Statutory Approvals Committee - minutes

Centre 0102 (Guys Hospital)

Preimplantation Genetic Diagnosis (PGD) application for Senior-Loken Syndrome (SLSN) type 1, OMIM #266900, type 3, OMIM #606995, type 4, OMIM #606996, type 5, OMIM #609254, type 7, OMIM #613615, type 8, OMIM #616307 and type 9, OMIM #616629

Date:	28 January 2021
Venue:	Microsoft Teams Meeting
Committee Members	Margaret Gilmore (Chair) Emma Cave Anne Lampe Ruth Wilde
Specialist Adviser	Peter Turnpenny
Legal Adviser	Gerard Hanratty - Browne Jacobson 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:

- 9th edition
- Standard Licencing and Approvals Pack

The following papers were considered by the committee:

- Executive Summary
- PGD Application form
- Redacted Peer review
- Genetic Alliance (UK) Statement
- 2019-07-25 Statutory Approvals Committee minutes, PGD for autosomal dominant polycystic kidney disease – type 2, OMIM #613095
- 2015-05-28 Statutory Approvals Committee minutes, PGD for Leber congenital amaurosis types 3-17, OMIM #604232, #604393, #604537, #613826, #613829, #613835, #608553, #611755, #613837, #610612, #612712, #613341, #613843, #614186, #615360
- 2011-06-30 Licence Committee minutes, PGD for Senior Loken Syndrome 6, OMIM #610189

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 conditions in the application for Senior-Loken Syndrome type 1 (SLSN1), OMIM #266900, type 3 (SLSN3), OMIM #606995, type 4 (SLSN4), OMIM #606996, type 5 (SLSN5), OMIM #609254, type 7 (SLSN7), OMIM 613615, type 8 (SLSN8), OMIM #616307 and type 9 (SLSN9), OMIM #616629 are consistent with the peer review:

1.3. The committee noted that the conditions Senior-Loken Syndrome type 1 (SLSN1), OMIM #266900, type 3 (SLSN3), OMIM #606995, type 4 (SLSN4), OMIM #606996, type 5 (SLSN5), OMIM #609254, type 7 (SLSN7), OMIM 613615, type 8 (SLSN8), OMIM #616307 and type 9 (SLSN9), OMIM #616629 are not on the list of approved PGD conditions.

1.4. The committee noted that the Genetic Alliance (UK) statement provided a perspective on the impact of the conditions on patients, their families and carers.

1.5. 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 Senior-Loken Syndrome type 1 (SLSN1), OMIM #266900, type 3 (SLSN3), OMIM #606995, type 4 (SLSN4), OMIM #606996, type 5 (SLSN5), OMIM #609254, type 8 (SLSN8), OMIM #616307 and type 9 (SLSN9), OMIM #616629, are 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. The committee noted the peer reviewer's comment that the pattern of inheritance for Senior-Loken Syndrome type 7, (SLSN7), OMIM #613615, is not stated in OMIM but that there is good evidence of homozygous/compound heterozygous mutations in the SDCCAG8 gene in the published literature, in keeping with an autosomal recessive inheritance pattern for this condition.

1.8. The committee noted that the age of onset and speed of progression of symptoms is variable between SLSN types, but both kidney problems (nephronophthisis) and eye problems (Leber Congenital Amaurosis) appear to be fully penetrant in each type.

1.9. The conditions Senior-Loken Syndrome type 1 (SLSN1), OMIM #266900, type 3 (SLSN3), OMIM #606995, type 4 (SLSN4), OMIM #606996, type 5 (SLSN5), OMIM #609254, type 7 (SLSN7), OMIM 613615, type 8 (SLSN8), OMIM #616307 and type 9 (SLSN9), OMIM #616629 are all characterised by kidney problems (nephronophthisis) leading to kidney failure and potential death, and eye problems (Leber Congenital Amaurosis) which can lead to blindness in childhood.

1.10. There is no treatment which can slow the progression of visual problems associated with these diseases, but those affected may benefit from visual aids. Kidney problems can be treated with medication, however, once these progress to end stage kidney failure it must be treated with dialysis or transplantation, and if successful, transplantation can lead to life-long dependence on anti-rejection medication.

1.11. The committee noted the executive's request to consider Senior-Loken Syndrome type 1 (SLSN1), OMIM #266900, type 3 (SLSN3), OMIM #606995, type 4 (SLSN4), OMIM #606996, type 5 (SLSN5), OMIM #609254, type 7 (SLSN7), OMIM 613615, type 8 (SLSN8), OMIM #616307 and type 9 (SLSN9), OMIM #616629 for inclusion on the list of conditions approved for PGD and agreed to consider the application on this basis.

1.12. However, the committee noted the recommendation of the peer reviewer that Senior-Loken Syndrome type 3 (SLSN3), OMIM #606995 should not be included on the list for which PGD can be applied due to insufficient evidence of any confirmatory gene mutation studies relating to this particular condition. The committee considered the advice of its specialist adviser who concurred that it would be inappropriate to offer PGD without more scientific evidence and agreed not to consider this condition.

2. Decision

2.1. The committee considered that, in the worst-case scenario, Senior-Loken Syndrome type1 (SLSN1), OMIM #266900, type 4 (SLSN4), OMIM #606996, type 5 (SLSN5), OMIM #609254, type 7 (SLSN7), OMIM 613615, type 8 (SLSN8), OMIM #616307 and type 9 (SLSN9), OMIM #616629, are serious, progressive and potentially fatal conditions which can present in utero and/or in early childhood. The conditions result in life-threatening kidney failure and severe visual impairment, with some of those affected being registered as legally blind. There is no treatment that can prevent the conditions and those affected will require a lifetime of medical intervention, including dialysis and/or kidney transplantation. The committee considered the potentially very severe physical and psychological effects on the quality of life of those affected by the conditions and acknowledged the helpfulness of the Genetic Alliance Statement in describing the major impact of the conditions on those living with them.

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 that a person with such an abnormality will, given the conditions' worst symptoms, have or develop a serious physical disability, a serious illness or any other serious medical condition.

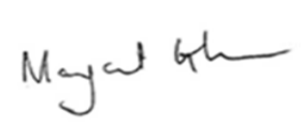
2.3. The committee was therefore satisfied that the following conditions meet the criteria for testing under paragraph 1ZA(1)(b) and (2) of Schedule 2 of the Act. The committee agreed to authorise testing for:

- Senior-Loken Syndrome type 1 (SLSN1), OMIM #266900
- Senior-Loken Syndrome type 4 (SLSN4), OMIM #606996
- Senior-Loken Syndrome type 5 (SLSN5), OMIM #609254
- Senior-Loken Syndrome type 7 (SLSN7), OMIM #613615
- Senior-Loken Syndrome type 8 (SLSN8), OMIM #616307
- Senior-Loken Syndrome type 9 (SLSN9), OMIM #616629

3. Chair's signature

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

Signature



Name

Margaret Gilmore

Date

23 February 2021