Statutory Approvals Committee – minutes

Centre 0035 (Oxford Fertility)

PGD for Mitochondrial DNA Depletion Syndrome 13 (MTDPS13)

OMIM #615471

Thursday, 29 August 2019

HFEA, Spey Meeting Room, Level 2, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe	
Members of the Executive	Moya Berry Catherine Burwood	Committee Secretary Licensing Manager (Observer)
Specialist Adviser	Dr. Alan Fryer	
Legal Adviser	Dawn Brathwaite	Mills & Reeve LLP
Observer	Darryn Hale	DAC Beachcroft LLP

Declarations of interest

- Members of the committee declared that they had no conflicts of interest in relation to this item.
- Apologies were received from Rachel Cutting and Tony Rutherford

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
- Redacted Peer Review
- Genetic Alliance UK statement
- Statutory Approvals Committee Minutes, 19 December 2019 - Mitochondrial DNA Depletion Syndrome 2, OMIM #609560
- Licence Committee Minutes, 9 July 2007 - Alpers Syndrome – (Mitochondrial DNA Depletion Syndrome 4, OMIM #203700)

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Alan Fryer, who confirmed that the conditions were as described in the papers.

1.2. The committee noted that the description in the PGD application for Mitochondrial DNA Depletion Syndrome 13 (MTDPS13), OMIM #615471 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 Mitochondrial DNA Depletion Syndrome 13 (MTDPS13), OMIM #615471 is inherited in an autosomal recessive pattern, 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 the penetrance of the condition is 100%.

1.9. Mitochondrial DNA Depletion Syndrome 13 (MTDPS13), OMIM #615471 is a recently described disorder of mitochondrial DNA production and replication. It is a very serious, life-limiting condition that usually presents in early infancy. Babies present with poor feeding and failure to thrive and may be noted to have congenital cataracts.

1.10. The disease is characterised by severe lactic acidosis, muscular hypotonia, and early onset encephalopathy with global developmental delay and brain atrophy. A high percentage of those affected die in early childhood, often as a result of metabolic decompensation during intercurrent infection. Those who survive into later childhood are usually non-verbal and are unable to sit unsupported.

1.11. There is no cure or treatments for this condition.

1.12. The committee noted the executive's request to consider Mitochondrial DNA Depletion Syndrome 13 (MTDPS13), OMIM #615471 for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.13. The committee noted that Mitochondrial DNA Depletion Syndrome 2, OMIM #609560 and Mitochondrial DNA Depletion Syndrome 4a, OMIM #203700 have already been approved for PGD.

1.14. The committee noted the recommendation of the peer reviewer to consider other Mitochondrial DNA Depletion Syndromes for approval as conditions for which PGD can be applied. The committee noted the risk of inheriting these conditions is 25% in each pregnancy if each parent carries a relevant mutation. In the worst-case scenario these conditions, are serious, resulting in death within the first year of life, with no additional treatment options.

These other disorders all have a similar poor prognosis, many being fatal in infancy except for Mitochondrial DNA Depletion Syndrome 8B. The conditions identified by the peer reviewer are:

- Mitochondrial DNA Depletion Syndrome 3 (MTDPS3), OMIM #251880
- Mitochondrial DNA Depletion Syndrome 5 (MTDPS5), OMIM #612073
- Mitochondrial DNA Depletion Syndrome 6 (MTDPS6), OMIM #256810
- Mitochondrial DNA Depletion Syndrome 7 (MTDPS7), OMIM #271245
- Mitochondrial DNA Depletion Syndrome 8A/B (MTDPS8A/B), OMIM #612075
- Mitochondrial DNA Depletion Syndrome 9 (MTDPS9), OMIM #245400
- Mitochondrial DNA Depletion Syndrome 15 (MTDPS15), OMIM #617156

2. Decision

2.1. The committee considered that, in the worst-case scenario Mitochondrial DNA Depletion Syndrome 13 (MTDPS13), OMIM #615471 is a rare and very serious, condition with onset at birth or infancy. There is no cure or treatment that can mitigate against this condition and death frequently occurs in early childhood.

2.2. The committee considered that in the worst-case scenario, Mitochondrial DNA Depletion Syndromes 3, 5, 6, 7, 8A, 9, and15, are conditions of similar severity and clinical presentation to Mitochondrial DNA Depletion Syndrome 13 (MTDPS13). The conditions all present in the neonatal period/infancy, with death occurring in the first year of life.

2.3. The committee agreed that as Mitochondrial DNA Depletion Syndrome 8B (MTDPS8B), OMIM #612075 is different to other Mitochondrial Depletion Syndromes, it was not appropriate to consider this condition under this application. It was agreed that only Mitochondrial DNA Depletion Syndrome 8A (MTDPS8A) would be recorded under the OMIM number #612075 on the HFEA website.

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 abnormalities 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.

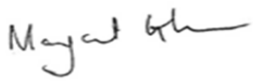
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Mitochondrial DNA Depletion Syndrome 13 (MTDPS13), OMIM #615471
- Mitochondrial DNA Depletion Syndrome 3 (MTDPS3), OMIM #251880
- Mitochondrial DNA Depletion Syndrome 5 (MTDPS5), OMIM #612073
- Mitochondrial DNA Depletion Syndrome 6 (MTDPS6), OMIM #256810
- Mitochondrial DNA Depletion Syndrome 7 (MTDPS7), OMIM #271245
- Mitochondrial DNA Depletion Syndromes 8A (MTDPS8A), OMIM #612075
- Mitochondrial DNA Depletion Syndrome 9 (MTDPS9), OMIM #245400
- Mitochondrial DNA Depletion Syndrome15 (MTDPS15), OMIM #617156

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
16 September 2019