Statutory Approvals Committee – minutes

Centre 0035 (Oxford Fertility)
Pre-implantation Genetic Diagnosis (PGD) application for Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 1 (OMIM #224050), Type 2 (OMIM #610185), Type 3 (OMIM #613227) and Type 4 (OMIM #615268)

Thursday 13 August 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe	
Members of the Executive	Dee Knoyle Catherine Burwood	Committee Secretary Senior Governance Manager (Observer)
Specialist Adviser	Dr Alison Male	
Legal Adviser	Tom Rider	Fieldfisher 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
- Correspondence with centre staff regarding the PGD application and its impact on the patient's funding treatment
- One academic paper describing the condition

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 centre 0035 has submitted an application to provide PGD for ATP8A2 related encephalopathy, OMIM #615268. The Executive has determined, using the OMIM website, that OMIM #615268 defines Cerebellar Ataxia, Mental Retardation and Dysequilibrium Syndrome Type 4 which results from homozygous mutation in the ATP8A2 gene. The centre has confirmed that 'ATP8A2 related encephalopathy' and 'Cerebellar Ataxia, Mental Retardation and Dysequilibrium Syndrome Type 4' define the same condition. The committee noted that there is sensitivity around the use of the term 'mental retardation' and that it is preferred that the term 'intellectual disability' is used instead.

1.3. The committee noted that the description in the application for Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 4, OMIM #615268 is consistent with the peer review.

1.4. The committee noted that an opinion on this application and the impact of the condition on individuals, families and carers was requested from Genetic Alliance UK, however the opinion was unavailable at the time this application was considered

1.5. 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.

1.6. The committee noted that the condition being applied for is not on the list of approved PGD conditions.

1.7. 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'.

1.8. 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 in each pregnancy, if both parents have a relevant mutation.

1.9. The committee noted that Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 4 is caused by homozygous mutations in the ATP8A2 gene. The condition is characterised by congenital cerebellar ataxia and intellectual disability. It causes severe cognitive and psychomotor developmental delay with intellectual disability, reduced muscle tone, abnormal balance and movement and, in some cases, blindness due to optic atrophy, and hearing impairment. Symptoms of the condition are exhibited from birth and penetrance is 100%; those affected by the condition are generally severely affected.

1.10. The committee noted that there is no cure for this condition, only supportive care such as physiotherapy to improve muscle tone and hearing aids to assist hearing deficits are available. Affected individuals are dependent on care and their lifespan may be severely shortened.

1.11. The committee noted the inspectorate's request to consider whether Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome 4, OMIM #615268, should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

1.12. The committee noted that the inspectorate also request that the committee considers whether the following conditions should also be approved for inclusion on the PGD List:

- CAMRQ1, i.e. Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 1, OMIM #224050 (caused by homozygous mutations in the VLDLR gene)
- CAMRQ2, i.e. Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 2, OMIM #610185 (caused by homozygous mutations in the WDR81 gene)
- CAMRQ3, i.e. Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 3, OMIM #613227 (caused by homozygous mutations in the CA8 gene).

1.13. The Peer Reviewer considers the above conditions all have a very similar phenotype and level of severity equal to Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 4, OMIM #615268 and the Specialist Adviser agreed. The committee also agreed to consider the above additional conditions for inclusion on the PGD List.

2. Decision

2.1. The committee considered that, in the worst case scenario, Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 1 (OMIM #224050), Type 2 (OMIM #610185), Type 3 (OMIM #613227) and Type 4 (OMIM #615268) are serious conditions present from birth.

2.2. These conditions affect the brain, causing severe cognitive and psychomotor developmental delay with intellectual disability. Affected individuals have reduced muscle tone, abnormal balance and movement and in some cases blindness and hearing impairment. The committee considered that these conditions cause both mental and physical disability and individuals with affected balance and coordination may have an increased risk of injury. The committee considered the psychological impact on an individual with severe intellectual disability, suffering injuries caused by their symptoms. The committee agreed that these conditions severely impact on the quality of life. The committee also considered that the conditions may shorten an individual's lifespan and there is no curative treatment.

2.3. 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 following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing for these conditions:

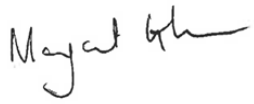
- Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 1, OMIM #224050
- Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 2, OMIM #610185
- Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 3, OMIM #613227
- Cerebellar Ataxia, Intellectual Disability and Dysequilibrium Syndrome Type 4, OMIM #615268

2.4. The committee noted that this particular application was processed with a delay on the part of the Executive and therefore agreed to hold an extraordinary meeting in order that the deadline could be met for the patient to receive funding for her treatment which is timebound. The committee was very sympathetic to the unusual set of circumstances which caused the delay to the Executive processing this application and urged the centre to ensure that all applications are processed as soon as possible in future in order to reduce any risk to the patient missing deadlines for funding of their treatment.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

13 August 2018