Statutory Approvals Committee – minutes

Item 2

Centre 0102 (Guys Hospital)

Pre-implantation Genetic Diagnosis (PGD) application for Blepharophimosis, Ptosis and Epicanthus Inversus Syndrome types 1 & 2 (BPES 1 & 2), OMIM #110100

Thursday, 22 February 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Anne Lampe Ruth Wilde Anthony Rutherford	
Members of the Executive	Dee Knoyle Paula Robinson Clare Ettinghausen	Committee Secretary Head of Planning & Governance (Observing) Director of Strategy & Corporate Affairs (Observing)
External adviser	Dr Mary Porteous	
Legal Adviser	Graham Miles	Blake Morgan 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 (2018)
- Redacted peer review (2015)
- Genetic Alliance opinion (2015)
- Two academic papers (Beaconfield et al 1991 and Mandal et al 2017) provided by the peer reviewer in 2018.
- One patient comment
- Email chain with the centre confirming their inclusion of a patient statement with the application and their desire that the Executive process the application
- July 2015 SAC Minutes - PGD for BPES 1 & 2 OMIM #110100

1. Consideration of application

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

1.2. The committee noted that the description in the application for Blepharophimosis, Ptosis and Epicanthus Inversus Syndrome types 1 & 2 (BPES 1 & 2), OMIM #110100 is consistent with the peer review.

1.3. The committee noted that in July 2015, the Person Responsible (PR) applied for BPES 1 & 2 to be approved for PGD. Genetic Alliance provided a patient perspective and supported the original application in 2015. However, this application was refused by the Statutory Approvals Committee and the conditions were not included on the list of approved PGD conditions. Although the committee was sensitive to the fact that the conditions are associated with altered facial appearance, in considering the worst case scenario of the symptoms associated with these conditions and taking into account the treatment options available, the committee concluded that the threshold for the statutory test of seriousness, which would allow the committee to licence this condition for PGD, was not met.

1.4. The committee noted that the PR has submitted a second application for BPES 1 & 2 with additional information, including academic papers provided by a second Peer Reviewer on the seriousness of the condition and a statement from a patient couple seeking PGD to avoid passing on the condition. The committee noted that the Executive considered that the additional information constituted a material and significant change to the information provided in the original application and therefore submitted the second application for consideration by the Statutory Approvals Committee.

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 BPES 1 & 2 are inherited in an autosomal dominant manner which means there is a 50% chance of having an affected child in each pregnancy, if either parent has a relevant mutation.

1.8. The committee noted that BPES 1 & 2 have high penetrance.

1.9. The committee noted that BPES 1 & 2 are conditions that affect the development of the eyelids. The conditions are apparent from birth. Those affected by BPES 1 & 2 have four main features: fusion of eyelids causing narrowing of the eye opening (blepharophimosis), droopy eyelids (ptosis), an upward fold of the skin of the lower eyelid near the inner corner of the eye (epicanthus inversus) and an increased distance between the inner corners of the eyes (telecanthus).

1.10. The committee noted that symptoms include a variety of ophthalmic problems. Babies can be born with fused eyelids, and may have to endure multiple operations, involving periods of time with bandaged eyes. Where the eyelids cannot open fully there is an ongoing possibility of visual impairment. In addition, there may be decreased tear production which causes discomfort and dry eyes, and may compromise vision. People with BPES have distinct facial features including a broad nasal bridge and a shortened distance between the nose and upper lip. The condition is variable but can seriously affect the psychological and mental well-being of the sufferer. Some patients report very difficult childhoods and adult life, due to this condition. Both BPES 1 & 2 are caused by changes in the same gene and the difference in the type is made on the basis of symptoms. Women with BPES 1 have the additional symptom of premature ovarian failure, which results in women either having difficulties conceiving, or not being able to conceive their own children at all.

1.11. The committee noted that treatment for BPES 1 & 2 involves surgically opening the eyelids at an appropriate time as delay can prevent normal sensory stimulation. In some instances plastic surgery may be performed to eventually create an eyelid. Children with BPES usually need multiple operations and skin grafts to create normal looking eyes. Individuals with BPES 1 & 2 have normal intelligence, however, psychologically they can suffer due to their unusual facial features. Glasses can treat refractive issues. Hormone replacement therapy may be used to treat premature ovarian failure.

1.12. The committee noted the inspectorate's request to consider whether BPES 1 & 2 OMIM #110100 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst case scenario, BPES 1 & 2 OMIM #110100 are serious conditions. The committee considered the original peer reviewer's comments made in 2015, that babies are born with severe eyelid malformations threatening their visual development. In the worst case scenario individuals born with this condition undergo surgery repeatedly with limited success at a young age, developing amblyopia in both eyes with permanently decreased vision and poor cosmetic outcome, causing the individual psychological distress and affecting social interaction. Females with BPES 1 may also experience primary amenorrhoea and infertility due to premature ovarian failure.

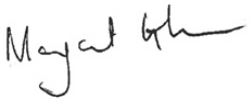
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 conditions Blepharophimosis, Ptosis and Epicanthus Inversus Syndrome types 1 & 2 (BPES 1 & 2), OMIM #110100 meet 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 Blepharophimosis, Ptosis and Epicanthus Inversus Syndrome types 1 & 2 (BPES 1 & 2), OMIM #110100.

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

7 March 2018