NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 34 draft remits and draft scopes and summary of comments and discussions at scoping workshops

Item	process	Topic
5.1	TA	Omalizumab for previously treated chronic spontaneous urticaria
5.2	TA	Ospemifene for treating postmenopausal vulvo-vaginal atrophy
5.3	TA	Apremilast for treating moderate to severe plaque psoriasis
5.4	TA	Apremilast for treating active psoriatic arthritis
5.5	TA	Brentuximab vedotin for treating CD30-positive Hodgkin's lymphoma after autologous stem cell transplant
5.6	TA	Cangrelor for preventing atherothrombotic events in people undergoing percutaneous coronary intervention or surgery
5.7	TA	TK cell therapy following haploidentical haematopoietic stem cell transplant for adults with acute leukaemia
5.8	TA	Thymosin beta-4 and ciclosporin for treating dry eye syndrome

Provisional Title	**Omalizumab for previously treated chronic spontaneous urticaria**		
Topic Selection ID Number	6383	**Wave / Round**	R44
TA ID Number	707		
Manufacturer	Novartis		
Anticipated licensing information	***confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of omalizumab within its licensed indication for previously treated chronic spontaneous urticaria.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of omalizumab for previously treated chronic spontaneous urticaria is appropriate. The proposed remit is appropriate. No changes are required. Comments received during consultation indicated that the specified population did not accurately reflect those who would be eligible for treatment with omalizumab. The clinical specialists at the scoping workshop advised that in clinical practice, if the condition does not respond adequately to a non-sedating H1 antihistamine, the dose would normally be escalated up to 4-times the licensed dose before trying another type of treatment (such as leukotriene receptor antagonists or immunosuppressants); therefore they considered that dose escalation should be included in the description of the population. It was noted that NICE cannot make recommendations on the use of a technology outside of its marketing authorisation; therefore proposing the use of omalizumab after unlicensed dose escalation of antihistamines was not appropriate. It was acknowledged that the current wording for the population in the scope does not specify the dose of antihistamines that a patient has not adequately responded to; therefore there is an opportunity for the manufacturer to present data on the effect of omalizumab after different treatment regimens, if available. Consultation comments suggested that the list of comparators was incomplete. It was noted that sulfasalazine was an anti-inflammatory drug (rather than an immunosuppressant) and should be removed from the list of comparators. They noted that mycophenolate mofetil is used in routine clinical practice in England to treat this condition and therefore was an appropriate comparator. The role of no further pharmacological treatment was also discussed and the clinical specialists confirmed that some people do not wish to take immunosuppressants because of their low risk–benefit ratio and their long-term adverse effects are likely to be of particular concern to younger people (especially children). They noted that some patients would not receive further pharmacological interventions but may continue receiving background therapies, such as dietary changes and PUVA (which is psoralen [a sensitising drug] in combination		

	with ultraviolet light). It was therefore agreed that 'no further pharmacological treatment' should be an alternative comparator. The scoping workshop attendees agreed that the outcomes in the draft scope were appropriate but that the list of symptoms was incomplete, and that it should be amended to include angioedema and lack of sleep. It was also agreed that steroid sparing should be included as an outcome. It was agreed that an STA would be the most appropriate process to consider this topic.
Population size	Chronic urticaria has a UK point prevalence of 1–5 per 1000, with a lifetime prevalence of 0.5–1%. Over 50% of people with chronic urticaria do not respond completely to antihistamines at licensed doses.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	No changes required, original comments apply: It is assumed that the prevalence of CSU is 1-5 per 1,000 people. Taking a mid-point of this range results in an estimate of around 65,000 people in England with CSU and refractory to antihistamines at any one time. Symptoms may last a few months or up to ten years, however it is not known how long symptoms may persist if omalizumab treatment is received. Based on the trials, it is assumed that active treatment is for 6 periods of 4 weeks. Assuming the treatment duration above and a midpoint dose of 150mg, there is a cost impact of around £99m. However this may be an over estimate as there could be offsetting savings from the reduced use of non-licensed treatments currently used as a second line option for CSU. The number of patients who would switch to omalizumab, the treatment duration, the dose and the treatment they move away from are not known. However, it is still anticipated that this topic has potential to be high cost.
Timeliness statement	Given the expected referral date of this topic and the knowledge that this technology received a positive CHMP opinion in January 2014, issuing timely guidance for this technology will not be possible.

