Statutory Approvals Committee - minutes

Centre 0102 (Guys Hospital)

Preimplantation Genetic Testing for Monogenic Disorders (PGT-M) - application for Cutis Laxa type 2B, OMIM #612940

Date:	24 June 2021
Venue:	Microsoft Teams Meeting
Committee Members:	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde Tim Child
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:	Members of the committee declared that they had no conflicts 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

1. Consideration of application

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

1.2. The committee noted that the description in the PGT-M application for Cutis Laxa type 2B, OMIM #612940, is consistent with the peer review.

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

1.4. The committee noted that the condition, Cutis Laxa type 2B, OMIM #612940 is also known as Cutis Laxa, autosomal recessive, type IIB (ARCL2B), OMIM #612940. As the OMIM website entry lists Cutis Laxa, autosomal recessive, type IIB (ARCL2B), OMIM #612940, as the primary name of the condition, the condition, for the purposes of this application, will be termed Cutis Laxa, autosomal recessive, type IIB (ARCL2B), OMIM #612940.

1.5. The committee noted that the Genetic Alliance (UK) statement provided a perspective on the impact of the condition 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 Cutis Laxa, autosomal recessive, type IIB (ARCL2B), OMIM #612940, is inherited in an autosomal recessive manner, which means there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation.

1.9. The committee noted that the penetrance of the condition is 100%.

1.10. Cutis Laxa, autosomal recessive, type IIB (ARCL2B), OMIM #612940, is a painful condition characterised by cutis laxa (loose skin), growth restriction from before birth, hyper extensive joints with dislocations, hypotonia and intellectual disability.

1.11. There is no cure for the condition and those affected may require multiple medical and surgical interventions to help ameliorate the symptoms.

1.12. The committee noted the executive's request to consider Cutis Laxa, autosomal recessive, type IIB (ARCL2B), OMIM #612940, for inclusion on the list of conditions approved for PGT-M. The committee agreed to consider the application on this basis.

1.13. The committee also noted the peer reviewer's recommendation to consider nine additional conditions for inclusion on the list for which PGT-M can be applied and agreed to consider the application on this basis.

1.14. The conditions for consideration are:

- Cutis Laxa, autosomal recessive, type IA (ARCL1A), OMIM #219100
- Cutis Laxa, autosomal recessive, type IB (ARCL1B), OMIM #614437
- Cutis Laxa, autosomal recessive, type IC (ARCL1C), OMIM # 613177
- Cutis Laxa, autosomal recessive, type IIA (ARCL2A), OMIM # 219200

- Cutis Laxa, autosomal recessive, type IIC (ARCL2C), OMIM # 617402
- Cutis Laxa, autosomal recessive, type IID (ARCL2D), OMIM # 617403
- Cutis Laxa, autosomal recessive, type IIIA (ARCL3A), OMIM # 219150
- Cutis Laxa, autosomal recessive, type IIIB (ARCL3B), OMIM # 614438
- Cutis Laxa, autosomal dominant 1 (ADCL1), OMIM #123700

1.15. The condition types are all inherited in an autosomal recessive manner, with the exception of Cutis Laxa, autosomal dominant 1 (ADCL1), OMIM #123700, which is inherited in an autosomal dominant manner. All conditions present in childhood and include cutis laxa (loose skin), joint hyperlaxity and dislocations, hernia, cataracts, corneal clouding, lipodystrophy, and osteopenia leading to bone fractures. For some of these conditions, peripheral pulmonary artery stenosis and cardiorespiratory failure, can prove fatal.

1.16. The committee also noted the recommendation of the peer reviewer to consider one further condition, Geroderma Osteodysplasticum, OMIM #231070. This condition is inherited in an autosomal recessive manner meaning there is a 25% chance of an embryo being affected by the condition in each pregnancy if each parent has a relevant mutation. The condition is characterised by cutis laxa (loose skin), hyperextensible joints, short stature, hypotonia, and congenital hip dislocation. In Geroderma Osteodysplasticum, OMIM #231070, the bones, particularly in the vertebrae, are susceptible to fracture due to osteopenia.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Cutis Laxa, autosomal recessive, type IIB (ARCL2B), OMIM #612940, is a rare, multi-system condition with symptoms present from birth. Those affected may experience painful joint dislocations, neurological and developmental delays. There is also an increased risk of premature cardiovascular disease leading to early death. The committee considered the potential significant psychological, emotional, and physical implications, on the quality of life of those affected by the condition.

2.2. The committee also considered the following conditions that can present from birth and have symptoms that are very similar to Cutis Laxa, autosomal recessive, type IIB (ARCL2B), OMIM #612940, in that they include cutis laxa (loose skin), joint hyperlaxity and dislocations, hernia, cataracts and osteopenia leading to bone fractures which in the worst-case scenario can significantly affect quality of life:

- Cutis Laxa, autosomal recessive, type IA (ARCL1A), OMIM #219100
- Cutis Laxa, autosomal recessive, type IB (ARCL1B), OMIM #614437
- Cutis Laxa, autosomal recessive, type IC (ARCL1C), OMIM # 613177
- Cutis Laxa, autosomal recessive, type IIA (ARCL2A), OMIM # 219200
- Cutis Laxa, autosomal recessive, type IIC (ARCL2C), OMIM # 617402
- Cutis Laxa, autosomal recessive, type IID (ARCL2D), OMIM # 617403
- Cutis Laxa, autosomal recessive, type IIIA (ARCL3A), OMIM # 219150
- Cutis Laxa, autosomal recessive, type IIIB (ARCL3B), OMIM # 614438
- Cutis Laxa, autosomal dominant 1 (ADCL1), OMIM #123700

2.3. The committee also considered the condition Geroderma Osteodysplasticum, OMIM #231070, in the worst-case scenario can lead to osteoporosis, associated with vertebrae compression and susceptibility to fractures, growth deficiency and developmental delays.

2.4. 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.

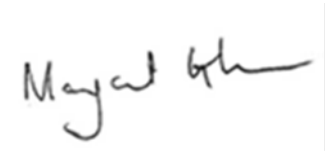
2.5. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Cutis Laxa, autosomal recessive, type IA (ARCL1A), OMIM #219100
- Cutis Laxa, autosomal recessive, type IB (ARCL1B), OMIM #614437
- Cutis Laxa, autosomal recessive, type IC (ARCL1C), OMIM # 613177
- Cutis Laxa, autosomal recessive, type IIA (ARCL2A), OMIM # 219200
- Cutis Laxa, autosomal recessive, type IIB; ARCL2B, OMIM #612940
- Cutis Laxa, autosomal recessive, type IIC (ARCL2C), OMIM # 617402
- Cutis Laxa, autosomal recessive, type IID (ARCL2D), OMIM # 617403
- Cutis Laxa, autosomal recessive, type IIIA (ARCL3A), OMIM # 219150
- Cutis Laxa, autosomal recessive, type IIIB (ARCL3B), OMIM # 614438
- Cutis Laxa, autosomal dominant 1 (ADCL1), OMIM #123700
- Geroderma Osteodysplasticum, OMIM #231070

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