Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Molybdenum Cofactor Deficiency Type B (MOCODB), OMIM #252160

Thursday, 28 June 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Ruth Wilde Anthony Rutherford	
Members of the Executive	Dee Knoyle Bernice Ash Paula Robinson Catherine Burwood Richard Chamberlain	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer) Temporary Committee Clerk (Observing for Induction)
Specialist Adviser	Professor Peter Turnpenny	
Legal Adviser	Tom Rider	Fieldfisher 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
- 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.

1.2. The committee noted that the description in the application for PGD for Molybdenum Cofactor Deficiency Type B (MOCODB), OMIM #252160, is consistent with the peer review.

1.3. The committee noted that Genetic Alliance provided a patient perspective and supported the 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 which means there is a 25% chance of an embryo being affected with the condition in each pregnancy, if both parents have a relevant mutation.

1.8. The committee noted that the condition MOCODB is due to inheriting faults in both copies of the MOCS2 gene. Patients present with neonatal seizures, feeding difficulties, severe developmental delay, brain atrophy and early childhood death.

1.9. The committee noted that penetrance is 100% in children who inherit two faulty copies of the MOCS2 gene.

1.10. The committee noted that in the most severe cases, intractable seizures and feeding difficulties are evident in the first few hours to days of life. Subsequently the children show severe profound intellectual disability and spasticity. Seizures are refractory to anti-epileptic drugs. There is failure to thrive, progressive microcephaly, low muscle tone and lens dislocation, and renal stones may occur in longer-term survivors.

1.11. The committee noted that although substitution therapy with Cyclic Pyranopterin Monophosphate (cPMP) has been successfully used in patients with Molybdenum Cofactor Deficiency Type A (mutations in the MOCS1 gene), there is currently no curative therapy for patients with Molybdenum Cofactor Deficiency Type B. Treatment is palliative.

1.12. Professor Turnpenny advised the committee that MOCODB is a severe neurological condition and that milder cases of MOCODB have been reported with a later onset and not all affected individuals have seizures. There is currently no curative treatment for MOCODB and no long term data available to show the efficacy of therapeutic drugs used to help manage the symptoms.

1.13. The committee noted the inspectorate's request to consider whether Molybdenum Cofactor Deficiency Type B (MOCODB), OMIM #252160, should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

1.14. The committee also noted the inspectorate's request to consider whether Molybdenum Cofactor Deficiency Type A, OMIM #252150, which is clinically similar, should be approved for inclusion on the PGD List. The committee decided not to consider this condition for inclusion on the PGD List at this time.

2. Decision

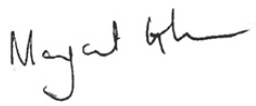
2.1. The committee considered that, in the worst case scenario, Molybdenum Cofactor Deficiency Type B (MOCODB), is a serious condition, given the age of onset can be as early as the first few hours of life. Babies have feeding difficulties and seizures and the condition can cause death during infancy. The condition affects the brain and causes severe developmental delay, profound intellectual disability and spasticity, severely impacting on the quality of life.

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 Molybdenum Cofactor Deficiency Type B (MOCODB) meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

30 July 2018