NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals and Highly Specialised Technologies

Consultation on Batch 62 draft remits, draft scopes and summary of comments and discussions at scoping workshops

Topic list

Topic ID: 1438

Topic title: Emapalumab for treating primary haemophagocytic lymphohistiocytosis in children and young people.

Topic ID: 1109

Topic title: Fenfluramine for treating Dravet syndrome.

Topic ID: 1202

Topic title: Budesonide for treating eosinophilic oesophagitis.

Topic ID: 1440

Topic title: TYRX Absorbable Antibacterial Envelope for preventing infection from pacemakers and implantable defibrillators.

Topic ID: 1111

Topic title: Autologous haematopoietic stem cell transplantation for treating multiple sclerosis.

Topic ID: 1414

Topic title: Esketamine for treatment-resistant depression.

Provisional Title: Emapalumab for treating primary haemophagocytic lymphohistiocytosis in children and young people.

Topic Selection ID Number: 8735.

Wave / Round: R210.

TAID Number: 1438.

Company: NovImmune/Sobi

Anticipated licensing information: ***Confidential information removed***

Draft remit

To evaluate the benefits and costs of emapalumab within its marketing authorisation for treating primary haemophagocytic lymphohistiocytosis for national commissioning by NHS England.

Main points from consultation

Following the consultation exercise and the scoping workshop, NICE is of the opinion that a **technology appraisal** of emapalumab for treating primary haemophagocytic lymphohistiocytosis (HLH) in children and young people is **appropriate**.

The proposed remit is not appropriate and should be amended in line with standard wording for technology appraisals.

Not all of the topic selection criteria for the highly specialised technologies programme are met; specifically:

- The technology will be used as part of a short-term treatment strategy, to control inflammation, prior to definitive therapy with HSCT. It will therefore not be used lifelong.

- Treatment of paediatric primary HLH is managed in 19 specialist paediatric haematology centres; it is unlikely that treatment will be concentrated in very few centres or used exclusively in the context of a highly specialised service.

It is therefore proposed that this topic is considered as an STA.

Population size

Approximately 15–50 people in England would be eligible for treatment with emapalumab per year.

Source: estimated by clinical and patient experts at the scoping workshop. Approx 13–15 patients per year have genetically confirmed primary HLH; up to 40–50

patients per year are thought to have primary HLH that requires treatment with chemotherapy. Estimated incidence of confirmed primary HLH is consistent with published incidence rate of 1.2 per million children per year.

Process (TA/HST): TA.

Proposed changes to remit

To appraise the clinical and cost effectiveness of emapalumab within its marketing authorisation for treating primary haemophagocytic lymphohistiocytosis.

Costing implications

The unit cost of emapalumab 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.

Provisional Title: Fenfluramine for treating Dravet syndrome

Topic Selection ID Number: 8110.

Wave / Round: R169.

TA ID Number: 1109.

Company: Zogenix.

Anticipated licensing information: ***Confidential information removed***

Draft remit

To appraise the clinical and cost effectiveness of fenfluramine within its marketing authorisation for treating Dravet syndrome.

Main points from consultation

Following the consultation exercise, NICE is of the opinion that an appraisal of fenfluramine for treating dravet syndrome is **appropriate**.

The proposed remit is appropriate. No changes are required.

Currently proposed as an STA.

Population size

The prevalent population with Dravet syndrome is estimated to be between 1,350 and 2,700 people in England.

There is no data on the number of people who would be considered to be inadequately controlled by anti-epileptic drugs, that is, the people that are likely to be treated with fenfluramine in clinical practice.

- Dravet syndrome is known to be drug resistant, and the clinical experts at the scoping workshop for cannabidiol (ID1211) considered the proportion eligible for treatment to be relatively high.

Process (TA/HST): TA.

Proposed changes to remit: None.

Costing implications

The unit cost of fenfluramine 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.

Provisional Title: Budesonide for treating eosinophilic oesophagitis

Topic Selection ID Number: 8965

Wave / Round: R226

TA ID Number: 1202

Company: Dr Falk Pharma

Licensing information
Marketing authorisation granted in January 2018

Wording of marketing authorisation: Jorveza is indicated for the treatment of eosinophilic oesophagitis (EoE) in adults (older than 18 years of age).

Draft remit

To appraise the clinical and cost effectiveness of budesonide within its marketing authorisation for treating active eosinophilic oesophagitis

Main points from consultation

Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of budesonide for treating eosinophilic oesophagitis is **appropriate**.

