Statutory Approvals Committee – minutes

Item 2

Centre 0119 (Birmingham Women's Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Hereditary Pancreatitis, OMIM #167800

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	Dee Knoyle Catherine Burwood Paula Robinson Victoria Askew	Committee Secretary Senior Governance Manager (Observer) Head of Planning and Governance (Observer) Inspections & 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

1. Consideration of application

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

1.2. The committee noted that the description in the application for PGD for Hereditary Pancreatitis, OMIM #167800 is consistent with the peer review.

1.3. The committee noted that the condition being applied for is not on the list of conditions approved for PGD.

1.4. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the application.

1.5. 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.

1.6. 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. Hereditary Pancreatitis, due to a PRSS1 mutation, is inherited in an autosomal dominant pattern which means there is 50% chance of an embryo inheriting the condition in each pregnancy, if either parent has a relevant mutation. There are rare families in the literature where specific mutations in SPINK1 have also been inherited in an autosomal dominant manner and resulted in a condition that fulfils the clinical diagnostic criteria for Hereditary Pancreatitis. CTRC mutations have also been shown to be strongly associated with early-onset pancreatitis.

1.8. Hereditary Pancreatitis due to some SPINK1 and CFTR mutations can be inherited in an autosomal recessive pattern which means there is a 25% chance of an embryo being affected with the condition in each pregnancy, if both parent have a relevant mutation.

1.9. The Peer Reviewer noted that whatever the cause, the symptoms and management of the condition are similar.

1.10. The application notes that a Missense variation in PRSS2 confers protection against Pancreatitis and should not be licenced for testing within this OMIM. The Specialist Advisor confirmed that testing for the condition could be licensed with reference to the OMIM number specified in the application.

1.11. The Specialist Advisor further confirmed that the recessive forms are less common than the dominant forms of the condition and that reducing alcohol consumption, smoking and avoiding certain drugs may reduce the risk of developing more severe symptoms.

1.12. The committee noted that the application discusses PRSS1-related Hereditary Pancreatitis as having a penetrance of up to 80%. The Peer Reviewer states that non-penetrance does occur in this condition and that, depending on the publication, the penetrance ranges from 40-90%. This variability may reflect an influence of ethnic background and/or lifestyle factors.

1.13. The committee noted that the condition causes recurrent episodes of acute pancreatitis producing severe abdominal pain, fever, nausea and vomiting, which can require hospitalisation and progress to multi-organ failure. Repeated episodes of pancreatitis and the damage that this causes can then lead to chronic pancreatitis and long-term health implications such as intractable abdominal pain, insulin-dependent diabetes mellitus and pancreatic cancer. The effects of the condition on some individuals are life-threatening.

1.14. The committee noted that Hereditary Pancreatitis is an incurable condition and treatment is focused on managing the symptoms. Hypoglycaemic drugs and sometimes insulin may be required to treat diabetes mellitus. Pancreatic enzymes can be given as a dietary supplement to assist when there are digestive enzyme insufficiencies. There is a significant impact on quality of life as it is difficult to predict when an attack may occur, and this can lead to periods of leave from school or work. Surgical procedures may also be required to deal with complications, including, rarely, complete removal of the pancreas and islet cell auto transplantation if possible. The lifetime risk for pancreatic cancer may be 20% and screening and preventative surgery for this is not straight forward. In the chronic form of the condition, the quality of life can be severely impaired due to severe chronic abdominal pain that may not be controlled even with the input of specialist pain clinic expertise.

1.15. The committee noted the inspectorate's request to consider whether Hereditary Pancreatitis, OMIM #167800 should be approved for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario Hereditary Pancreatitis, OMIM #167800 is a serious progressive condition which affects the pancreas, causing severe abdominal pain which is not always manageable, fever, nausea and vomiting. The condition can lead to digestive enzyme deficiency, diabetes mellitus and pancreatic cancer which may result in radical surgery. Symptoms can start from early childhood and most people with PRSS1- related disease develop the condition by the age of 20 years. The condition can be life-threatening and the quality of life of affected individuals may be severely impacted.

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 meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing for:

Hereditary Pancreatitis, OMIM #167800

Autosomal dominant forms due to due to PRSS1 mutations and CTRC and SPINK1 mutations in families that fulfil the diagnostic criteria for Hereditary Pancreatitis

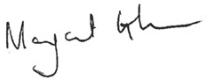
Autosomal recessive forms due to SPINK1 or CFTR mutations

2.3. The committee agreed that the Missense variation in PRSS2 that confers protection against Pancreatitis should not be licenced for testing within this OMIM.

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