Statutory Approvals Committee – minutes

Centre 0044 (The Centre for Reproductive and Genetic Health)

Pre-implantation Genetic Diagnosis (PGD) application for

Charcot Marie Tooth type 1B (CMT1B), OMIM #118200

Thursday, 24 May 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe	
Members of the Executive	Bernice Ash Dee Knoyle Paula Robinson Catherine Burwood Mhairi West	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer) Inspector (Observer - Induction)
Specialist Adviser	Dr Ed Blair	
Legal Adviser	Sarah Ellson	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
- Comment from centre re peer review
- Genetic Alliance UK Statement
- Licence Committee minutes, 19 July 2012, PGD Charcot Marie Tooth type 1A (CMT1A), OMIM #118220

1. Consideration of application

1.1. The committee welcomed the advice of its Specialist Adviser, Dr Ed Blair, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the application for PGD for Charcot Marie Tooth type 1B (CMT1B), OMIM #118200 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. The committee noted that the condition is inherited in an autosomal dominant pattern which means there is a 50% chance of an embryo being affected with the condition, if either parent has a relevant mutation.

1.8. The committee noted that CMT1B is a subtype of CMT type 1. CMT1 is characterized by abnormalities in myelin, the fatty substance covering nerve cells which assists in conducting nerve impulses. These abnormalities slow the transmission of nerve impulses to muscles and sensory cells. CMT type 1A (OMIM #118220) is considered by the applicant and Peer Reviewer to be very similar in symptoms to CMT1B and is already licensed for PGD.

1.9. The Legal Adviser confirmed the Executive's position, that the committee is not bound by its previous decisions and indicated that each application should be considered against the statutory test. The Legal Adviser recognised that applications might be distinguished but also indicated that consistency was an important principle of good regulation and therefore reasons should be provided for any decision which might appear inconsistent.

1.10. The committee noted that CMT1B is caused by mutation in the MPZ gene and accounts for 5-10% of CMT1 cases. Onset of symptoms may occur anytime from early childhood through to adulthood.

1.11. Symptoms of CMT include: muscle weakness and wasting (atrophy) of the feet, legs and hands, feet abnormalities, reduced sensation and balance difficulties caused by both muscle weakness and vestibular impairment, musculoskeletal or neuropathic pain, depressed or absent tendon reflexes. Obstructive sleep apnoea and restless leg syndrome have been reported in a significant proportion of CMT1 patients (37% and 40% respectively). Hearing loss sometimes occurs. The condition is slowly progressive over many years. Symptoms of CMT disease vary in severity, even within families, ranging from extremely mild disease that goes unrecognized by the affected individual and physician, to considerable weakness and disability. However, most affected patients have a moderate amount of physical disability and an individual with a mutation in one of the CMT1 genes is almost certain to demonstrate some signs of the condition. There is very little clinical difference between CMT1A and CMT1B.

1.12. The committee noted that there is no curative treatment, only management of symptoms. Individuals with CMT1 are often evaluated and managed by a multidisciplinary team that includes neurologists, physiatrists, orthopaedic surgeons, and physical and occupational therapists. Fatigue is frequently reported. Weakness and balance problems may lead to mobility difficulties. Hand weakness can affect daily activities, such as writing, fastening buttons, and turning doorknobs.

1.13. The committee noted that the Peer Reviewer considered that other subtypes of CMT1 'are clinically indistinguishable and would recommend that they are considered as a single entity', along with CMT1B. These CMT1 subtypes are listed below and are not currently approved for PGD:

Condition	OMIM	Gene affected
Charcot Marie Tooth type 1C (CMT1C)	#601098	LITAF
Charcot Marie Tooth type 1D (CMT1D)	#607678	EGR2
Charcot Marie Tooth type 1E (CMT1E)	#118300	PMP22
Charcot Marie Tooth type 1F (CMT1F)	#607734	NEFL

1.14. The committee noted the Person Responsible (PR) at the centre had confirmed that they would like the additional CMT1 subtypes to also be considered as conditions for which PGD can be applied.

1.15. The committee noted that CMT1A had already been approved for PGD.

1.16. The Specialist Adviser informed the committee that Charcot Marie Tooth type 1F (CMT1F), OMIM #607734 is also linked to Charcot Marie Tooth type 2E (CMT2E); this has a different mode of inheritance to the other subtypes of the condition, suggested for approval for the PGD List. The committee considered the advice of the Specialist Adviser and agreed that Charcot Marie Tooth type 1F (CMT1F), OMIM #607734 should not be considered for PGD approval at this stage.

1.17. The committee noted the inspectorate's request to consider whether Charcot Marie Tooth type 1B (CMT1B), OMIM #118200 should be approved for inclusion on the PGD List. The inspectorate also requested that the committee consider approving the additional CMT1 subtypes. The committee agreed to consider the application on this basis, with the exception of Charcot Marie Tooth type 1F (CMT1F), OMIM #607734 due to its differing mode of inheritance.

2. Decision

2.1. The committee considered that, in the worst case scenario, Charcot Marie Tooth type 1B (CMT1B), OMIM #118200 is serious given the condition is highly penetrant and progressive, may often have an early childhood onset, and can cause hand weakness and mobility difficulties. The condition in its most severe form can severely impact on the individual's quality of life.

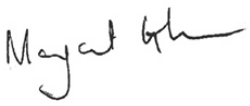
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 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:

- Charcot Marie Tooth type 1B (CMT1B), OMIM #118200
- Charcot Marie Tooth type 1C (CMT1C), OMIM #601098
- Charcot Marie Tooth type 1D (CMT1D), OMIM #607678
- Charcot Marie Tooth type 1E (CMT1E), OMIM #118300

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

19 June 2018