**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

CENTRE FOR HEALTH TECHNOLOGY EVALUATION

Technology Appraisals

# Consultation on Batch 65 draft remits and draft scopes and

# summary of comments and discussions at scoping workshops

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| **Topic ID** | **Topic title** |  |
| 1488 | Mexiletine for treating symptomatic myotonia in adults with non-dystrophic myotonic disorders |
| 1254 | Brolucizumab for treating wet age-related macular degeneration |
| 1372 | Galcanezumab for preventing migraine |
| 1523 | L-glutamine for treating sickle cell disease |
| 1419 | Secukinumab for treating non-radiographic axial spondyloarthritis |
| 1532 | Ixekizumab for treating axial spondyloarthritis after NSAIDs |
| 1179 | Dupilumab for treating chronic rhinosinusitis with nasal polyps |
| 1531 | Tafamidis for treating transthyretin amyloid cardiomyopathy |
| 1540 | Treosulfan with fludarabine for non-malignant disease before allogeneic stem cell transplant |
| 1515 | Bempedoic acid for treating primary hypercholesterolaemia or mixed dyslipidaemia |

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| **Provisional Title** | Mexiletine for treating symptomatic myotonia in adults with non-dystrophic myotonic disorders | | |
| **Topic Selection ID Number** | 9836 | **TA ID Number** | 1488 |
| **Company** | Lupin | | |
| **Licensing information** | Marketing authorisation granted: Dec 2018  Wording of marketing authorisation: Mexiletine is indicated for the symptomatic treatment of myotonia in adult patients with non-dystrophic myotonic disorders. | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of mexiletine within its marketing authorisation for treating myotonia in adults with non-dystrophic myotonic disorders | | |
| **Main points from consultation** | Following the consultation exercise and the scoping workshop in January 2019, with more information collected from the NHSE afterwards, NICE is of the opinion that an appraisal of mexiletine (200mg) for treating symptomatic myotonia in adults with non-dystrophic myotonia (NDM) is appropriate.  The proposed remit is not appropriate and should be amended as follows:  “*To appraise the clinical and cost effectiveness of mexiletine within its marketing authorisation for treating* ***symptomatic*** *myotonia in adults with non-dystrophic myotonic disorders.”* This is to be in line with the wording of marketing authorisation (MA). It was noted during the consultation that only people with symptomatic NDM will be eligible for treatment.”  Mexiletine has been used for many years as an oral antiarrhythmic with the brand name Mexitil. Although the product was removed from the European market in 2008 for commercial reasons, it is still available for this indication in the US and Canada. The product has been used as an effectively ‘unlicensed’ medicine for many years and as part of the standard of care for NDM (dosages currently used include 50mg, 100mg, and 200mg).  Stakeholders differed in their opinions regarding the appropriateness of an appraisal and whether it is needed given the re-purpose of the medication and the implications of different options for patients and the NHS. It was noted that with the licensing of mexiletine 200mg, the prescribing of imported 200mg is likely to be stopped in practice. Prescribing data for the year of 2018 suggests that about 60% of NMD patients in the NHS have and will need stay on unlicensed dosages (such as 50mg and 100mg). For example, the company’s MA does not cover children and young people.  It is considered appropriate to refer the topic as a TA.  Not all of the topic selection criteria for the highly specialised technologies programme are met, specifically:   * Main symptoms of NDM are muscle stiffness, weakness and pain, which are not considered clinically distinct or severely disabling during the consultation; * Unlicensed mexiletine has been used for than 10 years in the NHS and formed part of the standard of care, it is not expected to be used exclusively in the context of a highly specialised service. | | |
| **Population size** | Approximately 300 to 600 people in England would be eligible for treatment with mexiletine. | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit (in bold)** | To appraise the clinical and cost effectiveness of mexiletine within its marketing authorisation for treating **symptomatic** myotonia in adults with non-dystrophic myotonic disorders. | | |
| **Costing implications** | \*\*\*Confidential information removed\*\*\* If there are between 300 and 600 people in England eligible for treatment with mexiletine, the cost of treatment could range from between \*\*\*Confidential information removed\*\*\*. There may be offsetting costs from a reduction in use of physiotherapists, mobility aids and occupational assistance, however these savings cannot be accurately estimated. | | |
| **Timeliness statement** | Considering that this product has received a marketing authorisation for use in the UK, publication of timely guidance will not be possible. | | |

