Statutory Approvals Committee - minutes

Centre 0119 (Birmingham Women's Hospital)

Preimplantation Genetic Diagnosis (PGD) application for Emery Dreifuss Muscular Dystrophy 6, X-Linked (EDMD6), OMIM #300696

Date:	25 March 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe
Specialist Adviser:	Jenny Carmichael
Legal Adviser:	Tom Rider - FieldFisher
Members of the Executive:	Moya Berry - Committee officer Catherine Burwood - Licensing Manager
Observers:	Jason Kasraie, Authority Member (Induction)
Apologies:	No apologies were received for the meeting
Declarations of Interest:	Ruth Wilde declared a conflict of interest and was not present at the meeting for this item. No other members declared a conflict 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
- 2018-01-25, Statutory Approvals Committee minutes, PGD for Muscular Dystrophy, Congenital, LMNA-related (MDCL), OMIM #613205
- 2012-08-30, Licence Committee minutes, PGD for X-Linked Emery-Dreifuss Muscular Dystrophy, OMIM #310100.

1. Consideration of application

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

1.2. The committee noted that the description in the PGD application for X-Linked Emery Dreifuss Syndrome, OMIM #300696, 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 condition, X-Linked Emery Dreifuss Syndrome, OMIM #300696 is also known as Emery-Dreifuss Muscular Dystrophy 6, X-Linked (EDMD6), OMIM #300696. As the OMIM website entry lists Emery-Dreifuss Muscular Dystrophy 6, X-Linked (EDMD6), OMIM #300696 as the primary name of the condition, the condition, for the purposes of this application, will be termed Emery-Dreifuss Muscular Dystrophy 6, X-Linked (EDMD6), OMIM #300696.

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

1.6. 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.

1.7. 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 Emery-Dreifuss Muscular Dystrophy 6, X-Linked (EDMD6), OMIM #300696, is inherited in an X-linked recessive (XLR) manner. The risk of transmission of the relevant genetic abnormality means there is a 25% chance of an affected male child and 25% of a female carrier in each pregnancy. Female carriers are usually phenotypically normal but there is a theoretical risk that a female carrier could also present with symptoms of the condition.

1.9. If the mother is not a carrier but the father carries the mutation, there is a 50% chance in each pregnancy that a child will be a female carrier and may exhibit some symptoms of the condition. All male children of an affected father will not inherit his one X chromosome carrying the relevant genetic abnormality and will be unaffected by the condition.

1.10. The committee noted that the penetrance of the condition is 100% in affected males.

1.11. Emery-Dreifuss Muscular Dystrophy 6, X-Linked (EDMD6), OMIM #300696, is a progressive muscular dystrophy, characterised by joint contractures, muscle weakness and heart disease. The heart complications include hypertrophic cardiomyopathy and rhythm abnormalities which in severe cases can result in sudden death.

1.12. There is no cure for this condition. Treatment is supportive and focuses on reducing the impact of symptoms.

1.13. The committee noted the executive's request to consider Emery-Dreifuss Muscular Dystrophy 6, X-Linked (EDMD6), OMIM #300696, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.14. The committee also noted the recommendation of the peer reviewer to consider three other conditions for inclusion on the list for which PGD can be applied and agreed to consider the application on this basis. The conditions are Emery-Dreifuss muscular dystrophy 4 (EDMD4), OMIM #612998, Emery-Dreifuss muscular dystrophy 5 (EDMD5), OMIM #612999 and Emery-Dreifuss muscular dystrophy 7 (EDMD7), OMIM #614302. The conditions are all inherited in an autosomal dominant manner which means there is 50% chance of an embryo being affected by the condition in each pregnancy if either parent carries a relevant mutation. Penetrance is unclear. Symptoms of all these condition types include contractures, muscle weakness and heart disease.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Emery-Dreifuss Muscular Dystrophy 6, X-Linked (EDMD6), OMIM #300696, is a slowly progressive muscle weakness and muscle wasting disease that can present from childhood. Patients with severe forms of the disease may also lose the capacity to walk and may become wheelchair dependent. Complications from heart problems, which usually present in early adulthood, can become life-threatening and if left untreated can lead to sudden death. The committee considered the potentially serious physical and psychological impact on the quality of life of those affected with the condition.

2.2. The committee also considered the conditions, Emery-Dreifuss muscular dystrophy 4 (EDMD4), OMIM #612998, Emery-Dreifuss muscular dystrophy 5 (EDMD5), OMIM #612999 and Emery-Dreifuss muscular dystrophy 7 (EDMD7), OMIM #614302. These can present from infancy and in the worst-case scenario are degenerative conditions characterized by severe muscle weakness and atrophy and serious heart disease which may result in cardiac death.

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

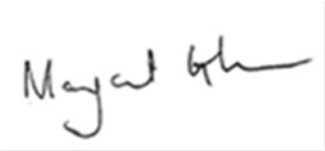
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Emery-Dreifuss muscular dystrophy 4 (EDMD4), OMIM #612998
- Emery-Dreifuss muscular dystrophy 5 (EDMD5), OMIM #612999
- Emery-Dreifuss muscular dystrophy 6 X-Linked (EDMD6), OMIM #300696
- Emery-Dreifuss muscular dystrophy 7 (EDMD7), OMIM #614302

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

16 April 2021