Provisional Title	**Ospemifene for treating postmenopausal vulvo-vaginal atrophy**		
Topic Selection ID Number	6639	**Wave / Round**	R62
TA ID Number	685		
Manufacturer	Shionogi		
Anticipated licensing information	***confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of ospemifene within its licenced indication for treating vulvo-vaginal atrophy in women who are post-menopausal.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that ospemifene for treating postmenopausal vulvo-vaginal atrophy should be included in the ongoing clinical guideline on menopause (diagnosis and management). The clinical guideline is expected to be published in July 2015. Consultees noted that the clinical guideline scope includes treatments for symptomatic relief and that this includes the use of selective oestrogen-receptor modulators for the treatment of urogenital symptoms. Consequently, considering ospemifene through the STA process will effectively duplicate effort in this area. The manufacturer also expressed an interest in pursuing this topic through the clinical guideline instead of the STA process. The clinical guidelines team indicated before consultation on the scope that even though the scope for the clinical guideline has already been finalised, they will add ospemifene.		
Population size	Approximately 4.3 million women in England and Wales (calculated as 45% of women over the age of 50 years who are postmenopausal)		
Process (MTA/STA/HST)	N/A – referral not sought. Topic should be included in the ongoing clinical guideline on menopause (due for publication in 2015).		
Proposed changes to remit (in bold)	N/A – referral is not sought.		
Costing implications of remit change	No changes required – original comments apply: There are estimated to be around 4.3 million postmenopausal women in England with vulvo-vaginal atrophy (aged 50 years and over). However, due to use the of non-prescription preparations, feeling the symptoms are not important, or being too embarrassed to discuss the problem with their doctor, the number may be under-reported. The manufacturer anticipates that no more than 5% of diagnosed women will be treated with ospemifene, if licensed. Although the eligible population is around 4.3 million, using the manufacturer's estimate, the eligible population is anticipated to be around 210,000 women.		

	The cost of ospemifene is not known, however in order for the topic to be 'high cost', using a population of 210,000, the annual cost of ospemifene would need to be around £70 per person per year more than comparator treatments. Ospemifene is administered for 12 weeks and the comparators are estimated to cost between around £10 and £40 for a 12 week period. Where these are not used there would be offsetting savings. Due to a large eligible population of 210,000, and perhaps much higher due to under-reporting, it is considered that this topic has potential to be high cost.
Timeliness statement	N/A – referral not sought

Provisional Title	**Apremilast for treating moderate to severe plaque psoriasis**		
Topic Selection ID Number	6551	**Wave / Round**	R60
TA ID Number	679		
Manufacturer	Celgene		
Anticipated licensing information	***confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of apremilast within its licensed indication for treating moderate to severe plaque psoriasis.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of apremilast is appropriate. The proposed remit is appropriate. No changes are required. Minor changes to the scope were proposed during consultation including: • Specifying that the population relates only to adults, in line with the clinical trials and anticipated marketing authorisation • Consideration of a subgroup who have had prior biologic therapy, if the evidence allows • Amending the outcomes to include "other complications of psoriasis, for example nail, scalp and joint outcomes" in line with suggestions during consultation. Consultees also agreed that biosimilars should be removed as comparators (as they are not currently available for this indication and are unlikely to represent established clinical practice at the time of appraisal). Consultees also commented that many patients with moderate to severe psoriasis do not receive systemic treatment due to contraindication or intolerability. There are also some patients with psoriasis whose disease does not respond to non-biologic systemic therapies but in whom biologic therapy is unsuitable. Best supportive care was considered a relevant comparator for these patients and has been included in the scope. Therefore the comparators in the scope are: • Systemic non-biological therapies (including acitretin, ciclosporin, methotrexate, phototherapy with or without psoralen) For people with severe psoriasis who have a contraindication to or are intolerant of systemic non-biological therapy, or for whom systemic therapy has been inadequately effective: • Systemic biological therapies (including etanercept, infliximab, adalimumab, and ustekinumab) For people in whom systemic biological therapy is contraindicated, ineffective, or not well tolerated:		

