Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352

Thursday, 25 January 2018

Church House Westminster, Dean's Yard, Westminster SW1P 3NZ

Committee members	Margaret Gilmore (Chair) Anne Lampe Tony Rutherford Ruth Wilde	
Members of the Executive	Dee Knoyle Bernice Ash Nana Gyamfi Chereena Harriott	Committee Secretary Committee Secretary (Observing) Licensing Information Officer (Observing) Inspections & Logistics Officer (Observing)
External Adviser	Dr Alison Male	
Legal Adviser	Dawn Brathwaite	Mills & Reeve 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 Statement

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 application for Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352 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 CCDS1 is a X-linked condition, which means if the mother is a carrier there is a 50% chance of an affected child in each pregnancy. Males will be more severely affected than females.

1.8. The committee noted that CCDS1 is caused by mutations in the SLC6A8 gene on the X chromosome. The condition affects mainly males and results in complete absence or severe reduction of creatine in the brain. Creatine plays a crucial role in energy metabolism.

1.9. The committee noted that symptoms and signs of CCDS1 usually manifest in infancy and include intellectual disability, behavioural problems and seizures (over 50% will have generalised or complex partial seizures). Other symptoms include decreased muscle tone and gastrointestinal and urogenital abnormalities. A small number of those affected will have intractable epilepsy. All reported males with the mutation are affected, with most having moderate to severe expression of symptoms including intellectual disability in adulthood. Females are usually unaffected or mildly affected, exhibiting mild intellectual and behavioural impairment and epilepsy, because the second normal X chromosome partially compensates for the SLC6A8 mutation. However, if the normal SLC6A8 gene is silenced, a female may be as severely affected as a male.

1.10. The committee noted that CCDS1 is one of three Cerebral Creatine Deficiency syndromes, the main difference between them being that CCDS1 does not respond to treatment but the other two types (CCDS2 and 3) do. Due to the underlying biochemical mechanism of CCDS1, it is likely to be fully penetrant, with a 50% penetrance of learning problems in female carriers.

1.11. The committee noted that there is no effective treatment that modifies CCDS1. Quality of life is compromised by seizures which can be difficult to treat, behavioural difficulties lead to challenges for both the family and affected individual, for both males and affected females.

1.12. The committee noted the inspectorate's request to consider whether Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352 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 Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352 is serious given that symptoms of the condition manifest as early as infancy and the condition affects the brain, causing seizures, intellectual disability and behavioural problems. Other symptoms include decreased muscle tone. The committee considered the impact on the quality of life of affected individuals with a severe mental disability and physical disability such as epilepsy.

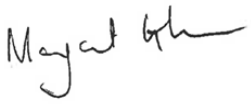
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352 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 Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

9 February 2018