Statutory Approvals Committee – minutes

Item 8

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Early Infantile Epileptic Encephalopathy type 7 (EIEE7), OMIM #613720

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	Dee Knoyle Bernice Ash Richard Chamberlain Paula Robinson Catherine Burwood	Committee Secretary Committee Secretary (Observer) Temporary Committee Clerk (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer)
Specialist Adviser	Professor Peter Turnpenny	
Legal Adviser	Graham Miles	Blake Morgan 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
- 2017-06-29 Statutory Approvals Committee Minutes – Early Infantile Epileptic Encephalopathy (EIEE) 48, OMIM #617276
- 2017-03-30 Statutory Approvals Committee Minutes - Early Infantile Epileptic Encephalopathy (EIEE) 10, OMIM #613402 (and other subtypes)

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 Early Infantile Epileptic Encephalopathy type 7 (EIEE7), OMIM #613720 is consistent with the peer review.

1.3. The committee noted that the Genetic Alliance opinion 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. EIEE7 is caused by mutations in the KCNQ2 gene and is inherited in an autosomal dominant manner, which means there is a 50% chance of an embryo being affected with the condition in each pregnancy, if either parent has a relevant mutation.

1.8. The committee noted that EIEE7 is a hereditary condition characterised by encephalopathy with multiple daily seizures beginning in the first week of life. Seizure frequency decreases in early childhood, with most children being seizure-free by three to four years of age. However, the seizures cause delay in neurological development and affected individuals have life-long neurological abnormalities, including movement disorders and intellectual disability.

1.9. The committee noted that seizures are mostly tonic, with associated focal motor and autonomic features. Other symptoms include generalised stiffening and automatisms. Encephalopathy is present from birth and persists during and after the period when seizures are uncontrolled, and results in delayed psychomotor development; intellectual disability; hypotonia; dystonia and spastic quadriparesis. Psychomotor developmental impairment is moderate in about one third of individuals and severe to profound in the remaining two thirds.

1.10. The committee noted that many patients at onset present with multiple daily seizures that are resistant to multiple old and new-generation antiepileptic drugs, alone or in combination. Sodium channel blockers have provided effective seizure control in some patients and should be considered first-line treatment. It has been suggested that early effective treatment reduces cognitive disability, however it remains a matter of debate whether early control of seizures translates to better neuropsychological outcome. During periods of seizure activity, patients require ongoing neurological monitoring. They should also have serial evaluation of neurologic, cognitive and behavioural problems. Management should focus on the optimisation of the patient’s functional and communication skills. A multidisciplinary team approach including physiotherapists, speech therapists, nutritionists and behavioural therapists is best suited to addressing the individual’s needs. Augmentative communication techniques can be valuable for many patients. The early years of frequent seizures are stressful for the family. Even though most patients become seizure-free in early childhood, many suffer lifelong neurological disability, which impacts many areas of daily life activity.

1.11. The Specialist Adviser to the committee, Professor Peter Turnpenny confirmed that EIEE7 belongs to a large family of conditions. The committee noted that EIEE types 3, 10, 12, 15, 16, 18, 21, 23, 25, 28, 29, 34, 35, 37, 38, 39, 40 and 48, have already been approved for PGD.

1.12. Professor Turnpenny also advised the committee that although seizures can improve, neurological development is severely affected and intellectual ability may be impaired. In the majority of cases the condition is caused by a de novo mutation, an alteration in a gene that is present for the first time in one family member as a result of a mutation in a germ cell (egg or sperm) of one of the parents, or in the fertilized egg itself. However, in an estimated 1% of cases the condition arises because of parental mosaicism, either germline or somatic (1% is based on general mosaicism risks). Mosaicism refers to the situation where the genetic variant is present in a proportion of cells and tissues, not all, with the result that there may be no clinical consequences.

1.13. Professor Turnpenny also confirmed that the condition is difficult to manage and a sodium channel blocker such as Mexiletine is also used in treatment. The committee noted that there is no curative treatment for EIEE7.

1.14. The committee noted the inspectorate's request to consider whether Early Infantile Epileptic Encephalopathy type 7 (EIEE7), OMIM #613720 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

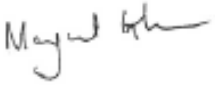
2.1. The committee considered that, in the worst case scenario, Early Infantile Epileptic Encephalopathy type 7 (EIEE7), OMIM #613720 is a serious condition which affects the brain and causes multiple daily seizures, beginning in the first week of life. Affected individuals have life-long neurological abnormalities, including intellectual disability and movement disorders which can interfere with day to day tasks. Management of the symptoms is difficult and there is no curative treatment. The quality of life for affected individuals is severely impacted.

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 Early Infantile Epileptic Encephalopathy type 7 (EIEE7), OMIM #613720 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing.

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