Item 4

Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Mitochondrial Complex 1 Deficiency caused by a mutation in the NDUFB3 gene, OMIM #603839

Thursday, 27 July 2017

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

Committee members	Margaret Gilmore (Chair) Anne Lampe Tony Rutherford Ruth Wilde Bobbie Farsides	
Members of the Executive	Dee Knoyle Paula Robinson	Committee Secretary Head of Planning & Governance
External adviser	Dr Peter Turnpenny	
Legal Adviser	Dawn Brathwaite	Mills & Reeve LLP
Observers		

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
- Two supporting papers submitted with the application
- Redacted peer review
- Alston et al. paper submitted by peer reviewer
- Genetic Alliance opinion
- Minutes of the Statutory Approvals Committee, approving the following as conditions for which PGD can be performed:
  - 17 December 2015 – Mitochondrial Complex 1 Deficiency caused by mutations in the NDUFS6 gene
  - 24 September 2015 – Mitochondrial Complex 1 Deficiency caused by mutations in the ACAD9 gene

1. Consideration of application

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

1.2. The committee noted that the condition applied for by the Person Responsible is Mitochondrial Complex 1 Deficiency caused by a mutation in the NDUFB3 gene, OMIM #252010. The peer reviewer noted that OMIM #252010 covers all forms of Complex 1 Deficiency and suggested that the gene OMIM number is used for clarity, #603839 which is consistent with the Peer Review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the application. This opinion was given for Mitochondrial Complex 1 Deficiency in general, rather than specifically for the condition resulting from mutation in the NDUFB3 gene, however the Executive considered the opinion to be valid for the committee when considering this application.

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 and there is a 25% chance of an embryo being affected with the condition if each parent has a relevant mutation.

1.8. The committee noted that Mitochondrial Complex 1 Deficiency is caused by an enzyme defect which affects multiple systems within the body. Symptoms are normally present from birth, with death in early infancy with this form of MC1D.

1.9. The committee noted that affected infants are typically of low birth weight and may be noted to have floppy muscles, feed poorly, and fail to thrive. Lactic acid may accumulate in the blood and there may be associated multi-organ failure leading to death. Those that survive the neonatal period may develop cardiomyopathy, seizures, brain damage and resulting learning disability. Mitochondrial Complex 1 Deficiency caused by a mutation in the NDUFB3 gene is variable but fully penetrant.

1.10. There is currently no curative treatment for Mitochondrial Complex 1 Deficiency. Many affected infants will die at an early age and it is a life-limiting illness requiring a range of supportive health care.

1.11. The committee noted the inspectorate’s request to consider whether Mitochondrial Complex 1 Deficiency caused by a mutation in the NDUFB3 gene, OMIM #603839 should be approved for inclusion on the PGD List.

1.12. The committee also noted that Mitochondrial Complex 1 Deficiency is caused by different genetic mutations and that the inspectorate had provided a list of these genetic causes for consideration.

2. Decision

2.1. The committee considered that Mitochondrial Complex 1 Deficiency caused by a mutation in the NDUFB3 gene, OMIM #603839, is serious. This is a rare condition which affects multiple systems within the body and is severely debilitating and fully penetrant. The onset of the condition is from birth and babies fail to thrive due to multi-organ failure leading to death in early infancy. Babies surviving the neonatal period may develop cardiomyopathy, seizures, brain damage and resulting learning disability.

2.2. The committee had regard to its decision tree and noted that on the basis of the information presented, given the condition's worst symptoms, it was satisfied that there is a significant risk 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 of Mitochondrial Complex 1 Deficiency caused by a mutation in the NDUFB3 gene does meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

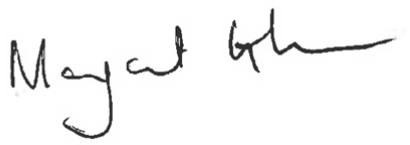
2.3. The committee agreed to authorise the testing for Mitochondrial Complex 1 Deficiency caused by a mutation in the NDUFB3 gene, OMIM #603839. The committee also agreed to use the gene OMIM number for clarity, rather than the condition OMIM number, as advised by the specialist adviser.

2.4. The committee agreed that, in the absence of a peer review, it would not be appropriate to consider any additional Mitochondrial Complex 1 Deficiency gene mutations for inclusion on the PGD List.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

24 August 2017