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| **Provisional Title** | Brolucizumab for treating wet age-related macular degeneration | | |
| **Topic Selection ID Number** | 8412 | **TA ID Number** | 1254 |
| **Company** | Novartis | | |
| **Anticipated licensing information** | \*\*\*Confidential information removed\*\*\* | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of brolucizumab within its marketing authorisation for treating wet age-related macular degeneration | | |
| **Main points from consultation** | Following the consultation exercise, NICE is of the opinion that an appraisal of brolucizumab for treating neovascular (wet) age-related macular degeneration is appropriate.  The proposed remit is appropriate. No changes are required. Thought will need to be given to the role of bevacizumab in the treatment of wet-AMD, and therefore as a potential comparator for brolucizumab.  Several stakeholders suggested a cost comparison with aflibercept or ranibizumab would be appropriate. | | |
| **Population size** | Approximately 500,000 people in England would be eligible for treatment with brolucizumab.  There were an estimated 415,000 people in UK with wet AMD in 2010 with a predicted estimate of 515,000 by 2020. | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit (in bold)** | None | | |
| **Costing implications** | The unit cost of brolucizumab is unknown so the resource impact of this technology cannot currently be estimated. | | |
| **Timeliness statement** | Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible. | | |

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| **Provisional Title** | Galcanezumab for preventing migraine | | |
| **Topic Selection ID Number** | 9626 | **TA ID Number** | 1372 |
| **Company** | Eli Lilly | | |
| **Licensing information** | Marketing authorisation granted: November 2018  Wording of marketing authorisation: ‘Emgality is indicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month’. | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of galcanezumab within its marketing authorisation for preventing migraine. | | |
| **Main points from consultation** | Following the consultation exercise, NICE is of the opinion that an appraisal of galcanezumab for treating migraine is appropriate.  The proposed remit is appropriate. No changes are required.  All stakeholders agreed the appraisal and remit were appropriate.  The company suggested a possible FTA compared to erenumab ACM2 delayed) and fremanezumab (ACM1 delayed to October 2019). | | |
| **Population size** | Approximately 43,000 people in England would be eligible for treatment with galcanezumab.  The prevalence of chronic migraine is unknown, although some clinicians consider the rate could be 1 in 1,000 people which would mean around 43,100 of the adult population in England (Information from costing briefing). | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit (in bold)** | None | | |
| **Costing implications** | The unit cost of galcanezumab is unknown so the resource impact of this technology cannot currently be estimated. | | |
| **Timeliness statement** | Considering that this product has received a marketing authorisation for use in the UK, publication of timely guidance will not be possible. Company have requested that appraisal commences in Q1 2020 which would be a delay to existing proposed timings. | | |

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| **Provisional Title** | L-glutamine for treating sickle cell disease | | |
| **Topic Selection ID Number** | 9870 | **TA ID Number** | 1523 |
| **Company** | Emmaus Medical Inc | | |
| **Anticipated licensing information** | \*\*\*Confidential information removed\*\*\* | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of L-glutamine within its marketing authorisation for preventing painful crises in sickle cell disease in people aged 5 years and over. | | |
| **Main points from consultation** | Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of L- glutamine for treating sickle cell disease is appropriate.  The proposed remit is not appropriate and should be amended. At the scoping workshop clinical experts noted the unmet need in people under 5 years of age. \*\*\*Confidential information removed\*\*\*  It is not clear which genotypes will be included in the MA (FDA approval includes all genotypes of sickle cell disease, some of which were not included in the trial evidence). A clinical expert explained that in clinical practice treatment is often dependent upon the phenotype rather than genotype. The draft scope specified people with sickle cell anaemia or Sickle βo-thalassaemia but was updated to sickle cell disease to include all genotypes of sickle cell disease to include all people with sickle cell disease who may be eligible for treatment. | | |
| **Population size** | Around 12,500 people in England have sickle cell disease. Of these around 6,600 (53%) are likely to suffer from acute complications and may be eligible for L-glutamine | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit (in bold)** | To appraise the clinical and cost effectiveness of L-glutamine within its marketing authorisation for preventing painful crises in sickle cell disease **~~in people aged 5 years and over~~**. | | |
| **Costing implications** | The unit cost of L-glutamine powder is unknown so the resource impact of this technology cannot currently be estimated. | | |
| **Timeliness statement** | Assuming that the anticipated date of the product launch is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology based on topic launch date will be possible. | | |

