Statutory Approvals Committee - minutes

Centre 0102 (Guys Hospital)

Preimplantation Genetic Diagnosis (PGD) application for Generalized epilepsy with febrile seizures plus, type 2 (GEFSP2); OMIM #604403

Date:	27 May 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde Jason Kasraie
Specialist Adviser:	Alison Male
Legal Adviser:	Graham Miles – Blake Morgan LLP
Members of the Executive:	Moya Berry - Committee officer Catherine Burwood - Licensing Manager
Observers:	Dina Halai- Senior Scientific Policy Manager HFEA India Hickey – Research Officer (Induction)
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
- PGD Application form
- Redacted Peer review
- Genetic Alliance (UK) Statement
- 2012-07-19 Licence Committee Minutes - PGD for Dravet Syndrome, OMIM #607208

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 PGD application for Generalized epilepsy with febrile seizures plus, type 2 (GEFSP2), OMIM #604403, is consistent with the peer review.

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

1.4. The committee noted that the Genetic Alliance (UK) statement provided a perspective on the impact of the condition on patients, their families, and carers.

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 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 Generalized epilepsy with febrile seizures plus, type 2 (GEFSP2), OMIM #604403, is inherited in an autosomal dominant manner, which means there is a 50% chance of an embryo being affected by the condition in each pregnancy if either parent has a relevant mutation.

1.8. The committee noted that research data suggests that the penetrance of the condition is high and may be up to 92%.

1.9. Generalized epilepsy with febrile seizures plus, type 2 (GEFSP2), OMIM #604403, is characterised by febrile and afebrile seizures, which can include tonic, clonic, tonic-clonic, myoclonic, or absence seizures. Patients with the condition are usually seizure-free in adulthood without the need for medications, however occasional seizures can occur in adulthood. There is a higher incidence of neuropsychological, behavioural, and cognitive problems in those with the condition. There is also the risk that sudden unexplained death in epilepsy can occur.

1.10. There is no curative treatment for this condition and seizure control with antiepileptic drugs is essential, although this may not always be effective.

1.11. The committee noted the executive's request to consider Generalized epilepsy with febrile seizures plus, type 2 (GEFSP2), OMIM #604403, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.12. The committee noted the recommendation of the executive to consider a number of additional conditions for inclusion on the list for which PGD can be applied. The peer reviewer considers there is reasonable evidence to support the applications for Generalized epilepsy with febrile seizures plus, type 1 (GEFSP1), OMIM #604233, Generalized epilepsy with febrile seizures plus, type 3 (GEFSP3), OMIM, #607681, and Generalized epilepsy with febrile seizures plus, type 5, susceptibility to, (GEFSP5), OMIM #613060. The committee agreed to consider the applications on this basis.

1.13. The committee noted the conditions are inherited in an autosomal dominant manner, meaning the risk of inheriting the condition is 50% in each pregnancy if either parent carries a relevant mutation. The penetrance of the condition types is not precisely characterised. Symptoms of these condition types include febrile and non-febrile seizures, the potential risk of developmental delay, and the risk of sudden death as a result of epilepsy.

1.14. The committee also noted the recommendation of the peer reviewer's request to consider the conditions Generalized epilepsy with febrile seizures plus, type 9 (GEFSP9), OMIM, #616172 and Generalized epilepsy with febrile seizures plus, type 10 (GEFSP10), OMIM #618482 for inclusion on the list for which PGD can be applied. Based on the advice of its specialist adviser, and the lack of available information to assess the severity of the conditions, the committee agreed it was not appropriate to consider these for PGD at this time.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Generalized epilepsy with febrile seizures plus, type 2 (GEFSP2), OMIM #604403, is a severe, life-threatening condition that presents in infancy and if left untreated can cause permanent and irreversible brain damage. Those affected may, as a result of the epilepsy. be at risk of sudden unexplained death. There is no cure for the condition, with some suffering drug resistant epilepsy, making the condition very difficult to control. The committee considered the potential serious physical and psychological impact on the quality of life of those living with the condition.

2.2. The committee also considered that the conditions Generalized epilepsy with febrile seizures plus, type 1 (GEFSP1), OMIM #604233, Generalized epilepsy with febrile seizures plus, type 3 (GEFSP3), OMIM, #607681, Generalized epilepsy with febrile seizures plus, type 5, susceptibility to, (GEFSP5), OMIM #613060, are, in the worst-case scenario, associated with the onset of seizures in infancy or early childhood and potential developmental delay. In severe cases the conditions persist into adulthood and may be resistant to medication.

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 that a person with such an abnormality will, given the condition's worst symptoms, have or develop a serious physical disability, a serious illness, or any other serious medical condition.

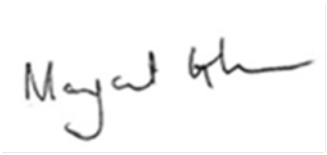
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Generalized epilepsy with febrile seizures plus, type 1 (GEFSP1), OMIM #604233
- Generalized epilepsy with febrile seizures plus, type 2 (GEFSP2), OMIM #604403
- Generalized epilepsy with febrile seizures plus, type 3 (GEFSP3), OMIM, #607681
- Generalized epilepsy with febrile seizures plus, type 5, susceptibility to, (GEFSP5), OMIM #613060

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

21 June 2021