Statutory Approvals Committee – minutes

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Combined Pituitary Hormone Deficiency type 2 (CPHD2), OMIM #262600

Thursday, 26 April 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Anthony Rutherford	
Members of the Executive	Bernice Ash Dee Knoyle Paula Robinson Catherine Burwood	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer)
Specialist Adviser	Professor Peter Turnpenny	
Legal Adviser	Gerard Hanratty	Browne Jacobson 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
- One comment from the public
- Email correspondence from Centre confirming to include additional conditions from Peer Reviewer's recommendations

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 application for PGD for Combined Pituitary Hormone Deficiency type 2 (CPHD2), OMIM #262600 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 a 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 CPHD2 is characterised by a deficiency of several hormones produced by the pituitary gland, which affects the development and functions of various parts of the body. Affected individuals are small, presenting with growth failure in early childhood. The condition generally presents between 9 months and 8 years of age with growth failure and/or failure to thrive.

1.9. The condition is characterised by failure of the pituitary gland to produce a variety of hormones including: Growth Hormone (GH), Thyroid Stimulating Hormone (TSH), Luteinising Hormone (LH), Follicle Stimulating Hormone (FSH), Prolactin (PrL) and, occasionally, Adrenocorticotrophic hormone (ACTH). The condition causes multiple developmental and physiological problems which may include: growth failure/short stature; hypoglycaemia; hypothyroidism; absent or delayed/incomplete secondary sexual development; infertility; ambiguous genitalia; hypogenitalism in males; and adrenal insufficiency/failure. There is significant variability of phenotype. The age of onset and order of presentation of the various hormone deficiencies varies. Often the order of appearance of hormone deficiency is GH, LH and FSH, TSH, and ACTH. Anterior pituitary function can deteriorate over time, such that penetrance is age dependent.

1.10. The committee noted the main principle of treatment in CPHD2 is replacement therapy with the appropriate hormones. Growth hormone deficiency is treated with growth hormone injections during childhood and adolescence. The various other hormone deficiencies are treated with hormone therapies as they arise. This may include hormone replacement therapy to induce secondary sexual characteristics and fertility. Treatment with hormone therapy and monitoring of hormone status is lifelong.

1.11. The committee noted that the Peer Reviewer recommended that CPHD types 1,3,4,5 and 6 also be considered for licensing as conditions for which PGD can be applied, because they share similar hormone deficiencies and symptoms. These conditions are stated below:

Condition	OMIM	Gene mutation (OMIM number)
Combined Pituitary Hormone Deficiency Type 1; (CPHD1)	#63038	POU1F1 (*173110)
Combined Pituitary Hormone Deficiency Type 3; (CPHD3)	#221750	LHX3 (*600577)
Combined Pituitary Hormone Deficiency Type 4; (CPHD4)	#262700	LHX4 (*602146)
Combined Pituitary Hormone Deficiency Type 5; (CPHD5)	#182230	HESX1 (*601802
Combined Pituitary Hormone Deficiency Type 6; (CPHD6)	#613986	OTX2 (*600037

1.12. The committee noted that CPHD types 1,3,4,5 and 6 can be inherited in either an autosomal recessive or autosomal dominant pattern (LHX4, OMIM #262700, follows autosomal dominant inheritance, not autosomal recessive as stated in both the application and Peer Review documentation).

1.13. The committee noted the Person Responsible (PR) at the centre had confirmed that they would like the conditions CPHD types 1,3,4,5 and 6, to also be considered as conditions for which PGD can be applied.

1.14. The committee noted the inspectorate requested that the committee consider whether Combined Pituitary Hormone Deficiency type 2 (CPHD2), OMIM #262600 should be approved for inclusion on the PGD List. The inspectorate also requested that the committee to consider approving CPHD types 1,3,4,5 and 6. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario, Combined Pituitary Hormone Deficiency type 2 (CPHD2), OMIM #262600, is serious given the condition may result in adrenal crisis or premature death, also considering the side effects of lifelong, onerous treatments, which can be very challenging to manage day by day. The condition can severely impact on the individual's quality of life and the family.

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 Combined Pituitary Hormone Deficiency type 2 (CPHD2), OMIM #262600, meets the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act.

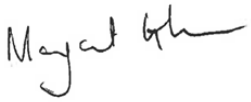
2.3. The committee agreed to authorise testing for the following conditions:

- Combined Pituitary Hormone Deficiency Type 1, (CPHD1), OMIM #63038
- Combined Pituitary Hormone Deficiency Type 2, (CPHD2), OMIM #262600
- Combined Pituitary Hormone Deficiency Type 3, OMIM #600577
- Combined Pituitary Hormone Deficiency Type 4, OMIM #602146
- Combined Pituitary Hormone Deficiency Type 5, OMIM #601802
- Combined Pituitary Hormone Deficiency Type 6, OMIM #600037

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

17 May 2018