	• Best supportive care Attendees considered that an MTA with secukinumab (from batch 33 for moderate to severe psoriasis after systemic therapy) would be preferable, but noted that this would affect the timeliness of recommendations for both technologies. An STA was therefore considered to be the most appropriate process to consider apremilast.
Population size	There are approximately 140,000 with moderate to severe plaque psoriasis in England.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	None required – original comments apply: It is estimated that the prevalence of psoriasis is around 1.63% and that around 20% (170,000) people have moderate to severe symptoms. Of these, around 85% (144,000) have plaque psoriasis. The number with an inadequate response, a contraindication, or who are intolerant to other systemic therapies is not definite. Assuming that the drug will be considered alongside biologics as a third-line treatment for psoriasis, the total eligible population would be around 7,100 (based on TA180 for ustekinumab), but as there are a wide range of treatments available, the number who receive apremilast is likely to be considerably lower. The alternative treatments are approximately £10,000 per annum, and people who don't respond at this stage progress to a programme of 'Best Supportive Care' which CG153 suggests commonly costs around £11,000 per annum. Where people choose apremilast rather than biologics there will be offsetting savings. The number who switch and the cost of the drug is unknown. It is considered that this topic has potential to be low 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 will be possible.

Provisional Title	**Apremilast for treating active psoriatic arthritis**		
Topic Selection ID Number	6552	**Wave / Round**	R60
TA ID Number	682		
Manufacturer	Celgene		
Anticipated licensing information	***confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of apremilast within its licensed indication for treating active psoriatic arthritis in people for whom disease-modifying anti-rheumatic drugs have been inadequately effective, not tolerated or contraindicated.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of apremilast for treating active psoriatic arthritis is appropriate. The proposed remit is appropriate. No changes are required. Minor changes to the scope were proposed during consultation including: • Specifying that the population relates only to adults, in line with the clinical trials and anticipated marketing authorisation • Amending the outcomes to include “other complications of psoriatic arthritis, for example nail, scalp and skin outcomes” in line with suggestions during consultation. Consultees agreed that biosimilars should be removed as comparators (as they are not currently available for this indication and are unlikely to represent established clinical practice at the time of appraisal). Consultees also commented that many patients with psoriatic arthritis are unable to receive treatment with DMARDs or biologics due to contraindications or intolerability. Best supportive care was considered a relevant comparator for these patients and has been included in the scope. The manufacturer advised that the participants in the pivotal trial had an inadequate response to 1 DMARD. Apremilast has been studied alone or in combination with one or more DMARDs. Patients could have a background DMARD treatment at baseline and continue that treatment throughout the study period. NICE Technology Appraisal guidance for psoriatic arthritis currently recommends systemic biological therapy in people who have an inadequate response to at least 2 DMARDs, therefore consultees considered that most people whose disease has inadequately responded to only 1 DMARD would receive a 2nd DMARD; therefore DMARDs should be included as a comparator for these patients. Therefore the comparators in the scope have been updated as follows: For people who have only received 1 prior disease modifying		

	anti-rheumatic drug (DMARD) • Disease modifying anti-rheumatic drugs For people whose disease has inadequately responded to at least 2 DMARDs or who are intolerant of or contraindicated to DMARDs: • Biologic therapies (including etanercept, adalimumab, infliximab and golimumab) For people in whom DMARDs and biologic therapies are not tolerated or contraindicated: • Best supportive care
Population size	The prevalence of psoriatic arthritis in England and Wales in 2011 was estimated to be around 56,100 to 168,200 people.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	Slightly updated due to clarification of comparators: The unit cost for apremilast for this indication is unknown. Based on TA220 (Psoriatic arthritis - golimumab), it is estimated that there are around 60,000 adults with psoriatic arthritis in England and that around 2.4% (1500) receive biologics. It is estimated that around 30% (450) have an inadequate response, contraindication, or intolerance to biologics. Eligibility for apremilast also includes those people who have an inadequate response, contraindication, or intolerance to DMARDs. This number is unknown. The exact number of the total population who would be eligible for treatment is unknown, but is anticipated to be higher than 450. The comparator/alternative treatment costs vary considerably and the cost of the new technology is unknown, so the potential cost impact cannot 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.