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| **Provisional Title** | Secukinumab for treating non-radiographic axial spondyloarthritis | | |
| **Topic Selection ID Number** | 8821 | **TA ID Number** | 1419 |
| **Company** | Novartis | | |
| **Anticipated licensing information** | \*\*\*Confidential information removed\*\*\* | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of secukinumab within its marketing authorisation for treating non-radiographic axial spondyloarthritis. | | |
| **Main points from consultation** | Following the consultation exercise, NICE is of the opinion that an appraisal of secukinumab for treating non-radiographic axial spondyloarthritis is appropriate.  The proposed remit is appropriate. No changes to the remit or scope are required. | | |
| **Population size** | Approximately 24000 people in England would be eligible for treatment with secukinumab based on the population for TA383 (2016). This assumes that the eligible patient population is the same as for other NICE recommended TNF inhibitors. | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit (in bold)** | None | | |
| **Costing implications** | The list price of secukinumab is around £1,200 for 2 pre-filled disposable injections of 150mg per 1ml. The company has agreed a PAS discount which would reduce the annual cost of treatment. The resource impact will depend on the incremental cost of the new technology after any discount is applied, compared to the cost of current comparators after any discounts for comparators are also applied. | | |
| **Timeliness statement** | Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible. | | |

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| **Provisional Title** | Ixekizumab for treating axial spondyloarthritis after NSAIDs | | |
| **Topic Selection ID Number** | 9688 | **TA ID Number** | 1532 |
| **Company** | Eli Lilly | | |
| **Anticipated licensing information** | \*\*\*Confidential information removed\*\*\* | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of ixekizumab within its marketing authorisation for treating axial spondyloarthritis. | | |
| **Main points from consultation** | Following the consultation exercise NICE is of the opinion that an appraisal of ixekizumab for treating axial spondyloarthritis is appropriate.  The proposed remit is appropriate. No changes to the remit or scope are required. | | |
| **Population size** | Non-radiographic axial spondyloarthritis: Approximately 24,000. Based on RIA template for TA383 (2016). Assumes (supported by consultation comments) that patient population is the same as those considered for TNF-alpha inhibitors. Radiographic axial spondyloarthritis: Approximately 23,000. Based on RIA template for TA407 (2016). | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit (in bold)** | None | | |
| **Costing implications** | If licensed, ixekizumab will be an additional biological treatment option alongside current biological treatments. The NHS indicative price for ixekizumab is £1,125 for 1 prefilled pen (BNF). The company has agreed a PAS discount which would reduce the annual cost of treatment. Some of the comparator biological treatments have PAS discounts and therefore the resource impact cannot be provided here. | | |
| **Timeliness statement** | Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible. | | |

