Statutory Approvals Committee – minutes

Centre 0044 (The Centre for Reproductive and Genetic Health) Pre-implantation Genetic Diagnosis (PGD) application for Pachyonychia Congenita Type 2, OMIM #167210 Pachyonychia Congenita Type 3, OMIM #615726 Pachyonychia Congenita Type 4, OMIM #615728 and Palmoplantar Keratoderma, Nonepidermolytic, Focal or Diffuse, OMIM #615735

Thursday, 27 September 2018

HFEA, 10 Spring Gardens, London, SW1A 2BU

Committee members	Margaret Gilmore (Chair) Bobbie Farsides (Deputy Chair) Ruth Wilde	
Members of the Executive	Dee Knoyle Bernice Ash Catherine Burwood Paula Robinson	Committee Secretary Committee Secretary (Observer) Senior Governance Manager Head of Planning and Governance (Observer)
Specialist Adviser	Professor Peter Turnpenny	
Legal Adviser	Dawn Brathwaite	Mills & Reeve 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
- Licence Committee minutes 26 August 2010: PGD for Pachyonychia Congenita Type 1

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 for the following conditions listed in the application for PGD is consistent with the peer review:

- Pachyonychia Congenita Type 2, OMIM #167210
- Pachyonychia Congenita Type 3, OMIM #615726
- Pachyonychia Congenita Type 4, OMIM #615728
- Palmoplantar Keratoderma, Nonepidermolytic, Focal or Diffuse, OMIM #615735

1.3. The committee noted that the conditions being applied for are not on the list of conditions approved for PGD; however, Pachyonychia Congenita Type 1 (OMIM #167200) has been on the list since August 2010.

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

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 Pachyonychia Congenita Types 2, 3 and 4 and Palmoplantar Keratoderma, Nonepidermolytic, Focal or Diffuse, are all inherited in an autosomal dominant manner which means there is a 50% chance of an embryo being affected with the condition in each pregnancy, if either parent has a relevant mutation.

1.8. The committee noted that five different genes that code for the protein keratin have been found to cause the condition:

- Pachyonychia Congenita Type 1 is caused by mutation in the *KRT16* gene
- Pachyonychia Congenita Type 2 is caused by mutation in the *KRT17* gene
- Pachyonychia Congenita Type 3 is caused by mutation in the *KRT6A* gene
- Pachyonychia Congenita Type 4 is caused by mutation in the *KRT6B* gene
- Palmoplantar Keratoderma, Nonepidermolytic, Focal or Diffuse, is caused by mutation in the *KRT6C* gene

1.9. The committee noted that the most common features of the condition include plantar hyperkeratosis (thickened skin on the soles of the feet) with very painful underlying blisters and calluses; these make walking difficult or even impossible because of plantar pain. Affected individuals also have thickened and abnormally shaped fingernails and toenails, various types of cysts (i.e. steatocystoma and pilosebaceous cysts - two types of sebaceous gland cysts) in the armpits, groin, back, or scalp; follicular hyperkeratosis (lumpy accumulation of tissue at the base of hairs on the elbows, knees, and waistline), leukokeratosis (thickened white patches on the tongue, in the mouth, or on the inside of the cheek); sores at the corner of the mouth; and natal teeth. Some affected individuals develop calluses on the palms of the hands (palmar hyperkeratosis) and experience excessive sweating on the palms and soles; a hoarse cry or voice caused by white film on the larynx (voice box); and/or intense pain when beginning to eat or swallow. Although rare, laryngeal involvement may cause life-threatening respiratory distress requiring intervention. Affected individuals usually have normal intellectual development, however may suffer from significant psychological problems as a consequence of the chronic pain. Penetrance is almost complete with around 97% of patients experiencing some symptoms and some are profoundly affected by the limitations in mobility caused by the pain.

1.10. The committee noted that Pachyonychia Congenita is incurable so treatment primarily centres on symptomatic pain relief, hygienic grooming practices including paring of hyperkeratotic areas, and treatment of secondary infection when indicated. The pain associated with plantar focal blistering may require the use of crutches, canes, or wheelchairs. Special orthotics or insoles, wicking socks, ventilated footwear or cushioned footwear can help to lessen the pain although pain varies from day to day. This intense pain has a major impact on quality of life, as does the limitations on mobility caused by this pain.

1.11. The committee noted the inspectorate's request to consider whether the following conditions should be approved for inclusion on the list of conditions approved for PGD and agreed to consider the application on this basis:

- Pachyonychia Congenita Type 2, OMIM #167210
- Pachyonychia Congenita Type 3, OMIM #615726
- Pachyonychia Congenita Type 4, OMIM #615728
- Palmoplantar Keratoderma, Nonepidermolytic, Focal or Diffuse, OMIM #615735

2. Decision

2.1. The committee considered that, in the worst case scenario, Pachyonychia Congenita Type 2, 3 and 4 and Palmoplantar Keratoderma, Nonepidermolytic, Focal or Diffuse are serious conditions with multiple symptoms which may cause difficulty breathing and be life threatening. The conditions cause chronic pain when walking due to very painful blisters and calluses on the soles of the feet, limiting mobility and resulting in some individuals requiring a wheelchair. Affected individuals have difficulty swallowing food, experiencing severe pain when eating. The condition mainly affects the feet and hands and also causes thickening of the finger nails and toe nails resulting in abnormality. The age of onset could be as early as the first year of life or in early childhood. Management of the symptoms is difficult, especially the treatment of secondary infections and there is no curative treatment. The quality of life for affected individuals is severely impacted.

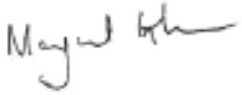
2.2. The committee had regard to its explanatory note and confirmed that, on the basis of the information presented, it was satisfied that there is a particular risk that an embryo may have the abnormality in question and that there is a significant risk, given the condition's worst symptoms, that a 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 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:

- Pachyonychia Congenita Type 2, OMIM #167210
- Pachyonychia Congenita Type 3, OMIM #615726
- Pachyonychia Congenita Type 4, OMIM #615728
- Palmoplantar Keratoderma, Nonepidermolytic, Focal or Diffuse, OMIM #615735

3. Chairs signature

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

Signature



Name

Margaret Gilmore

Date

22 October 2018