The proposed remit is not appropriate and should be amended as follows:

Remove 'active' from the remit to be consistent with the marketing authorisation.

Clinical experts considered this to be an area of unmet need and would welcome guidance on the use of this drug. Although other formulations of budesonide are used to treat EoE, they are unlicensed for this indication and only used in a few centres.

Population size

Approximately 700 people per year have EoE in England.
(source: costing comments for topic consideration – Mar 2017)

Process (TA/HST): TA.

Proposed changes to remit

To appraise the clinical and cost effectiveness of budesonide within its marketing authorisation for treating ~~active~~ eosinophilic oesophagitis

Costing implications

The unit cost of this formulation of budesonide is unknown so the resource impact of this technology cannot currently be estimated. However if the orodispersible tablet

will be similarly priced to budesonide granules sachets and inhalation powder, the cost of 8 weeks treatment at 1mg twice a day will be around £1,700. Therefore if uptake is around 1% of the 700 people potentially eligible for treatment, the cost of treatment with budesonide will be around £12,000.

Timeliness statement

Considering that this product has a marketing authorisation for use in the UK, publication of timely guidance will not be possible.

Provisional Title: TYRX Absorbable Antibacterial Envelope for preventing infection from pacemakers and implantable defibrillators

Topic Selection ID Number: N/A – from MTEP.

Wave / Round: N/A.

TA ID Number: 1440.

Company: Medtronic

CE mark information
TYRX is indicated for pacemakers and implantable defibrillators, which includes cardiac resynchronisation therapy devices.

TYRX received its CE mark in 2014.

Draft remit

To appraise the clinical and cost effectiveness of TYRX within its CE mark for preventing infection from pacemakers and implantable defibrillators.

Main points from consultation

Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of TYRX for treating pacemakers and defibrillators is **appropriate**.

The proposed remit is not appropriate and should be amended as follows:

- TYRX is intended to be used with pacemakers and defibrillators. This implicitly includes cardiac resynchronisation devices because they either pace or defibrillate. The devices in the remit of the scope have been updated to 'cardiac implantable electronic devices (CIED)' so that all relevant devices are included.

Population:
TYRX is intended to be used in all patients requiring CIED's but it is likely to be of more benefit and therefore used in people who are at high risk of a CIED infection. Stakeholders noted that it is very difficult to agree on a definition of 'high risk' and are awaiting the results of the WRAP-IT study to define this. The scope includes people at high risk of infection as a subgroup.

Comparators:
Pouches that are not impregnated with antibiotics are not relevant comparators given the focus of the scope is the prevention of CIED infections. Collatemp G is a collagen sheet impregnated with gentamicin which is intended to be used to reduce the rate of surgical site infections. It can be used with CIEDs and has therefore been included as a comparator in the scope

Population size

Approximately 44,000 people in England would be eligible for treatment with TYRX Absorbable Antibacterial Envelope.

The above calculation is based on the National Institute of Cardiovascular Outcomes Research (NICOR) 2017 report on the National Audit of Cardiac Rhythm Management Devices: April 2016 – March 2016. The report states between April 2015 and March 2016, 34,000 pacemakers and 13,000 ICDs were implanted (both new and replacements) in England.

Process (TA/HST): TA.

Proposed changes to remit

To appraise the clinical and cost effectiveness of TYRX within its CE mark for preventing infection from cardiac implantable electronic devices ~~pacemakers and implantable defibrillators.~~

Costing implications

The cost of the TYRX absorbable antibacterial envelope is £719 per unit (exclusive of VAT), this is an additional cost as the TYRX is used in addition to standard care. Approximately 1-2% of the 44,000 people who have a CIED implanted would develop an infection. However the consultees noted that only people at high risk of infection would receive TYRX but the size of this group is uncertain. If there are approximately 44,000 people who are potentially eligible for treatment, uptake would need to be greater than 45% for this device to cost more than £15 million
The cost of TYRX could be offset against savings as a result of reduced device related infections and reduced hospital admissions however, these savings cannot currently be quantified.

Timeliness statement

Considering that this product has a CE Mark for use in the UK, publication of timely guidance will not be possible.

Provisional Title: Autologous haematopoietic stem cell transplantation for treating multiple sclerosis

Topic Selection ID Number: 8436.

Wave / Round: R195.

