Statutory Approvals Committee – minutes

Item 4

Centre 0044 (Centre for Reproductive and Genetic Health)

Pre-implantation Genetic Diagnosis (PGD) application for

Catecholaminergic Polymorphic Ventricular Tachycardia type 4 (CPVT4), OMIM #614916

Thursday, 29 November 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Anthony Rutherford Ruth Wilde Emma Cave	
Members of the Executive	Catherine Burwood Dee Knoyle Paula Robinson Victoria Askew	Senior Governance Manager (Secretary) Committee Secretary (Observer) Head of Planning and Governance (Observer) Inspections and Logistics Officer (Observer)
Specialist Adviser	Dr Alan Fryer	
Legal Adviser	Ros Foster	Browne Jacobson LLP
Observers	Rachel Cutting (New Member induction - observer)	

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
- Licence Committee minutes, March 2012, PGD for CPVT2 (OMIM #611938)
- Statutory Approvals Committee minutes, January 2014, PGD for CPVT1 (OMIM #604772)

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 Catecholaminergic Polymorphic Ventricular Tachycardia type 4 (CPVT4), OMIM #614916 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 inheriting the condition in each pregnancy, if either parent has a relevant mutation. CPVT4 causes a cardiac arrhythmia during times of stress or exercise which can result in episodes of fainting, cardiac arrest and sudden death. These symptoms can be exhibited from childhood onwards.

1.8. The committee noted that two subtypes of Catecholaminergic Polymorphic Ventricular Tachycardia have previously been licensed for use in PGD by the HFEA: Catecholaminergic Polymorphic Ventricular Tachycardia type 2 (CPVT2), OMIM #611938, was approved in March 2012, and Catecholaminergic Polymorphic Ventricular Tachycardia type 1 (CPVT1), OMIM #604772, was approved in January 2014. The committee noted the minutes of these approvals in the papers.

1.9. The committee noted that Catecholaminergic Polymorphic Ventricular Tachycardia type 3 (CPVT3), OMIM #614021, and Catecholaminergic Polymorphic Ventricular Tachycardia type 5 with or without muscle weakness (CPVT5), OMIM #615441, are not approved by the HFEA as conditions for which PGD can be applied.

1.10. CPVT3 and CPVT5 are autosomal recessive conditions, resulting from homozygous or compound heterozygous mutations in the TECRL and TRDN genes, respectively. The risk of inheriting CPVT3 or CPVT5 is 25% in each pregnancy if both parents each carry a causative TECRL or TRDN mutation. CPVT3 and CPVT5 also cause cardiac arrhythmia during times of stress or exercise which can result in episodes of fainting, cardiac arrest and sudden death. These symptoms can be exhibited from childhood onwards.

1.11. The committee noted that here is no cure for CPVT3, CPVT4 or CPVT5, so treatment is used to manage symptoms. If left untreated the disease may be lethal. In CPVT in general, beta-blockers are the first therapeutic choice with a proven efficacy in about 60% of individuals. Flecainide can also be given along with betablockers to patients who have recurrence of fainting or complex arrhythmias during exercise. Implantable cardioverter defibrillator (ICD) implantation in addition to beta-blockers with or without flecainide is recommended in

individuals who experience cardiac arrest, recurrent fainting or polymorphic/bidirectional ventricular tachycardia despite optimal therapy. Left cardiac sympathetic denervation (LCSD) may be considered in those with a diagnosis of CPVT who experience recurrent fainting, polymorphic/bidirectional ventricular tachycardia, or several appropriate ICD shocks while on beta-blocker and flecainide in those who are intolerant of or with a contraindication to beta-blocker therapy.

1.12. The committee noted the inspectorate's request to consider whether CPVT4, OMIM #614916 should be approved for inclusion on the PGD List. The committee agreed to the request from the inspectorate that it also consider approving CPVT3, OMIM #614021, and CPVT5, OMIM #615441.

2. Decision

2.1. The committee considered that, in the worst case scenario, Catecholaminergic Polymorphic Ventricular Tachycardia type 3 (CPVT3), OMIM #614021, Catecholaminergic Polymorphic Ventricular Tachycardia type 4 (CPVT4), OMIM #614916 and and Catecholaminergic Polymorphic Ventricular Tachycardia type 5 with or without muscle weakness (CPVT5), OMIM #615441 are serious conditions, which can cause sudden death. Quality of life for sufferers may be impaired due to living with the anxiety caused by this knowledge. The management of these conditions is not always effective and has risks associated.

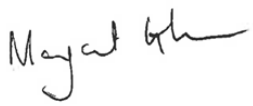
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the conditions' worst symptoms, that a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

- Catecholaminergic Polymorphic Ventricular Tachycardia type 3 (CPVT3), OMIM #614021
- Catecholaminergic Polymorphic Ventricular Tachycardia type 4 (CPVT4), OMIM #614916
- Catecholaminergic Polymorphic Ventricular Tachycardia type 5 with or without muscle weakness (CPVT5), OMIM #615441

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

19 December 2018