Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Hyperphosphatasia with Intellectual Disability Syndrome 3 (HPMRS3) OMIM #614207

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
- One additional paper form peer reviewer
- Comment from centre re peer review
- Genetic Alliance UK Statement
- SAC minutes, 23 January 2017, Mabry Syndrome (Hyperphosphatasia with intellectual disability syndrome 1), Type 1, OMIM #239300
- SAC minutes, 28 August 2014, Mabry Syndrome (Hyperphosphatasia with intellectual disability syndrome 4), Type 4 OMIM # 615716

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 Hyperphosphatasia with intellectual disability syndrome 3, OMIM #614207 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 recessive pattern which means 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 Hyperphosphatasia 3 is a genetic condition that is characterised by severe developmental delay, poor or absent speech and low muscle tone. It is caused by mutations in the PGAP2 gene. Hyperphosphatasia 3 onset is from birth or infancy.

1.9. The committee noted that Hyperphosphatasia 3 is part of the Hyperphosphatasia with intellectual disability group of moderate to severe postnatal neurodegenerative disorders. All types of Hyperphosphatasia are associated with moderate to severe learning disability and seizures. Symptoms of Hyperphosphatasia 3 also include poor or absent speech development, delay in development of motor skills with hypotonia, raised alkaline phosphatase and hyperphosphatemia (abnormally raised levels of phosphate in the blood), microcephaly (small head) and cerebral atrophy (loss of neurons and neuronal connections). There can be some clinical variability in expression. However, in most cases the condition is severe and penetrance complete (100%).

1.10. Some of the symptoms can be managed, but the condition is not curable. Seizures are frequently resistant to anti-epileptic medication. Management should focus on helping the child to achieve optimal function and skills. A multidisciplinary team of paediatricians, physiotherapists, speech therapists and special need teachers are required. Most patients present with poor development in early childhood. This affects quality of life outcomes, leading to a life lacking independence and requiring continuous care and management.

1.11. The committee noted that the Peer Reviewer had identified that Hyperphosphatasia 4 has already been licensed by the HFEA, describing other types of Hyperphosphatasia which are similar conditions to Hyperphosphatasia 3. The Peer Reviewer referenced the paper (Altassan et al), which documented the similarity in the phenotype between the 7 different Hyperphosphatasia syndromes that make up Mabry syndrome; this group of disorders are a cause of significant morbidity. The Peer Reviewer suggested that the committee consider all 7 types of this condition, in this application, as they are almost indistinguishable. Conditions 2,5,6 and 7 are stated below.

Condition	OMIM	Gene affected
Hyperphosphatasia with intellectual disability syndrome 2	#614749	PIGO
Hyperphosphatasia with intellectual disability syndrome 5	#616025	PIGW
Hyperphosphatasia with intellectual disability syndrome 6	#616809	PIGY
Hyperphosphatasia with intellectual disability syndrome 7, also known as Coloboma, Congenital Heart Disease, Ichthyosiform Dermatosis, Intellectual disability and Ear Anomalies Syndrome	#280000	PIGL

1.12. The committee noted the Person Responsible (PR) at the centre had confirmed that they would like the additional types of Hyperphospatasia with Intellectual disability syndrome to also be considered as conditions for which PGD can be applied.

1.13. The committee noted that alongside Hyperphosphatasia with intellectual disability syndrome 1, OMIM #239300, Hyperphosphatasia with intellectual disability syndrome 4, OMIM #615716 had also already been licensed for PGD by the HFEA.

1.14. The committee noted the inspectorate's request to consider whether Hyperphosphatasia with intellectual disability syndrome 3, OMIM #614207 should be approved for inclusion on the PGD List. The inspectorate also requested that the committee consider approving the additional types of Hyperphosphatasia with intellectual disability syndrome. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario, Hyperphosphatasia with intellectual disability syndrome 3, OMIM #614207 is serious given the condition is chronic, with symptoms including seizures, heart disease, brain malformations and intellectual disability. The condition severely impacts on the individual's quality of life and the family.

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 Hyperphosphatasia with intellectual disability syndrome 3, OMIM #614207, meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

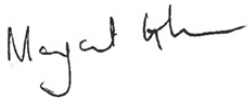
2.3. The committee agreed to authorise testing for the following conditions:

- Hyperphosphatasia with intellectual disability syndrome 2, OMIM #614749
- Hyperphosphatasia with intellectual disability syndrome 3, OMIM #614207
- Hyperphosphatasia with intellectual disability syndrome 5, OMIM #616025
- Hyperphosphatasia with intellectual disability syndrome 6, OMIM #616809
- Hyperphosphatasia with intellectual disability syndrome 7, also known as Coloboma, Congenital Heart Disease, Ichthyosiform Dermatosis, Intellectual disability and Ear Anomalies Syndrome (CHIME), OMIM #280000

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

17 May 2018