Statutory Approvals Committee – minutes

Centre 0035 (Oxford Fertility)

Pre-implantation Genetic Diagnosis (PGD) application for Muckle-Wells Syndrome (MWS), OMIM #191900

Thursday, 31 August 2017

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Anne Lampe Tony Rutherford Ruth Wilde Bobbie Farsides	
Members of the Executive	Dee Knoyle	Committee Secretary
External adviser	Dr Jenny Carmichael	
Legal Adviser	Sarah Ellson	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
- Statutory Approvals Committee minutes for 29 June 2017
- Original Executive summary considered on 29 June 2017
- PGD Application Form
- Redacted peer review
- Genetic Alliance Opinion
- Additional information on treatments provided by the external adviser on 29 June 2017
- Peer reviewer's comments on additional information on treatments
- Centre's response to the additional information on treatments and peer reviewer's comments

1. Background

1.1. Oxford Fertility, centre 0035 submitted an application to provide PGD for Muckle-Wells Syndrome (MWS), OMIM #191900. This application was considered by the Statutory Approvals Committee on 29 June 2017. Dr Alan Fryer, the Specialist Adviser who attended this meeting, provided information about the availability, effectiveness and side-effects of treatment for the condition that had not been addressed by the Peer Reviewer or the centre. The committee considered that this information was relevant to the determination of the application and therefore decided to adjourn its decision to allow the centre and original Peer Reviewer to comment on this new information. Both have reviewed this information and the centre was forwarded the peer reviewer's comments and has provided a response.

2. Consideration of application

2.1. The committee welcomed the advice of its Specialist Adviser, Dr Jenny Carmichael, who confirmed that the condition was as described in the papers.

2.2. The committee noted that the description in the application for Muckle-Wells Syndrome (MWS), OMIM #191900 is consistent with the Peer Review.

2.3. The committee noted that the Genetic Alliance opinion provided a patient perspective and supported the application.

2.4. 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.

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

2.6. 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'.

2.7. The committee noted that Muckle-Wells Syndrome (MWS), OMIM #191900 is inherited in an autosomal dominant pattern which means there is a 50% chance of having an affected child in each pregnancy, if either parent has a relevant mutation.

2.8. MWS is known as a cryopyrin associated periodic syndrome (CAPS). It is characterised by episodes of fever, rash and joint pain. Symptoms may be exacerbated by cold, or triggered by other stimuli. Patients may also develop progressive hearing loss and kidney problems. Symptoms begin in infancy or early childhood.

2.9. Common symptoms of MWS include recurrent rashes, intermittent fevers, joint pain, recurrent conjunctivitis and progressive hearing loss. In some MWS cases amyloidosis develops later in life. Amyloidosis causes an abnormal accumulation of the protein amyloid in a patient's tissues and organs which causes damage and often kidney failure if untreated. Symptoms can appear suddenly, but can also be triggered by cold exposure as well as stress or exercise. Episodes may last between 24 to 48 hours. Symptoms of other CAPS conditions, such as Familial cold autoinflammatory syndrome (FCAS) can be similar to Muckle-Wells syndrome. There is significant phenotypic overlap with FCAS and it is caused by mutations in the same CIAS1/NLRP3 gene. Per the peer review, there are not many case reports but penetrance appears to be 100%, albeit with a variable phenotype.

2.10. Treatments include the use of painkillers and non-steroidal anti-inflammatory drugs to alleviate joint pain and rashes. A variety of drug treatments are also available to those with CAPS disorders, including MWS; these vary in effectiveness. Hearing aids may help to correct progressive hearing loss. Kidney transplant may be required if amyloidosis causes kidney failure and this may have a significant impact on quality of life. Kidney complications may impact on the life expectancy of MWS patients.

2.11. The committee noted that there is only one treatment available in the UK - Ilaris (Canakinumab), a monoclonal antibody to interleukin-1 beta which was approved by the FDA in 2009 as a treatment for children and adults with CAPS, including FCAS and MWS. This treatment is administered once every four weeks and the average cost is approximately $500,000 per year. This treatment has been approved in the UK by the National Institute for Health and Care Excellence (NICE). This treatment is very expensive and may require approval for affected individuals on a case by case basis.

2.12. The committee noted the inspectorate's request to consider whether Muckle-Wells Syndrome (MWS), OMIM #191900 should be approved for inclusion on the PGD List. The committee agreed to consider the application on this basis.

3. Decision

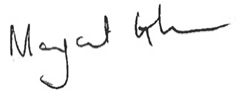
3.1. The committee considered that Muckle-Wells Syndrome (MWS), OMIM #191900 is serious, given the significant risk of developing symptoms including fever, painful joints, progressive hearing loss and kidney failure requiring a transplant. Kidney complications may impact on life expectancy. This is a chronic condition with acute exacerbation that can be disabling and limit mobility, having severe impact on an individual's quality of life. The onset of the condition is in early infancy or early childhood and there is no curative treatment. For individuals at the severe end of the spectrum, only a small number have partially responded to treatment using Ilaris (Canakinumab). This treatment involves frequent injections and may alleviate symptoms in some cases, however long term effects of using this treatment on individuals who have already developed the symptoms of the condition is unknown. Also, there is no research available to show the effectiveness of long term use of this treatment as prophylactic to prevent the disease from developing or to slow down the progression of the condition on individuals known to be gene carriers who have not yet developed any symptoms. All research currently available is based on treatment of patients who have already developed the symptoms of the condition.

3.2. The committee had regard to its explanatory note and noted that on the basis of the information presented, given the condition's worst symptoms, it was satisfied that there is both a particular risk and a significant risk 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 of Muckle-Wells Syndrome (MWS), OMIM #191900 does meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise the testing for Muckle-Wells Syndrome (MWS), OMIM #191900.

4. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

2 October 2017