Statutory Approvals Committee - minutes

Centre 0035 (Oxford Fertility)

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) - application for Kozlowski type of spondylometaphyseal dysplasia, OMIM #184252, Spondyloepiphyseal dysplasia, Maroteaux type, OMIM #184095, Parastremmatic dysplasia, OMIM #168400, and Metatropic dysplasia, OMIM #156530

Date:	24 June 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde
Specialist Adviser:	Ed Blair
Legal Adviser:	Neil Ward – Mills & Reeve LLP
Members of the Executive:	Moya Berry - Committee officer Catherine Burwood - Licensing Manager
Apologies:	No apologies were received for the meeting
Declarations of Interest:	Tim Child declared a conflict of interest and was not present at the meeting for this item. No other members declared a conflict 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
- PGT-M Application form
- Redacted Peer review
- Genetic Alliance (UK) Statement
- 2019-09-26 Statutory Approvals Committee Minutes - Spondyloepiphyseal Dysplasia with Congenital Joint Dislocations, OMIM #143095
- 2019-05-30 Statutory Approvals Committee Minutes - Spondylometaepiphyseal Dysplasia Short Limb Hand Type, OMIM #271665
- 2015-08-15 Statutory Approvals Committee Minutes - Spondyloepimetaphyseal dysplasia, Strudwick type, OMIM #184250

1. Consideration of application

1.1. The committee welcomed the advice of its specialist adviser, Dr Ed Blair, who confirmed that the conditions were as described in the papers.

1.2. The committee noted that the description in the PGT-M application for Kozlowski type of spondylometaphyseal dysplasia, OMIM #184252, Spondyloepiphyseal dysplasia, Maroteaux type, OMIM #184095, Parastremmatic dysplasia, OMIM #168400, and Metatropic dysplasia, OMIM #156530, is consistent with the peer review.

1.3. The committee noted that the conditions being applied for are not on the list of approved PGT-M conditions.

1.4. The committee noted that the conditions, Kozlowski type of spondylometaphyseal dysplasia, OMIM #184252 and Parastremmatic dysplasia, OMIM #168400 are also known as Spondylometaphyseal dysplasia, Kozlowski type, (SMDK), OMIM #184252 and Parastremmatic Dwarfism, OMIM #168400. As the OMIM website entry lists Spondylometaphyseal dysplasia, Kozlowski type, (SMDK), OMIM #184252 and Parastremmatic Dwarfism, OMIM #168400 as the primary names for these conditions, the conditions, for the purposes of this application, will be termed Spondylometaphyseal dysplasia, Kozlowski type, (SMDK), OMIM #184252 and Parastremmatic Dwarfism, OMIM #168400.

1.5. The committee noted that the Genetic Alliance (UK) statement provided a perspective on the impact of the conditions 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 PGT-M. The committee was also satisfied that the centre has experience of carrying out PGT-M and that generic patient information about its PGT-M 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 Spondylometaphyseal dysplasia, Kozlowski type (SMDK), OMIM #184252, Spondylo-epiphyseal dysplasia, Maroteaux type, OMIM #184095, Parastremmatic Dwarfism, OMIM #168400, and Metatropic dysplasia, OMIM #156530, are inherited in an

autosomal dominant manner, which means there is a 50% chance of an embryo being affected by the condition in each pregnancy if either parent has a relevant mutation.

1.9. The committee noted that the conditions are not fully penetrant. Symptoms can be variable, although presentation within a family is similar.

1.10. Spondylometaphyseal dysplasia, Kozlowski type (SMDK), OMIM #184252, Spondylo-epiphyseal dysplasia, Maroteaux type, OMIM #184095, Parastremmatic Dwarfism, OMIM #168400, and Metatropic dysplasia, OMIM #156530, are characterised by skeletal dysplasia involving shortened digits, short stature varying from mild to severe, progressive spinal abnormality and abnormalities of the long bones and pelvis. Bilateral progressive sensorineural hearing loss can also occur. In severe cases death in utero or in childhood can occur.

1.11. There is no cure for these conditions and treatment is focused on symptom management.

1.12. The committee noted the executive's request to consider Spondylometaphyseal dysplasia, Kozlowski type (SMDK), OMIM #184252, Spondylo-epiphyseal dysplasia, Maroteaux type, OMIM #184095, Parastremmatic Dwarfism, OMIM #168400, and Metatropic dysplasia, OMIM #156530, for inclusion on the list of conditions approved for PGT-M. The committee agreed to consider the application on this basis.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Spondylometaphyseal dysplasia, Kozlowski type (SMDK), OMIM #184252, Spondylo-epiphyseal dysplasia, Maroteaux type, OMIM #184095, Parastremmatic Dwarfism, OMIM #168400, and Metatropic dysplasia, OMIM #156530 are rare, progressive, conditions that can present in utero. The conditions, which involve multiple joints, may lead to those affected suffering chronic lifelong pain. Some may also experience difficulty with walking and require the use of a wheelchair to aid mobility. There is no cure for the conditions, and in some cases death in early childhood can occur from respiratory failure. The committee considered the serious implications for, and the potential severe impact on, the quality of life of those affected by the conditions.

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 abnormalities in question and that there is a significant risk that a person with such abnormalities will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness, or any other serious medical condition.

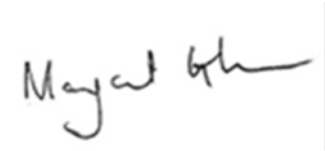
2.3. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Spondylometaphyseal dysplasia, Kozlowski type (SMDK), OMIM #184252
- Spondylo-epiphyseal dysplasia, Maroteaux type, OMIM #184095
- Hypotonia, Parastremmatic Dwarfism, OMIM #168400
- Metatropic dysplasia, OMIM #156530

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

21 July 2021