Statutory Approvals Committee – minutes

Centre 0201 (Edinburgh Assisted Conception Unit) Pre-implantation Genetic Diagnosis (PGD) application for Microcephaly Seizures and Developmental Delay MCSZ (Early Infantile Epileptic Encephalopathy - EIEE 10), OMIM #613402

Thursday, 30 March 2017

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Anthony Rutherford Bobbie Farsides	
Members of the Executive	Dee Knoyle Erin Barton	Secretary Governance Manager
External adviser	Dr Alison Male	
Legal Adviser	Sarah Ellson	Fieldfisher
Observers		

Declarations of interest

- Members of the panel 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 Opinion
- Academic papers
  - The American Journal of Human Genetics 96, 474–479.
  - Neurogenetics (2013) 14:43–51

1. Consideration of application

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

1.2. The committee noted that the description in the PGD application for Microcephaly Seizures and Developmental Delay MCSZ (EIEE 10), OMIM #613402 is consistent with the Peer Review.

1.3. The committee noted that the Genetic Alliance opinion provided a patient's 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 conditions being applied for are 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 the condition demonstrates 100% penetrance and the onset of symptoms is from birth.

1.9. The committee noted that MCSZ (EIEE10) is one of a group of conditions that cause Early Infantile Epileptic Encephalopathy. An affected individual will usually have a very small head (microcephaly) and will develop frequent seizures within the first 2 months of life which are associated with severe developmental delay. It is thought that there is an underlying brain pathology which is exacerbated by the seizures contributing further to severe cognitive and behavioural impairment.

1.10. Death in infancy is common and children that do survive are likely to be severely mentally impaired.

1.11. In some families seizures can be controlled but the child will still develop a progressive neurological problem (ataxia) as a result of cerebellar atrophy (loss of tissue in the balance centre of the brain) requiring a wheelchair and will also exhibit a significant intellectual impairment.

1.12. The committee noted that there is no curative treatment for the condition.

1.13. The committee noted the inspectorate’s recommendation to consider the approval of Microcephaly Seizures and Developmental Delay MCSZ (EIEE 10) to be included on the PGD List and to also include further types of Early Infantile Epileptic Encephalopathy (EIEE) which are individually rare but have a very similar clinical course and are considered clinically indistinguishable from EIEE10. These types include:

EIEE Type	OMIM #	Gene affected
EIEE 3	609304	SLC25A22
EIEE 12	613722	PLCB1
EIEE 15	615006	ST3GAL3
EIEE 16	615338	TBC1D24
EIEE 18	615476	SZT2
EIEE 21	615833	NECAP1
EIEE 23	615859	DOCK7
EIEE 25	615905	SLC13A5
EIEE 29	616339	AARS
EIEE 34	616645	SLC12A5
EIEE 35	616647	ITPA
EIEE 37	616981	FRRS1L
EIEE 38	617020	ARV1
EIEE 39	612949	SLC25A12
EIEE 40	617065	GUF1

1.14. After taking advice from the Specialist Adviser the committee agreed to consider the application on this basis.

1.15. The committee noted that the peer reviewer recommended the approval of two other highly potential similar conditions EIEE 48 and EIEE 50. The committee noted these were not part of the original application and felt it did not have adequate information to consider them for the PGD List.

2. Decision

2.1. The committee considered that the condition is serious. Babies are born with a very small head (microcephaly) and have severe developmental delay. Affected children have significant intellectual impairment, cognitive and behavioural impairment and progressive neurological problems requiring a wheelchair. The committee noted the Genetic Alliance Opinion which provided the patient perspective and testimonials from the families caring for children affected with the condition, living with the knowledge that the condition is progressive, there is no curative treatment and death is inevitable. The committee noted that death in infancy is common and children that do survive are likely to be severely mentally impaired.

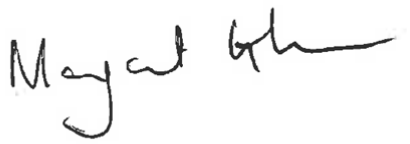
2.2. The committee had regard to its explanatory note and noted that on the basis of the information presented, given the condition's worst symptoms, it was satisfied that there is a significant risk that a person with the abnormality will have or develop a serious physical or mental disability, a serious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

2.3. The committee agreed to authorise the testing of embryos for Microcephaly Seizures and Developmental Delay MCSZ (EIEE 10), OMIM #613402. The committee also agreed to authorise the testing of embryos for all of the additional clinically indistinguishable conditions listed at paragraph 1.13.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

30 March 2017