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| **Provisional Title** | Dupilumab for treating chronic rhinosinusitis with nasal polyps | | |
| **Topic Selection ID Number** | 8622 | **TA ID Number** | 1179 |
| **Company** | Sanofi | | |
| **Anticipated licensing information** | \*\*\*Confidential information removed\*\*\* | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of dupilumab within its marketing authorisation for treating chronic rhinosinusitis with nasal polyps. | | |
| **Main points from consultation** | Following the scoping workshop, NICE is of the opinion that an appraisal of dupilumab for treating chronic rhinosinusitis with nasal polyps is appropriate.  The proposed remit is appropriate. No changes are required. All stakeholders agreed that an appraisal and the draft remit are appropriate.  Overlaps with other eosinophilic conditions, such atopic dermatitis and asthma (for which there is NICE TA guidance and guidance in development respectively) were discussed at the scoping workshop. The disease is often concomitant with these conditions and all could potentially be treated at the same time. However, it was agreed that the population for this indication are primarily having treatment for chronic rhinosinusitis with nasal polyps. Subgroups based on these comorbidities were added to the scope.  Stakeholders were of the view that dupilumab would most likely be used after surgery if polyps have recurred. However, it was agreed that the remit should remain broad and no changes are required. | | |
| **Population size** | The population size is difficult to establish, but an estimate of the potential population is below:   * 10% of people have chronic rhinosinusitis = 5.6 million * 25 – 30% of this population will have chronic rhinosinusitis with nasal polyps = 1.4 million to 1.7 million * ~60% of this population have had surgery = 800,000 to 1,000,000 * ~50% of this population may have had >1 surgery = 400,000 to 500,000   \*Actual population may be more restricted than the figures presented here as treatment may be reserved for severe cases. | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit (in bold)** | None | | |
| **Costing implications** | The list price of dupilumab is around £1,300 for 2 pre-filled disposable injections of 150mg per 1ml (BNF). In clinical trials 2 different doses were used. The first dose was 300mg every 2 weeks along with mometasone furoate daily. The annual cost per person for this dosage will be around £32,900, along with the cost of mometasone furoate, which is around £2 for every bottle of nasal spray needed (NHS Electronic Drug Tariff).  The second dose in the clinical trial was 300mg daily every 2 weeks up to week 24, then every 4 weeks for a total of 52 weeks along with mometasone furoate daily. The annual cost per person for this dose will be around £24,000, along with the cost of mometasone furoate, which is around £2 for every bottle of nasal spray needed (NHS Electronic Drug Tariff).  However, there is a commercial arrangement in place for dupilumab which would reduce the estimated annual cost. | | |
| **Timeliness statement** | Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology would be possible. However, NICE have agreed to a request from the company to delay submission for this topic until after marketing authorisation. Timely guidance may still be possible based on expected launch date. | | |

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| **Provisional Title** | Tafamidis for treating transthyretin amyloid cardiomyopathy | | |
| **Topic Selection ID Number** | 9509 | **TA ID Number** | 1531 |
| **Company** | Pfizer | | |
| **Anticipated licensing information** | \*\*\*Confidential information removed\*\*\* | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of tafamidis within its marketing authorisation for treating transthyretin amyloid cardiomyopathy. | | |
| **Main points from consultation** | Following the scoping workshop, NICE is of the opinion that an appraisal of tafamidis for treating transthyretin amyloid cardiomyopathy is appropriate.  The proposed remit is appropriate. No changes are required. All stakeholders agreed that an appraisal and the draft remit are appropriate.  At the workshop it was discussed whether for the population with hereditary disease, patisiran and inotersen (which are currently undergoing NICE HST evaluation for treatment of polyneuropathy caused by hereditary transthyretin amyloidosis) should be comparators. It was agreed that only a small number of people would have a mixed phenotype (that is both cardiomyopathy and polyneuropathy). However, for these people, patisiran and inotersen would potentially be comparators if recommended by NICE. Therefore, they have been left in the scope, but clarity has been added that this is only relevant for people with a mixed phenotype and is subject to ongoing NICE evaluation.  It was agreed that tafamidis did not meet the criteria to be evaluated through the HST process. This was primarily because there are currently 600 people known to have wild-type cardiomyopathy, and these numbers are expected to increase substantially over the next few years due to the development of non-invasive cardiac diagnostic tests. As such, management is likely to move to local centres rather than be concentrated in a few specialised centres. | | |
| **Population size** | Approximately 800 people in England would be eligible for treatment with tafamidis.  Numbers of people on National Amyloidosis Centre database: Wild type ATTR cardiomyopathy n=600  Hereditary ATTR cardiomyopathy n=200 | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit (in bold)** | None | | |
| **Costing implications** | The NHS indicative price for 30 capsules of tafamidis each of 20mg is around £10,700 (BNF). According to the BNF, treatment should be 20mg once daily, this would result in an annual cost of around £130,000 per person. However, in clinical trials some people were treated with 80mg of tafamidis daily, this treatment would result in an annual cost of around £520,000. | | |
| **Timeliness statement** | Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible | | |

