Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Episodic Kinesigenic Dyskinesia type1 (EKD1), OMIM #128200

Thursday, 26 April 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Anthony Rutherford	
Members of the Executive	Bernice Ash Dee Knoyle Paula Robinson Catherine Burwood Clare Ettinghausen	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer) Director of Strategy and Corporate Affairs (Observer)
Specialist Adviser	Professor Peter Turnpenny	
Legal Adviser	Gerard Hanratty	Browne Jacobson 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
- Email from centre confirming condition - Paroxysmal Choreoathetosis, OMIM #602066, to be considered within the application.

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 Episodic Kinesigenic Dyskinesia type1 (EKD1), OMIM #128200 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. The committee noted that the condition is inherited in an autosomal dominant pattern which means there is a 50% chance of an embryo being affected with the condition, if either parent has a relevant mutation.

1.8. The committee noted that EKD1 is caused by mutations in the PRRT2 gene and is a neurogenetic condition characterised by recurrent and brief attacks of involuntary movement triggered by sudden motion, such as standing up quickly or being startled. The involuntary movements include slow, prolonged muscle contractions; small, fast, ‘dance-like’ motions; writhing movements of the limbs; or, rarely, flailing movements of the limbs. Attacks may also involve migraine on one side of the body. Individuals do not lose consciousness during an episode and do not experience symptoms between episodes. The frequency of attacks can range widely from one per month to many per day, and while usually lasting a few seconds to five minutes in duration, attacks can sometimes last several hours. Affected infants may have epilepsy and convulsions (afebrile seizures), with no neurologic sequelae - in 40% of patients.

1.9. The age of onset of the condition is variable, ranging from four months to 57 years, but is typically in childhood or adolescence (median 9 years of age). The condition exhibits high penetrance of 80-90% in both males and females, but symptoms are phenotypically variable, even in the same family, and it tends to affect males more than females. Symptoms can decrease or remit with age.

1.10. The committee noted treatments are available and attacks are reduced or prevented by the anticonvulsants phenytoin and carbamazepine, typically given at lower doses than are used to treat epilepsy. Other effective anti-epileptic drugs include oxcarbazepine, ethosuximide, and lamotrigine. If attacks are not effectively controlled, they can cause psychological burden and poorer quality of life. Depression and anxiety are more prevalent in patients affected with EKD1.

1.11. The committee noted that the Peer Reviewer suggested that the condition Convulsions, Familial Infantile, with Paroxysmal Choreoathetosis, OMIM #602066, should be considered for addition to the PGD list. This second condition is similar to EKD1 in that it is also caused by heterozygous mutations in the PRRT2 gene, follows autosomal dominant inheritance and its symptoms include episodic dyskinesia and infantile seizures.

1.12. The committee noted the Person Responsible (PR) at the centre had confirmed that they would like the condition Convulsions, Familial Infantile, with Paroxysmal Choreoathetosis, OMIM #602066 to also be considered as conditions for which PGD can be applied.

1.13. The committee noted the inspectorate's request to consider whether Episodic Kinesigenic Dyskinesia type1 (EKD1), OMIM #128200 should be approved for inclusion on the PGD List. The inspectorate also requested that the committee considers approving the condition Convulsions, Familial Infantile, with Paroxysmal Choreoathetosis, OMIM #602066 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, Episodic Kinesigenic Dyskinesia type1 (EKD1), OMIM #128200 is serious given it is a lifelong condition, severely impacting on the quality of life of those with the condition and their families. Severe involuntary movements can also be extremely embarrassing and stigmatizing in a public setting. The committee also considered the potential symptomatic side effects of available treatments.

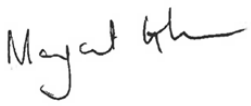
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 Episodic Kinesigenic Dyskinesia type1 (EKD1), OMIM #128200 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee agreed to authorise testing for Episodic Kinesigenic Dyskinesia type1 (EKD1), OMIM #128200. The committee also agreed to authorise testing for Convulsions, Familial Infantile, with Paroxysmal Choreoathetosis, OMIM #602066.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

17 May 2018