

Statutory Approvals Committee – minutes

Centre 0314 (Leeds Fertility)

Pre-implantation Genetic Diagnosis (PGD) application for Neuroferritinopathy also known as Neurodegeneration with Brain Iron Accumulation 3 (NBIA3), OMIM #606159

Thursday, 30 January 2020

HFEA, Spey Meeting Room, Level 2, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde	
Members of the Executive	Moya Berry Catherine Burwood	Committee Officer Licensing Manager
Specialist Adviser	Professor Peter Turnpenny	
Legal Adviser	Dawn Brathwaite	Mills & Reeve LLP

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:

- 9th 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

1. Consideration of application

- 1.1. The committee welcomed the advice of its specialist adviser, Professor Peter Turnpenny, who confirmed that the condition was as described in the papers.
- 1.2. The committee noted that the description in the PGD application for Neuroferritinopathy, OMIM #606159 is consistent with the peer review.
- 1.3. The committee also noted that Neuroferritinopathy, OMIM #606159 is referred to as Neurodegeneration with Brain Iron Accumulation 3 (NBIA3) on the OMIM website. The committee therefore agreed, at the request of the executive, to refer to the condition for the purposes of this application, as Neurodegeneration with Brain Iron Accumulation 3 (NBIA3), OMIM #606159, to ensure consistency with the OMIM website.
- 1.4. The committee noted that the condition being applied for is not on the list of approved PGD conditions.
- 1.5. The committee noted that the Genetic Alliance UK statement provided a perspective on the impact of the condition on patients, their families and carers.
- 1.6. 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 Neurodegeneration with Brain Iron Accumulation 3 (NBIA3), OMIM #606159, is inherited in an autosomal dominant pattern, 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.
- 1.9. The committee noted the penetrance of the condition is 100% by the age of 60 years.
- 1.10. The condition Neurodegeneration with Brain Iron Accumulation 3 (NBIA3), OMIM #606159, typically presents in adult life (mean age 40 years), although onset in the early teenage years, and in the sixth decade, have been reported. The condition causes progressive problems with movement, including involuntary jerking motions, rhythmic shaking, difficulty coordinating movements and uncontrolled tensing of muscles. Affected individuals have difficulty swallowing and speaking and some develop a gradual decline in their ability to think and reason. Personality changes such as reduced inhibitions and emotional lability may occur as the disorder progresses. Over time, mental decline and behavioural issues may become significant problems.
- 1.11. There is no cure for the condition and management focuses on the treatment of symptoms. Surgical intervention may be an option but may not resolve issues and is not without significant risk.
- 1.12. The committee noted the executive's request to consider Neurodegeneration with Brain Iron Accumulation 3 (NBIA3), OMIM #606159, for inclusion on the list of conditions for approved PGD. The committee agreed to consider the application on this basis.
- 1.13. The committee noted the recommendation of the executive to include a number of other types of NBIA for which PGD can be applied. The peer reviewer considers that there is reasonable

evidence that the following condition types have symptoms which are generally more severe than Neurodegeneration with Brain Iron Accumulation 3 (NBIA3), as they are associated with childhood onset, are life-limiting, and more frequently cause a multi-system disorder. The conditions for consideration are:

- Neurodegeneration with Brain Iron Accumulation 1 (NBIA1), OMIM #234200
- Neurodegeneration with Brain Iron Accumulation 2A (NBIA2A), OMIM #256600
- Neurodegeneration with Brain Iron Accumulation 2B (NBIA2B), OMIM #610217
- Neurodegeneration with Brain Iron Accumulation 4 (NBIA4), OMIM #614298
- Neurodegeneration with Brain Iron Accumulation 5 (NBIA5), OMIM #300894
- Neurodegeneration with Brain Iron Accumulation 6 (NBIA6), OMIM #615643

1.14. The committee noted the executive's recommendation not to include the following conditions on the list for which PGD can be applied. These are: Neurodegeneration with Brain Iron Accumulation 7 (NBIA7), OMIM #617916, and Neurodegeneration with Brain Iron Accumulation 8 (NBIA8), OMIM #617917, as gene assignments are thus far based on only one patient in both conditions.

2. Decision

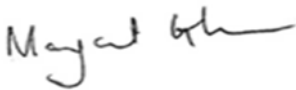
- 2.1.** The committee considered that, in the worst-case scenario Neurodegeneration with Brain Iron Accumulation 3 (NBIA3), OMIM #606159, is a slowly progressive neurological condition leading to severe movement disorder, indistinct speech and swallowing difficulties. Symptoms may develop in teenage years. In some cases, a moderate dementia may develop. There is no cure or mitigating treatments for the condition. The committee considered the possible adverse impact on the quality of life for patients living with this condition.
- 2.2.** The committee considered that in the worst-case scenario the following conditions, are severe life-limiting disorders associated with childhood onset.
- Neurodegeneration with Brain Iron Accumulation 1 (NBIA1), OMIM #234200
 - Neurodegeneration with Brain Iron Accumulation 2A (NBIA2A), OMIM #256600
 - Neurodegeneration with Brain Iron Accumulation 2B (NBIA2B), OMIM #610217
 - Neurodegeneration with Brain Iron Accumulation 4 (NBIA4), OMIM #614298
 - Neurodegeneration with Brain Iron Accumulation 5 (NBIA5), OMIM #300894
 - Neurodegeneration with Brain Iron Accumulation 6 (NBIA6), OMIM #615643
- 2.3.** The committee agreed that Neurodegeneration with Brain Iron Accumulation 7 (NBIA7), OMIM #617916, and Neurodegeneration with Brain Iron Accumulation 8 (NBIA8), OMIM #617917, should not be considered for PGD at this time.
- 2.4.** 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.
- 2.5.** 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:

- Neurodegeneration with Brain Iron Accumulation 1 (NBIA1), OMIM #234200
 - Neurodegeneration with Brain Iron Accumulation 2A (NBIA2A), OMIM #256600
 - Neurodegeneration with Brain Iron Accumulation 2B (NBIA2B), OMIM #610217
 - Neurodegeneration with Brain Iron Accumulation 3 (NBIA3), OMIM #606159
 - Neurodegeneration with Brain Iron Accumulation 4 (NBIA4), OMIM #614298
 - Neurodegeneration with Brain Iron Accumulation 5 (NBIA5), OMIM #300894
 - Neurodegeneration with Brain Iron Accumulation 6 (NBIA6), OMIM #615643
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3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

24 February 2020