Statutory Approvals Committee – minutes

Item 6

Centre 0017 Newcastle Fertility Centre at Life

Application to perform PGD for congenital mitochondrial encephalomyopathy/mitochondrial myopathy with diabetes OMIM #500002/*590025

Thursday, 26 July 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Ruth Wilde	
Members of the Executive	Richard Chamberlain Dee Knoyle Bernice Ash Paula Robinson Catherine Burwood	Temporary Committee Clerk Committee Secretary (Observer) Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer)
External Adviser	Professor Peter Turnpenny	
Legal Adviser	Graham Miles	Blake Morgan LLP
Apologies	Anthony Rutherford	

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
- Genetic Alliance UK statement

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Professor Peter Turnpenny who confirmed that the condition was as described in the papers. The committee noted that that the description in the application to perform PGD for Congenital mitochondrial encephalomyopathy/ mitochondrial myopathy with diabetes, OMIM #500002/*590025, is consistent with the peer review.

1.2. The committee noted that Centre 0017 – The Newcastle Fertility Centre at Life, is licensed to provide embryo testing and has submitted an application to provide PGD for Congenital mitochondrial encephalomyopathy/mitochondrial myopathy with diabetes, OMIM #500002/*590025. Congenital mitochondrial encephalomyopathy/mitochondrial myopathy with diabetes is not on the approved PGD condition list.

1.3. The committee noted that the condition is to be referred to by the executive as Mitochondrial myopathy with diabetes, and if the committee was to approve the application it would be added to the PGD list with that same wording.

1.4. The committee noted that the condition can be associated with congenital or early onset of poor tone, swallowing difficulties, delayed cognitive development, weakness and unsteadiness associated with markedly delayed motor development. Survival into adult life leads to the development of a multisystem disease involving diabetes mellitus, cardiomyopathy, proximal and facial weakness, ataxia and cerebellar dysarthria. There are no treatments.

1.5. The committee noted that Mitochondrial myopathy is inherited from the mother through the maternal line, i.e. is matrilinear. Mitochondrial myopathy with diabetes is caused by a mutation in the mitochondrial MTTE gene OMIM *590025 which codes for the mitochondrial tRNA for glutamic acid.

1.6. The committee noted that penetrance is dependent on the proportion of mitochondria in each cell which carries the MTTE mutation relative to the normal gene (the heteroplasmy level) but this relationship is not clear cut. It is therefore extremely difficult to give an accurate estimate of the risk of an embryo being affected by a mitochondrial DNA mutation-related condition such as Mitochondrial myopathy with diabetes.

1.7. The purpose of testing is to establish whether the embryo has a particular abnormality causing Mitochondrial myopathy with diabetes, OMIM #500002/*590025.

1.8. The committee noted that the centre has provided all information on the relevant form to the HFEA as required by General Direction 0008.

1.9. The committee noted that the peer reviewer supported the application but had commented on the effect of variations in heteroplasmy and the efficacy of PGD testing making it difficult to assess the level of heteroplasmy in a blastomere that could be considered safe and unlikely to cause symptoms. Setting a threshold for PGD would be difficult and would require careful counselling of the family.

1.10. The committee noted that Genetic Alliance UK actively endorse a decision by HFEA to issue a license for PGD in this instance as it provides an additional option to parents who find themselves to be at risk of having a child affected by this condition.

1.11. The committee noted that the centre is licensed to provide embryo testing. The committee noted that the centre is seeking approval from the committee for PGD procedure for mitochondrial myopathy with diabetes, OMIM #500002/*590025.

1.12. The committee noted that the disease is associated with early onset of poor muscle tone, swallowing difficulties, delayed motor and cognitive development, weakness and unsteadiness. There can be considerable variation in the condition partially based on the individual's level of heteroplasmy. The committee considered the worst-case scenario.

1.13. The committee agreed with the peer reviewer that careful counselling of the parents in terms of likelihood of success and threshold levels used would be essential.

1.14. The committee referred to its decision tree taking into account the issues discussed above. 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.

2. Decision

2.1. The committee considered the condition to be very serious and noted it is associated with early onset of poor muscle tone, swallowing difficulties, delayed motor and cognitive development, weakness and unsteadiness.

2.2. There was considerable variation in the condition partially based on the individual's level of heteroplasmy. The committee noted that the worst-case scenario cardiomyopathy as part of the condition may be fatal.

2.3. The committee considered the advice of the peer reviewer who had pointed out the risks to children are dependent on the proportion of mitochondria in each cell which carries the MTTE mutation relative to the normal gene (the heteroplasmy level) but this relationship is not clear cut. It is therefore extremely difficult to give an accurate estimate of the risk of an embryo being affected by a mitochondrial DNA mutation-related condition such as Mitochondrial myopathy with diabetes.

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, 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 Mitochondrial myoplathy with diabetes OMIM #500002/*590025, meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

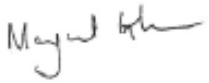
2.5. The committee decided to grant a licence for the Newcastle Fertility Centre at Life Centre 0017 for PGD with Mitochondrial myoplathy with diabetes, OMIM #500002/*590025.

2.6. The committee wished to express their concerns that parents should be adequately counselled to ensure that they were aware of the risks involved. The committee also considered and wished to highlight the HFEA Code of Practice, paragraph 10.5 which states the following; 'When deciding if it is appropriate to provide PGD in particular cases, the centre should consider the circumstances of those seeking treatment rather than the particular heritable condition.'

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

30 August 2018