Statutory Approvals Committee – minutes

Centre 0102 (Guy's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for

Loeys-Dietz syndrome type 3 (LDS), OMIM #613795

Thursday, 25 January 2018

Church House Westminster, Dean's Yard, Westminster SW1P 3NZ

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford Ruth Wilde	
Members of the Executive	Bernice Ash Dee Knoyle Nana Gyamfi Chereena Harriott	Committee Secretary Committee Secretary (Observing) Licensing Information Officer (Observing) Inspections and Logistics Officer (Observing)
Specialist Adviser	Dr Alison Male	
Legal Adviser	Dawn Braithwaite	Mills & Reeve 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
- Genetic Alliance UK Statement for LDS type 3
- Genetic Alliance UK Statement for LDS type 1 (2016)

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 application for Loeys-Dietz syndrome type 3 (LDS), OMIM #613795 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 the condition is caused by mutations in a gene called SMAD3 which result in a high risk of developing arterial aneurysms and dissections, especially affecting the aorta (the major blood vessel that leaves the heart to carry blood around the body) and cerebral arteries (blood vessels supplying the brain); however, any artery can be affected. Arteries can become weaker and stretch and develop a bulge (aneurysm). LDS is associated with a significantly increased risk of early-onset mortality. Age of onset is very variable; the condition can present at birth with congenital heart abnormalities. Arterial aneurysms and dissection can occur at any age, including in childhood.

1.9. Symptoms of the condition consist of stretching (dilatation) of blood vessels which can result in sudden tearing (dissection) causing severe life-threatening haemorrhage. Cerebral artery dissection causes stroke, with the potential for death or serious irreversible handicap. LDS also presents with skeletal features including concave chest, protruding chest that affect lung function; cervical spine instability; loss of joint movement especially in the fingers affecting fine motor function; and joint laxity, which can cause pain. Organ rupture can occur particularly in the spleen, intestines and womb, other features include: easy bruising, poor wound healing and scarring. LDS3 is more likely to cause osteoarthritis than other types of LDS as (LDS1 and 2). The penetrance of arterial dilatation is over 50%.

1.10. The committee noted that affected individuals live with significant, potentially life-threatening risks. Treatment is not curative, and may involve major surgery. Individuals may also experience daily pain and disability associated with various symptoms of the condition.

1.11. The committee noted that penetrance is nearly 100%.

1.12. The committee noted the Peer Reviewer's observation that there are 4 types of Loeys-Dietz syndrome - type 1 is due to mutations in TGFBR1, type 2 due to mutations in TGFBR2, type 3 due to mutations in SMAD3 (OMIM *603109) and type 4 to mutations in TGFB2. Mutations in all four genes cause similar cardiovascular, craniofacial, cutaneous, and skeletal features.

1.13. The committee noted the inspectorate's request to consider whether Loeys-Dietz syndrome type 3, OMIM # 613795, should be approved for inclusion on the PGD List. The inspectorate also requested that the committee consider approving Loeys-Dietz syndrome type 4, OMIM #614816, resulting from autosomal dominant mutation of the TGFB2 gene (OMIM *190220). The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that Loeys-Dietz syndrome type 3, OMIM # 613795 is serious given it is an unpredictable and catastrophic condition, with a high risk of ruptures occurring at any time, the life-threatening consequences and the associated necessary surgical interventions. The committee considered this a devastating condition which can have severe effects on the quality of life of those with the condition and their families.

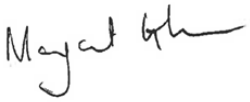
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 condition Loeys-Dietz syndrome type 3, OMIM # 613795 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

2.3. The committee agreed to authorise testing for Loeys-Dietz syndrome type 3, OMIM # 613795. The committee also agreed to authorise testing for Loeys-Dietz syndrome type 4, OMIM #614816.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

9 February 2018