Statutory Approvals Committee – minutes

Centre 0201 (Edinburgh Assisted Conception Unit)

Pre-implantation Genetic Diagnosis (PGD) application for

Osteogenesis Imperfecta Type VII (OI Type VII), OMIM #610682

Thursday, 26 October 2017

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

Committee members	Margaret Gilmore (Chair) Anne Lampe Anthony Rutherford Bobbie Farsides	
Members of the Executive	Bernice Ash Dee Knoyle Susanna Nyarko-Parkin	Committee Secretary Committee Secretary (Observing) Governance Officer (Observing)
External adviser	Peter Turnpenny	
Legal Adviser	Jane Williams	Mills & Reeve LLP
Observers	Gerard Hanratty	Browne Jacobson 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:

- 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 opinion
- Email communication from PR stating that he would like other types of the condition to be considered
- Licence committee minutes:

  - 25 September 2014; Centre 0102, Application to include embryo testing for Osteogenesis Imperfecta Type VIII, OMIM #610915
  - 24 October 2013; Centre 0101, Application to include embryo testing for Osteogenesis Imperfecta Type IV, OMIM #166220, Type V OMIM
  - 24 February 2011: Centre 0044; Application to include embryo testing for Osteogenesis Imperfecta Type IA, OMIM #166240
  - 25 February 2010; Centre 0101, Application to include embryo testing for Osteogenesis Imperfecta Type III, OMIM #259420
  - 26 March 2009; Centre 0101 Application to include embryo testing for Osteogenesis Imperfecta Type II, OMIM #120160

1. Consideration of application

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

1.2. The committee noted that the description in the application for Osteogenesis Imperfecta Type VII (OI Type VII), OMIM #610682 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 recessive pattern which means there is a 25% chance of an embryo being affected with the condition if each parent has a relevant mutation.

1.8. The committee noted that all forms of Osteogenesis Imperfecta are connective tissue disorders leading to fragile bones which are prone to fracture. At its worst, OI type VII is a severe condition that can be detected prenatally and be extremely life limiting. Children that survive beyond early childhood have short limbs with abnormality, spinal curvature with abnormality and chest wall abnormality, secondary to long bone, vertebral and rib fractures.

1.9. The clinical phenotype in OI can range from a slightly increased risk of fracture following trauma to multiple fractures present at birth. OI type VII is 100% penetrant if a child inherits a mutation from both parents. Symptoms of this condition can be detected in utero by ultrasound scanning and include shortening and abnormality of the limbs and narrowing of the chest secondary to rib fractures. A proportion of affected infants die perinatally or in infancy of respiratory insufficiency. For those children that survive there is a significant risk of serious respiratory insufficiency due to chest abnormality. Multiple fractures of the vertebrae and long bones result in significant pain for the child and lead to mobility problems.

1.10. There are no proven treatments that modify the course of OI type VII. Osteogenesis Imperfecta type VII may result in death in the perinatal period. The peer reviewer reported that Bisphosphonates have been used in patients with severe OI type VII. During 3 years of pamidronate therapy, lumbar spine and bone mineral density increased and lumbar vertebral bodies improved in shape in patients with OI type VII. However, fracture rates and mobility scores did not show statistically significant changes in this small study cohort.

1.11. The committee noted that other types of Osteogenesis Imperfecta have already been approved for PGD, specifically types I, Ia, II, III, IV, V, VI and VIII.

1.12. The committee noted that Genetic Alliance and the peer reviewer had been asked to comment on the other types of OI not currently approved for PGD, and their suitability for addition to the list of conditions for which PGD can be applied. This would include the following additional types; IX (OI type IX, OMIM #259440), X (OI type X, OMIM #613848), XI (OI type XI, OMIM #610968), XII (OI type XII, OMIM #613849), XIII (OI type XIII, OMIM #614856), XIV (OI type XIV, OMIM #615066), XV (OI type XV, OMIM #615220), XVI (OI type XVI, OMIM #616229) and XVII (OI type XVII, OMIM #616507).

1.13. The committee noted that the peer reviewer had expressed some concern regarding the addition of type XVI (OI type XVI, OMIM #616229) to the PGD list as more research is necessary. The Specialist Adviser stated that XVI (OI type XVI, OMIM #616229) is based on one case report and the molecular basis has not been fully characterised. Further reports are required to secure the delineation of this form of OI.

1.14. The committee noted that the PR at the centre has confirmed that he would like OI types IX-XVII, to also be considered as conditions for which PGD can be applied.

1.15. The committee noted the inspectorate's request to consider whether Osteogenesis Imperfecta type VII (OI type VII), OMIM #610682 should be approved for inclusion on the PGD List. The inspectorate also recommended that the committee consider the following additional OI conditions; IX (OI type IX, OMIM #259440), X (OI type X, OMIM #613848), XI (OI type XI, OMIM #610968), XII (OI type XII, OMIM #613849), XIII (OI type XIII, OMIM #614856), XIV (OI type XIV, OMIM #615066), XV (OI type XV, OMIM #615220), XVI (OI type XVI, OMIM #616229) and XVII (OI type XVII, OMIM #616507). Noting the comments of the peer reviewer and on the advice of the Specialist Adviser, the committee agreed that OI condition XVI (OI type XVI, OMIM #616229) should not be considered within the application before them, given that more information on this condition is needed. The committee accordingly agreed to consider the application as recommended by the inspectorate but excluding OI condition XVI (OI type XVI, OMIM #616229).

2. Decision

2.1. The committee considered that Osteogenesis Imperfecta type VII (OI type VII), OMIM #610682 is serious, given the significant risk of severe early onset of the condition in early infancy or early childhood. The condition is life limiting, causes severe pain and disability over long periods of time for those who survive early childhood, and there is no curative treatment. The committee also considered the impact of the condition on the family and their quality of life.

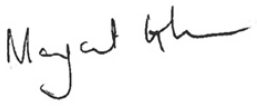
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 condition Osteogenesis Imperfecta type VII (OI type VII), OMIM #610682 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 Osteogenesis Imperfecta type VII (OI type VII), OMIM #610682. The committee also agreed to authorise testing for Osteogenesis Imperfecta types IX (OI type IX, OMIM #259440), X (OI type X, OMIM #613848), XI (OI type XI, OMIM #610968), XII (OI type XII, OMIM #613849), XIII (OI type XIII, OMIM #614856), XIV (OI type XIV, OMIM #615066) and XV (OI type XV, OMIM #615220).

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

16 November 2017