Statutory Approvals Committee – minutes

Centre 0101 (CARE Nottingham)

Pre-implantation Genetic Diagnosis (PGD) application for Hereditary Angioedema (HAE) Type I & II, OMIM #106100 & Hereditary Angioedema (HAE) Type III, OMIM #610618

Thursday, 28 June 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 Bernice Ash Paula Robinson Catherine Burwood Richard Chamberlain	Committee Secretary Committee Secretary (Observer) Head of Planning and Governance (Observer) Senior Governance Manager (Observer) Temporary Committee Clerk (Observing for Induction)
Specialist Adviser	Dr Alan Fryer	
Legal Adviser	Tom Rider	Fieldfisher 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
- Condition Names - confirmation from the centre
- 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 conditions were as described in the papers.

1.2. The committee noted that the description in the application for Hereditary Angioedema (HAE) Type I & Type II, OMIM #106100 and Hereditary Angioedema (HAE) Type III, OMIM #610618 is consistent with the peer review.

1.3. The committee noted that Genetic Alliance 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 conditions being applied for are 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 HAE Type I & Type II and HAE Type III 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 penetrance figures are unknown but HAE Type III has variable expressivity, later age of onset and lower penetrance.

1.9. The committee noted that affected individuals could have spontaneous attacks of angioedema (severe swelling) without itching which can affect the extremities, face, GI tract and the larynx. Patients experience attacks that can be potentially life threatening or cause pain and discomfort. Attacks can be triggered by infections, minor trauma or injury and stress, ACE-inhibitors and oestrogens. When attacks affect the gastrointestinal tract they can cause nausea, vomiting and severe abdominal pain. In the most severe cases the larynx is affected which can cause life threatening swelling due to airway obstruction. These episodes occur without warning in 50% of cases and with some prodromal symptoms or rash in 50%. A high percentage of affected patients (28%) can have more than one attack per week, often necessitating emergency or intensive care. Attacks can last 3-4 days. These can involve multiple visits to the hospital or admissions (Bork, 2010).

1.10. The committee noted that there is significant bearing on the quality of life for affected individuals, as reported in several published reports utilising patient surveys. Patients without adequate diagnosis can have an estimated mortality rate of 25-40% from laryngeal asphyxiation. Depression and anxiety are common in patients.

1.11. There is currently no cure for the disease. Acute Airway compromise in emergency situations is best dealt with by airway intubation by a skilled anaesthetist. Severity of acute attacks can be decreased or duration of attacks reduced using C1-inhibitor concentrate. This can also be utilised prophylactically in pregnancy to reduce attack frequency and minimise vaginal swelling in order to achieve a successful vaginal delivery. Historically, androgens and their derivatives can be used for long-term prophylaxis New therapies such as Icatibant and Ecallantide have also been shown to be effective in treating attacks by reducing the duration of symptoms. Side effects are reported with newer therapies.

1.12. The committee noted the inspectorate's request to consider whether HAE Type I & Type II OMIM #106100 and HAE Type III OMIM #610618, 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, Hereditary Angioedema (HAE) Type I & Type II, OMIM #106100 and Hereditary Angioedema (HAE) Type III, OMIM #610618 are serious conditions. These conditions cause swelling resulting in severe pain and discomfort and at worst, are disabling and life threatening. Symptoms usually develop by the time individuals reach their twenties. Individuals may require urgent treatment during an attack of angioedema, especially where the larynx is affected as they are at risk of asphyxiation. A detailed treatment plan and access to urgent care is required as spontaneous attacks, which could be triggered by something minor, could occur without warning and last for a period of days. There is no curative treatment for these conditions and attacks can only be reduced in frequency, they cannot be completely prevented. All of the therapies may have side effects.

2.2. The committee considered that the individual's quality of life may be severely affected by HAE. The committee also considered the psychological burden not knowing when an attack might occur and potentially cause early death.

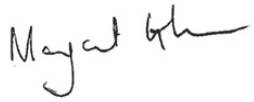
2.3. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act and agreed to authorise testing for these conditions:

- Hereditary Angioedema (HAE) Type I & Type II, OMIM #106100
- Hereditary Angioedema (HAE) Type III, OMIM #610618

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

30 July 2018