Other considerations	If evidence allows the following a subgroup analyses will be considered: • previous treatment (including previous treatment with DMARDs and TNF-α inhibitors) • reason for treatment failure with TNF-α inhibitors (for example lack of efficacy or adverse events) Guidance will only be issued in accordance with the marketing authorisation.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: Technology Appraisal No. 220, Apr 2011, 'Golimumab for the treatment of psoriatic arthritis'. A review proposal is currently being considered for this topic. Technology Appraisal No. 199, Aug 2010, 'Etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis (superseded technology appraisals No. 104 & 125)'. A review proposal is currently being considered for this topic. Technology Appraisal in Preparation, 'Ustekinumab for treating active and progressive psoriatic arthritis'. Earliest anticipated date of publication May 2014. Proposed Technology Appraisal, 'Secukinumab for treating active, progressive psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs'. Publication TBC. Related Guidelines: Clinical Guideline No.153, Oct 2012, 'Psoriasis: the management of psoriasis'. Related Quality Standards: Quality Standard No.40, Aug 2013, 'Psoriasis'. http://www.nice.org.uk/guidance/qualitystandards/qualitystandards.jsp
Related National Policy	None

Provisional Title	**Brentuximab vedotin for treating CD30-positive Hodgkin's lymphoma after autologous stem cell transplant**		
Topic Selection ID Number	6931 and 5031	**Wave / Round**	R80
TA ID Number	722		
Manufacturer	Takeda UK		
Anticipated licensing information	***confidential information removed*** This technology is already licenced for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma following autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option.		
Draft remit	To appraise the clinical and cost effectiveness of brentuximab vedotin within its licensed indication for treating people with CD30-positive Hodgkin's lymphoma after autologous stem cell transplant.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of brentuximab vedotin for treating CD30-positive Hodgkin's lymphoma is appropriate. The proposed remit is appropriate. No changes are required. This appraisal will consider the use of brentuximab vedotin in the population with relapsed or refractory disease covered by the existing licence as well as those expected to be covered under the pending licence extension. The population considered will be "*People with CD30-positive Hodgkin's lymphoma following autologous stem cell transplant:* • *with relapsed or refractory disease, or* • *who are at high risk of residual disease."* Consultees considered that the population in the scope who are considered to be at high risk of residual disease should be defined in line with eligibility criteria from the clinical trials and the definitions used in clinical practice and should include people with: • primary refractory disease; or • disease relapse within 1 year of completing first-line treatment; or • a positive PET scan prior to autologous stem cell transplant; or • extra-nodal involvement at the time of relapse prior to autologous stem cell transplant. Attendees at the scoping workshop stated that the ChlVPP regimen (chlorambucil, vinblastine, procarbazine and prednisolone) is used in the NHS for treating relapsed or refractory disease and should be included as a comparator. Attendees advised that response measures are predictive of progression-free survival and can guide subsequent therapy choices (for example, whether a patient can have an allogeneic stem cell transplant). It was agreed that both objective response rate and complete response rate should be included as outcome measures, although it was acknowledged that the number of patients who show a complete response may be low.		

	The manufacturer expressed concerns about the small population size and the associated difficulty in conducting an appraisal. It questioned the value of conducting an appraisal for such a small patient group but agreed that an STA was the most appropriate process to consider this topic if it is referred for appraisal.
Population size	In 2011 there were 164 autologous stem cell transplants for Hodgkin's lymphoma in the UK and the Republic of Ireland. It is unclear how many of these patients would be considered to be at high risk of residual disease and therefore eligible for brentuximab vedotin.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	None
Costing implications of remit change	Updated comments from 6931 slightly due to clarification of population size (previously calculated as 175): Brentuximab vedotin is administered by intravenous infusion at 1.8mg/kg every 21 days. Using information from the briefing note it is assumed that 16 cycles will be used plus follow up appointments every 6 months for 2 years with a total cost per patient of around £120,000. Using the approximate eligible population of around 165, the cost impact is around £20 million. Although there may be some offsetting savings from other treatment options not chosen, this topic has the potential to be high 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 the license extension component included within this technology appraisal will be possible. However, as brentuximab vedotin is already licenced for the treatment of adult patients with relapsed or refractory CD30+ Hodgkin lymphoma following autologous stem cell transplant (ASCT) or following at least two prior therapies when ASCT or multi-agent chemotherapy is not a treatment option, issuing timely guidance for this component of the Technology Appraisal will <u>not</u> be possible.

