Statutory Approvals Committee – minutes

Item 1

Centre 0044 (The Centre for Reproductive and Genetic Health)

Pre-implantation Genetic Diagnosis (PGD) application for

Familial Creutzfeldt-Jakob disease (fCJD), OMIM #123400

Thursday, 14 December 2017

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

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Ruth Wilde	
Members of the Executive	Dee Knoyle	Committee Secretary
External adviser	Dr Alan Fryer	
Legal Adviser	Eve Piffaretti	Blake Morgan 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
- SAC minutes 25 February 2016, approving Gerstmann-Straussler-Scheinker syndrome, OMIM #137440, as a condition for which PGD can be applied.

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 application for Familial Creutzfeldt-Jakob disease (fCJD), OMIM #123400 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. fCJD is inherited in an autosomal dominant manner which means there is a 50% chance of having an affected child in each pregnancy, if either parent has a relevant mutation.

1.8. fCJD is caused by mutations in the same gene - PRNP – as Gerstmann-Straussler-Scheinker disease. The main symptoms of fCJD are cognitive difficulties, psychiatric problems and neurological problems.

1.9. fCJD typically presents between the ages of 30 and 50 years, but can present outside of this age range. fCJD usually begins with progressive confusion and memory impairment. Symptoms including ataxia (balance problems and clumsiness) and myoclonus (abrupt jerking movements of muscle groups and/or entire limbs) then follow. Associated neurological problems may also occur (e.g. seizures and stroke-like episodes). Ataxia is progressive and leads to repeated falls. This often leads to wheelchair use to avoid injury. The condition can vary between individuals and individuals with fCJD who have two copies of the Met allele at position 129 will, in general, have an earlier diagnosis and a shorter disease course. The majority (60-90%) of mutation carriers exhibit signs of the condition by the fifth decade.

1.10. Treatment is palliative and aimed at easing discomfort, no cure is available. Quality of life is adversely affected due to the distress of dementia, behavioural change and loss of speech and mobility. Patients need increasing levels of assistance with tasks of daily living and will eventually be incapacitated and fully dependent on medical and nursing care in the later stages of the disease. The condition is fatal - the time from onset to death can be anything from a few months to five years.

1.11. The committee noted the inspectorate’s request to consider whether Familial Creutzfeldt-Jakob disease (fCJD), OMIM #123400, should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

1.12. The committee noted the Peer Reviewer's comment that the following three inherited prion diseases are almost clinically indistinguishable particularly in the end stages and that they result from mutations in the same gene, PRNP:

- Familial Creutzfeldt-Jakob disease (fCJD), OMIM #123400 which is this application;
- Gerstmann-Straussler-Scheinker disease, OMIM #137440 which is already licensed;
- Familial Fatal Insomnia, OMIM #600072 which has yet to be licensed.

1.13. The committee noted the inspectorate's recommendation to consider separately adding Familial Fatal Insomnia, OMIM #600072, to the list of conditions for which PGD can be applied.

1.14. The committee noted that the Specialist Adviser also recommended that the committee considers adding a further two conditions to the list of conditions for which PGD can be applied:

- Huntington disease-like 1 (HDL1), OMIM #603218
- Prion disease with protracted course, OMIM #606688

1.15. The Special Adviser confirmed that these conditions, OMIM #603218 and OMIM #606688 show the same symptoms, the same penetrance and mode of inheritance and are due to mutations in the same gene, PRNP. They also were almost clinically indistinguishable, particularly in the end stages and have the same fatal outcome as the condition that is the subject of this application fCJD OMIM #123400. The committee had regard to its decision tree and noted that these conditions had the same proposed purpose of testing the embryos in paragraph 1ZA(1)(b) of Schedule 2 of the Act.

1.16. The committee heard evidence on the symptoms and prognosis for the conditions suggested by the Peer Reviewer and the Specialist Adviser and concluded that they were the same as those caused by the mutations in the same gene as outlined in this application for fCJD OMIM #123400. On this basis, the committee decided to consider these additional conditions with this application too.

2. Decision

2.1. The committee considered that Familial Creutzfeldt-Jakob disease (fCJD), OMIM #123400 is a serious neurodegenerative disorder. The committee heard that this is a devastating, fatal condition which can develop as early as the teenage years but more often develops from the age of 30 onwards. Affected individuals develop dementia and loss of speech as the disease progresses. Mobility is severely affected and the sufferers become wheelchair bound which impacts on their quality of life. Once symptoms develop, death will normally result within a few months to five years.

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 Familial Creutzfeldt-Jakob disease (fCJD), OMIM #123400 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee noted that Familial Fatal Insomnia, OMIM #600072, Huntington disease-like (HDL1), OMIM #603218, Prion disease with protracted course, OMIM #606688 were inherited prion diseases which are almost clinically indistinguishable from Familial Creutzfeldt-Jakob disease (fCJD), OMIM #123400, particularly in the end stages. The committee was also satisfied that these conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act on this basis.

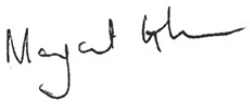
2.4. The committee agreed to authorise testing for the following:

- Familial Creutzfeldt-Jakob disease (fCJD), OMIM #123400
- Familial Fatal Insomnia, OMIM #600072
- Huntington disease-like (HDL1), OMIM #603218
- Prion disease with protracted course, OMIM #606688

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

22 December 2017