanna Nyarko-Parkin	Committee Secretary Committee Secretary (Observing) Governance Officer (Observing)
External adviser	Dr Mary Porteous	
Legal Adviser	Jane Williams	Mills & Reeve LLP
Observers	Gerard Hanratty	Browne Jacobson 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:

- 8th 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
- Redacted Peer Review
- Statutory Approval Committee Minutes – 25 February 2016 – approved Nemaline Myopathy type 2, OMIM #256030

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Dr Mary Porteous, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the application is consistent with the peer review, however the application was submitted for Congenital Myopathy aka Nemaline Myopathy, OMIM #161800. This OMIM number is specific to Nemaline Myopathy type 3, resulting from mutations in the alpha 1 actin gene (ACTA1). The Executive suggest that the committee considers naming the condition Nemaline Myopathy type 3, OMIM #161800 which follows the naming format used for the other subtype already approved. However, the Specialist Adviser suggest that the committee considers naming the condition Nemaline Myopathy ACTA 1, OMIM #161800 as this allows for types of the condition inherited in an autosomal recessive and autosomal dominant manner.

1.3. The committee noted that, at the time this application was submitted, an opinion from Genetic Alliance was not available.

1.4. 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.

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

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 the condition is inherited in an autosomal recessive pattern which means there is a 25% chance of an embryo being affected with the condition if each parent has a relevant mutation. If inherited in this manner, the condition is usually at the severe end of the spectrum and life limiting and death can occur during infancy due to cardiorespiratory insufficiency. Few have been reported to survive into the second decade of life.

1.8. The committee noted that the condition can also be inherited in an autosomal dominant pattern which means there is a 50% chance of having an affected child in each pregnancy, if either parent has a relevant mutation. If the condition is inherited in this manner, the age of onset for most affected individuals is in early adulthood with individuals experiencing muscle weakness, hypotonia and respiratory problems. This is a slightly less severe form of the condition, sometimes known as 'typical Nemaline Myopathy' which is more common than the severe form. The weakness predominantly involves proximal musculature, with involvement of the facial, bulbar, and respiratory muscles.

1.9. The committee noted that the specific ACTA1 mutation(s) inherited are likely to determine whether the condition follows an autosomal dominant or recessive expression pattern.

1.10. The penetrance is high for both the autosomal recessive form and the milder autosomal dominant form of the condition.

1.11. Nemaline Myopathy is a rare disorder (1 in 50,000 individuals affected) that primarily affects skeletal muscles, which are muscles that the body uses for movement. Muscle weakness can worsen over time and lead to the development of spinal curvature (scoliosis). Affected individuals may also have feeding and swallowing difficulties, foot and joint abnormalities (contractures).

1.12. There are several types of the condition. The severe congenital type is the most life-threatening and development of respiratory distress eventually requires artificial ventilation. There is no curative treatment for this condition, treatment is symptomatic only. Most individuals with this type do not survive past early childhood due to respiratory failure. In milder cases individuals with the condition can have respiratory insufficiency with poor breathing at night and significant mobility difficulties, requiring a wheelchair.

1.13. The committee noted the inspectorate's request to consider whether Nemaline Myopathy ACTA 1, OMIM #161800 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that Nemaline Myopathy ACTA 1 is serious given that there is a significant risk that a baby could be born with severe muscle weakness, develop breathing difficulties and have difficulties swallowing. Affected individuals have muscle weakness affecting the muscles that the body uses for movement. The committee considered that restricted mobility would severely impact on the individual's quality of life. The condition is life limiting and children could die during infancy.

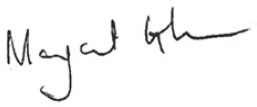
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a person with the abnormality will have or develop a serious physical or mental disability, a serious illness or any other serious medical condition. The committee was therefore satisfied that the condition Nemaline Myopathy ACTA 1, OMIM #161800 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee agreed to authorise testing for Nemaline Myopathy ACTA 1, OMIM #161800.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

16 November 2017