Statutory Approvals Committee - minutes

Centre 0035 (Oxford Fertility)

Panhypopituitarism, X-linked; PHPX, OMIM #312000

Date:	25 March 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde
Specialist Adviser:	Jenny Carmichael
Legal Adviser:	Tom Rider - FieldFisher
Members of the Executive:	Moya Berry - Committee officer Catherine Burwood - Licensing Manager
Observers:	Jason Kasraie- Authority Member (Induction)
Apologies:	No apologies were received for the meeting
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:

- HFEA Code of Practice 9th edition
- Standard Licensing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGD Application form
- Redacted Peer review
- Genetic Alliance (UK) Statement
- Academic paper (ARYA et al, 2019) provided by the peer reviewer

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Jenny Carmichael, who confirmed that the condition was as described in the papers.

1.2. The committee noted that the description in the PGD application for X-linked panhypopituitarism, OMIM #312000, is consistent with the peer review.

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 condition, X-linked panhypopituitarism, OMIM #312000 is also known as Panhypopituitarism, X-linked; PHPX, OMIM #312000. As the OMIM website entry lists Panhypopituitarism, X-linked; PHPX, OMIM #312000 as the primary name of the condition, the condition, for the purposes of this application, will be termed Panhypopituitarism, X-linked; PHPX, OMIM #312000.

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

1.6. 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.

1.7. 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'.

1.8. The committee noted that Panhypopituitarism, X-linked; PHPX, OMIM #312000, is inherited in an X-linked recessive manner. The risk of transmission of the relevant genetic abnormality means there is a 25% chance of an affected male child and 25% of a female carrier in each pregnancy. Female carriers are usually phenotypically normal but there is theoretical risk that a female could also present with symptoms of the condition.

1.9. If the father has the genetic abnormality, there is a 50% chance in each pregnancy that a child will be a female carrier. As stated above, female carriers are usually phenotypically normal. All male children of an affected father will not inherit his affected X chromosome so will be unaffected by the condition.

1.10. The committee noted that the penetrance of the condition is not known but appears to be very high in published reports of affected families.

1.11. Panhypopituitarism, X-linked; PHPX, OMIM #312000, is characterised by multiple pituitary hormone deficiencies or isolated growth hormone deficiency, structural pituitary and/or other midline cranial abnormalities, brain abnormalities and mild to severe intellectual disability. Some patients can also present with neural tube defects, with associated disabilities including lower limb weakness or paralysis and bladder and bowel dysfunction. Other symptoms include severe intrauterine growth retardation, cranio-facial and optical abnormalities, and poor control of blood sugar. The condition can result in neonatal death or death in infancy.

1.12. There is no cure for this condition and lifelong hormone replacement may be used, with doses modified as children grow, with the aim of avoiding some of the severe life-limiting complications of the condition that result from endocrine dysregulation. Growth hormone can be

given by injection to help growth and stature. Neural tube defects can be surgically treated but some individuals are left unable to walk and have bowel and bladder dysfunction. Hormone replacement cannot prevent all infant deaths and intellectual impairment.

1.13. The committee noted the executive's request to consider Panhypopituitarism, X-linked; PHPX, OMIM #312000, for inclusion on the list of conditions approved for PGD. The committee agreed to consider the application on this basis.

1.14. The committee also noted the recommendation of the peer reviewer to consider a further condition for inclusion on the list for which PGD can be applied and agreed to consider the application on this basis. Mental retardation, X-linked, with panhypopituitarism, OMIM #300123, is of a similar phenotype with overlapping clinical features to Panhypopituitarism, X-linked; PHPX, OMIM #312000, with all of those affected having severe intellectual disability.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Panhypopituitarism, X-linked; PHPX, OMIM #312000, is a severe condition that presents prenatally or at birth. Those affected with the condition will require lifelong daily injections to correct hormone imbalance, but there still remains a significant risk of intellectual impairment and death in infancy. The committee considered the potentially very serious physical and psychological impact on the quality of life of those affected with the condition.

2.2. The committee also considered the condition Mental retardation, X-linked, with panhypopituitarism, OMIM #300123, is, in the worst-case scenario, a serious condition resulting in multiple hormone deficiencies, brain anomalies, severe intellectual disability and death in infancy.

2.3. 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.

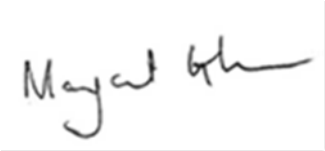
2.4. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Panhypopituitarism, X-linked; PHPX, OMIM #312000
- Mental retardation, X-linked, with panhypopituitarism, OMIM #300123

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

16 April 2021