Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Autosomal Dominant Polycystic Kidney Disease - type 2 (ADPKD2) OMIM #613095

Thursday, 25 July 2019

HFEA Foyle Meeting Room, Level 1, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Emma Cave Tony Rutherford	
Members of the Executive	Moya Berry Catherine Burwood	Committee Secretary Licensing Manager (Observer)
Specialist Adviser	Peter Turnpenny	
Legal Adviser	Jane Williams	Mills & Reeve LLP

Declarations of interest

- Members of the committee declared that they had no conflicts of interest in relation to this item.
- Apologies were noted from Rachel Cutting (Committee Member).

The committee had before it:

- 9th 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
- Patient Statement
- Licence Committee Minutes- 24 June 2010 - PGD for Autosomal Dominant Polycystic Kidney Disease – type 1 (ADPKD1), OMIM #173900
- Licence Committee Minutes- 22 July 2009 - PGD for Autosomal Recessive Polycystic Kidney Disease – type 4, OMIM #263200

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Professor Peter Turnpenny, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for Autosomal Dominant Polycystic Kidney Disease - type 2 (ADPKD2), OMIM #613095 was consistent with the peer review. The committee also noted that the condition appears on the OMIM website as Polycystic Kidney Disease type 2 (PKD2), OMIM #613095, omitting the reference to 'autosomal dominant' and the committee agreed that going forward, the condition would be known as this.

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

1.4. The committee noted that the Genetic Alliance UK statement provided a perspective on the impact of the condition on patients, their families and carers.

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. The committee noted that PKD2 is inherited in an autosomal dominant pattern, which means there is a 50% chance of an embryo being affected with the condition in each pregnancy if either parent has a relevant mutation.

1.8. The committee noted the penetrance of the condition is over 95%.

1.9. PKD2 is characterised by the development of kidney cysts which cause high blood pressure and renal compromise, progressing to end-stage renal disease (ESRD), which is fatal without kidney transplant or dialysis. There is also an increased risk of patients developing painful cysts within the liver which can disrupt liver function and a serious risk that patients may develop aneurysms within the brain, which can rupture causing a fatal or debilitating cerebral haemorrhage.

1.10. There is no cure for the condition and treatment focuses on managing symptoms. Some patients may need neurosurgery to treat aneurysms.

1.11. The committee noted the inspectorate's request to consider Polycystic Kidney Disease-type 2 (PKD2) #613095 for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.12. The committee also noted the recommendation of the peer reviewer to consider the following similar types of Polycystic Kidney Disease for approval as conditions for which PGD can be applied:

- Polycystic Kidney Disease-type 3 (PKD3) OMIM #600666
- Polycystic Kidney Disease-type 5 (PKD5) OMIM #617610
- Polycystic Kidney Disease-type 6 (PKD6) OMIM #618061

1.13. Both PKD5 and PKD6 are characterised by the development of kidney cysts causing high blood pressure and renal compromise, progressing to end stage renal failure, which is fatal without kidney transplant or dialysis. These treatments themselves carry risks to the patient and impact on quality of life. In PKD5, symptoms are more severe than PKD2 (the condition being applied for) and end stage renal failure is generally seen before the age of 30 years, with onset of deteriorating renal function in childhood or adolescence. In PKD6 patients may be symptomatic from their 30s with ESRD usually occurring from the 6th decade onwards. Approximately 50% of affected individuals develop liver cysts, which can compromise function.

1.14. The committee noted that individuals affected by PKD3 have more variable symptoms of both renal and/or severe liver disease, which in some cases may require renal dialysis or transplantation, usually from middle age but childhood onset has been reported. Individuals with the condition are also at an increased risk of developing aneurysms in the brain.

1.15. The committee noted that the risk of inheriting both PKD3 and PKD6 is 50% if either parent carries a relevant mutation and with PKD5 it is 25% if each parent carries a relevant mutation, as it follows autosomal recessive inheritance. There is no cure for the conditions but medical treatments can mitigate symptoms.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Polycystic Kidney Disease-type 2 (PKD2), OMIM #613095 is a serious multi-system and progressive condition that can be fatal. There is no treatment that can prevent the condition and once diagnosed patients require a lifetime of medical intervention. The committee noted the serious effect on the quality of life for those affected by this disease.

2.2. The committee considered that, in the worst-case scenario both Polycystic Kidney Disease-type 5, OMIM 617610 and Polycystic Kidney Disease-type 6 are serious conditions that without life-long medical treatment are fatal.

2.3. Regarding PKD3, after careful consideration, given its variable presentation, the committee agreed to licence this condition having considered the worst-case scenario. The committee noted that in the worst-case scenario patients affected by PKD3 may develop serious renal and liver disease and/or cerebral aneurysms that may be fatal.

2.4. 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 abnormalities in question and that there is a significant risk that a person with such an abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

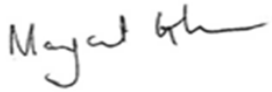
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Polycystic Kidney Disease-type 2 (PKD2) OMIM #613095
- Polycystic Kidney Disease-type 3 (PKD3) OMIM #600666
- Polycystic Kidney Disease-type 5 (PKD5) OMIM #617610
- Polycystic Kidney Disease-type 6 (PKD6) OMIM #618061

3. Chairs signature

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

Signature



Name
Margaret Gilmore

Date
14 August 2019