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| **Provisional Title** | Treosulfan with fludarabine for non-malignant disease before allogeneic stem cell transplant | | |
| **Topic Selection ID Number** | 10128 | **TA ID Number** | 1540 |
| **Company** | Medac | | |
| **Anticipated licensing information** | \*\*\*Confidential information removed\*\*\* | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of treosulfan with fludarabine within its marketing authorisation as a conditioning treatment for non-malignant diseases prior to allogeneic haematopoietic stem cell transplantation. | | |
| **Main points from consultation** | Following the scoping workshop (by teleconference), NICE is of the opinion that an appraisal of treosulfan with fludarabine for treating as a conditioning treatment for non-malignant diseases prior to allogeneic haematopoietic stem cell transplantation is not appropriate.  Before DP3 the current scope for non-malignant disease was separated from ID1508 for malignant disease. This was because of concerns of a diverse population (children, young people and adults with malignant and non-malignant disease) and potentially different comparators. The current CHMP positive opinion does not include children and young people with non-malignant disease therefore the population in the scope was restricted to adults only. This is because there is currently no trial evidence for children, but the company have an on-going trial to address this, and \*\*\*Confidential information removed\*\*\*  The current population (adults with non-malignant disease) is likely to be very small because people with non-malignant disease mainly have allogenic stem cell transplantation when they are children. In addition, treosulfan is already being used in clinical practice for this indication (off-label). For these reasons, an appraisal at this time is unlikely to add value to the NHS. This view was supported by the clinical experts and the company during the scoping teleconference and in their written comments. | | |
| **Population size** | Approximately 10-15 adults in England would be eligible for treatment with treosulfan with fludarabine.  This is based on clinical expert opinion from the scoping teleconference. | | |
| **Process (TA/HST)** | Not applicable | | |
| **Proposed changes to remit** | None | | |
| **Costing implications** | Unit costs and dosing information for this indication are not available. Based on the unit cost and dosing of treosulfan for the palliative treatment of epithelial ovarian cancer, the drug cost of treatment with treosulfan in combination with fludarabine is around £3,300 per person. Assuming 15 people are treated each year the annual cost of treatment is around £49,200 | | |
| **Timeliness statement** | N/A – referral not sought. | | |

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| **Provisional Title** | Bempedoic acid for treating primary hypercholesterolaemia or mixed dyslipidaemia | | |
| **Topic Selection ID Number** | 9861 | **TA ID Number** | 1515 |
| **Company** | Esperion Therapeutics, but commercialisation by Daiichi Sankyo | | |
| **Anticipated licensing information** | \*\*\*Confidential information removed\*\*\* | | |
| **Draft remit** | To appraise the clinical and cost effectiveness of bempedoic acid within its marketing authorisation for treating primary hypercholesterolaemia or mixed dyslipidaemia | | |
| **Main points from consultation** | Following the consultation exercise, NICE is of the opinion that an appraisal of bempedoic acid for treating primary hypercholesterolaemia or mixed dyslipidaemia is appropriate.  The proposed remit is appropriate. No changes are required. All stakeholders agreed that an appraisal and the draft remit are appropriate.  A minor point about the comparator section of the scope, which separates out relevant populations was raised. The company wanted to replace “optimised statin therapy” with “maximum tolerated statin dose” as a more accurate description.  An additional group was added into the comparator section, as suggested by the company:  “When maximally tolerated statin dose with ezetimibe does not appropriately control LDL-C:   * Evolocumab with a statin and ezetimibe * Alirocumab with a statin and ezetimibe”   The scope now has essentially 3 populations:   1. When maximum statin dose does not control LDL-C 2. When maximum statin dose plus ezetimibe does not control LDL-C 3. When statins contraindicated/not tolerated | | |
| **Population size** | Approximately 13,000 people in England would be eligible for treatment with bempedoic acid based on the costing report for alirocumab and evolocumab. | | |
| **Process (TA/HST)** | TA | | |
| **Proposed changes to remit** | None | | |
| **Costing implications** | The unit cost of bempedoic acid is unknown so the resource impact of this technology cannot currently be estimated. | | |
| **Timeliness statement** | Assuming that the anticipated date of the marketing authorisation is the latest date that we are aware of and the expected referral date of this topic, issuing timely guidance for this technology will be possible. | | |