Statutory Approvals Committee - minutes

Centre 0101 (CARE Nottingham)

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) - application for Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352, Cerebral Creatine Deficiency Syndrome 2 (CCDS2), OMIM #612736, Cerebral Creatine Deficiency Syndrome 3 (CCDS3), OMIM #612718

Date:	26 August 2021
Venue:	HFEA, 2nd Floor, 2 Redman Place, London E20 1JQ via Microsoft Teams
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde Tim Child
Specialist Adviser:	Alan Fryer
Legal Adviser:	Tom Rider - FieldFisher LLP
Members of the Executive:	Moya Berry - Committee Officer Catherine Burwood - Licensing Manager
Apologies:	No apologies were received for the meeting
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:

- HFEA Code of Practice 9th edition
- Standard Licensing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGT-M Application Form
- Redacted Peer Review
- Supporting Document - Guanidinoacetate methyltransferase (GAMT) deficiency: Outcomes in 48 individuals and recommendations for diagnosis, treatment, and monitoring, Stockler-Ipsiroglu et al, 2013
- 2018-01-25 Statutory Approvals Committee Minutes, PGD for Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352

1. Consideration of application

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

1.2. The committee noted that the description in the PGT-M application for Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352, Cerebral Creatine Deficiency Syndrome 2 (CCDS2), OMIM #612736 and Cerebral Creatine Deficiency Syndrome 3 (CCDS3), OMIM #612718, is consistent with the peer review.

1.3. The committee noted that the conditions being applied for are not on the list of approved PGT-M conditions with the exception of Cerebral Creatine Deficiency Syndrome 1 (CCDS1), OMIM #300352 which is on the approved PGT-M list and therefore an application is not required.

1.4. The committee noted that a Genetic Alliance (UK) statement had not been provided for this application.

1.5. The committee had regard to its decision tree. The committee noted that the centre is licensed to carry out PGT-M. The committee was also satisfied that the centre has experience of carrying out PGT-M and that generic patient information about its PGT-M programme and associated consent forms had previously been received by the HFEA.

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 Cerebral Creatine Deficiency Syndrome 2 (CCDS2), OMIM #612736 and Cerebral Creatine Deficiency Syndrome 3 (CCDS3), OMIM #612718, are inherited in an autosomal recessive manner, which means there is a 25% chance of an embryo being affected by the conditions in each pregnancy if each parent has a relevant mutation.

1.8. The committee noted that the penetrance of these conditions is 100%.

1.9. Cerebral Creatine Deficiency Syndrome 2 (CCDS2), OMIM #612736 and Cerebral Creatine Deficiency Syndrome 3 (CCDS3), OMIM #612718, are characterised by global developmental delay. Speech delay may be particularly severe and is present in all affected children. Intellectual disability of variable severity is typically present. Additional symptoms may also

include seizure disorders, muscle weakness, behaviour disorders, autistic behaviours, movement disorders, gastrointestinal problems, and failure to thrive.

1.10. There is no cure for the conditions. Treatment can include anti-epileptic medication as well as significant dietary manipulation which may not always improve outcomes in individuals.

1.11. The committee noted the executive's request to consider Cerebral Creatine Deficiency Syndrome 2 (CCDS2), OMIM #612736 and Cerebral Creatine Deficiency Syndrome 3 (CCDS3), OMIM #612718, for inclusion on the list of conditions approved for PGT-M. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Cerebral Creatine Deficiency Syndrome 2 (CCDS2), OMIM #612736 and Cerebral Creatine Deficiency Syndrome 3 (CCDS3), OMIM #612718 are severe, progressive, and potentially life-threatening conditions with symptoms present in infancy. Those affected usually suffer intellectual disability and global development delay. Seizures may be difficult to control. The committee considered the potential significant psychological, emotional, and physical implications, on the quality of life of those affected by the conditions.

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 abnormalities in question and that there is a significant risk that a person with such abnormalities will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness, or any other serious medical condition.

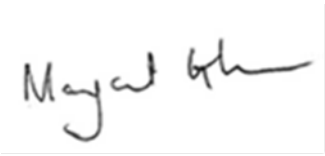
2.3. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Cerebral Creatine Deficiency Syndrome 2 (CCDS2), OMIM #612736
- Cerebral Creatine Deficiency Syndrome 3 (CCDS3), OMIM #612718

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

21 September 2021