TA ID Number: 1111.

Company: No commercial sponsor.

Anticipated licensing information
No marketing authorisation or CE mark being sought.
AHSCT is a therapeutic medical procedure and is not a 'commercial product' which requires a marketing authorisation.

Draft remit

To appraise the clinical and cost effectiveness of autologous haematopoietic stem cell transplantation (AHSCT) for treating multiple sclerosis.

Main points from consultation

Following the scoping workshop and second consultation exercise, NICE is of the opinion that an appraisal of autologous haematopoietic stem cell transplantation for treating relapsing–remitting multiple sclerosis is **not appropriate**.

AHSCT is already commissioned by NHS England in specific circumstances as a treatment for some immune mediated diseases including severe, resistant multiple sclerosis.

Stakeholders considered that an appraisal was appropriate because routine commissioning may make it easier for patients to access the procedure, which is currently only performed in Sheffield and London.

However, during the consultation it was noted that several of the conditioning chemotherapies used as part of the procedure are used outside of their marketing authorisations. The main trial (NCT00273364, due to report in 2021) uses cyclophosphamide and anti-thymocyte globulin to prepare the immune system. Neither are licensed for stem cell transplantation, or for use in people with multiple sclerosis. None of the other chemotherapies that could be used have marketing authorisations that include stem cell transplantation.

Because none of the chemotherapy drugs used in the procedure have marketing authorisations covering such use, a technology appraisal cannot be formally referred within regulation 7. Instead a referral would need to be sought via regulation 5 and not carry any formal funding requirements. A technology appraisal without the support of a funding requirement is unlikely to add value in this area where a clinical commissioning policy already exists.

There is currently a review proposal to update CG186 multiple sclerosis in adults: management. This guideline does not currently cover disease-modifying treatments, and it is not proposed to do so in the update. However, as the update is yet to be scoped, stakeholders may raise this issue during the consultation.

Population size

Approximately 18,800 people in England would be eligible for treatment with AHSCT.

This estimate is based on the number of people with active relapsing-remitting MS previously treated with disease-modifying therapy estimated in the 'Resource impact report' of TA 493; Cladrabine tablets for treating relapsing-remitting multiple sclerosis. This matches the trial population but does not include people with other forms of multiple sclerosis who might be eligible for treatment with AHSCT.

Process (TA/HST): N/A – referral not sought.

Proposed changes to remit: N/A – referral not sought.

Costing implications

Autologous haematopoietic stem cell transplantation (AHSCT) for treating multiple sclerosis is administered as a one off treatment and it is estimated to cost £30,000 per person. If uptake is around 1% of the 18,800 people potentially eligible for treatment, the cost will be around £6 million. The cost for AHSCT is a single one-off cost as opposed to the recurrent ongoing costs of disease modifying treatments for MS.

Timeliness statement: N/A – referral not sought.

Provisional Title: Esketamine for treatment-resistant depression

Topic Selection ID Number: 9514

Wave / Round: R255

TA ID Number: 1414

Company: Janssen

Anticipated licensing information: ***Confidential information removed***

Draft remit

To appraise the clinical and cost effectiveness of esketamine within its marketing authorisation for the treatment of major depressive disorder.

Main points from consultation

Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of esketamine for treating treatment-resistant depression is **appropriate**.

The proposed remit is not appropriate and should be amended as follows: “To appraise the clinical and cost effectiveness of esketamine within its marketing authorisation for the management of treatment-resistant depression.”

The draft remit for consultation focused on the treatment of major depressive disorder. At consultation, stakeholders highlighted that people with treatment-resistant depression (in whom esketamine was studied/is expected to be indicated) were a subgroup of the population with major depressive disorder. The remit has been amended accordingly.

Population size

Approximately 146,300 people in England would be eligible for treatment with esketamine.

Around 1.4 million adults in England may be affected by depression, around 768,200 (54%) will have moderate to severe depression and around 614,600 (80%) of these people will be prescribed a pharmacological treatment. It is believed that around 245,800 (40%) of people will not respond to the first line treatment and around 146,300 people (60%) will not respond to the second line of treatment and may be suitable for esketamine.

Process (TA/HST): TA.

Proposed changes to remit

To appraise the clinical and cost effectiveness of esketamine within its marketing authorisation for the ~~treatment of major depressive disorder~~ management of treatment-resistant depression.

Costing implications

The unit cost of esketamine 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.