Provisional Title	**Cangrelor for preventing atherothrombotic events in people undergoing percutaneous coronary intervention or surgery**		
Topic Selection ID Number	6664 and 4379	**Wave / Round**	R63 & R67
TA ID Number	698		
Manufacturer	The Medicine Company		
Anticipated licensing information	***confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of cangrelor within its licensed indication for preventing atherothrombotic events in people with coronary heart disease undergoing percutaneous coronary intervention or surgery.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of cangrelor for preventing atherothrombotic events in people undergoing percutaneous coronary intervention or surgery is appropriate. Consultees were concerned that the wording of the draft remit did not reflect the second indication accurately and could be wrongly interpreted as a pre-anaesthetic medication. They felt that the second indication, in the 'bridging setting' needed to be clearly stated in the remit. The experts explained that people on oral P2Y12 inhibitors (clopidogrel, ticagrelor, prasugrel) who are awaiting surgery are generally required to discontinue their use due to the bleeding risks involved. However, interruption of oral antiplatelet therapy is associated with an increased risk of thrombotic events and cangrelor is being positioned as a bridging therapy in this situation until oral P2Y12 inhibitors can be subsequently continued after surgery. Attendees also felt that the phrase 'preventing atherothrombotic events' should be changed to 'the reduction in atherthrombotic events' as it was not reasonable to expect that cangrelor would prevent all atherothrombotic events. In light on the suggestions received during consultation, the proposed remit should be amended to: "To appraise the clinical and cost effectiveness of cangrelor within its licensed indication for the reduction of atherothrombotic events in people with coronary heart disease undergoing percutaneous coronary intervention or in people awaiting surgery requiring interruption of antiplatelet therapy". Attendees considered that the population in the scope should also be amended in line with the proposed changes to the remit, as follows: • People with coronary heart disease undergoing percutaneous coronary intervention • People awaiting surgery requiring interruption of oral P2Y12 inhibitor therapy The clinical specialists clarified that a loading dose of an oral P2Y12 inhibitor is considered part of standard care of patients undergoing PCI. Attendees heard from the manufacturer that cangrelor will not replace the loading dose of oral P2Y12		

	inhibitors. Therefore attendees agreed that the intervention in the scope should be amended to 'cangrelor plus standard care'. Consultees commented that the proposed comparators listed in the scope for people with coronary heart disease undergoing percutaneous coronary intervention (that is, prasugrel, clopidogrel and ticagrelor) are not appropriate as they are all P2Y12 inhibitors and will be given in addition to cangrelor rather than be replaced by it. They considered that a more appropriate comparator for this population is: "established clinical management without cangrelor (including a loading dose of an oral P2Y12 inhibitor [clopidogrel/prasugrel/ticagrelor])". For people on anti-platelet therapy undergoing surgery: The clinical specialists commented that bridging treatment with glycoprotein IIb/IIIa inhibitors and/or heparin is rarely used in clinical practice and should be removed from the list of the comparators. Attendees also heard that aspirin is usually continued in patients with coronary stents undergoing surgery and only oral P2Y12 inhibitor use is interrupted. Attendees suggested amending 'discontinuation of all anti-platelet therapy' to 'discontinuation of oral P2Y12 anti-platelet therapy'. The comparators in the scope have therefore been amended as follows: For people with coronary heart disease undergoing percutaneous coronary intervention • Established clinical management without cangrelor (including a loading dose of an oral P2Y12 inhibitor [clopidogrel/prasugrel/ticagrelor]) For people on oral P2Y12 inhibitor therapy requiring interruption awaiting surgery • No oral P2Y12 anti-platelet therapy Attendees emphasised that an appraisal of cangrelor as a bridging therapy addressed substantial unmet need and was more likely to be a step change in this setting and therefore this indication should be given priority over the other indication.
Population size	The manufacturer estimated up to 61,000 patients may be eligible for treatment, which includes 50,000 patients undergoing PCI and 11,000 patients on oral P2Y12 therapy undergoing surgery.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of cangrelor within its licensed indication for **the reduction** of atherothrombotic events in people with coronary heart disease undergoing percutaneous coronary intervention and i**n people awaiting** surgery **requiring interruption of antiplatelet therapy**.
Costing implications of remit change	Both sets of costing comments updated to reflect clarification of the two populations and the appropriate comparators: **6664:** Cangrelor is intended for use as a bridging agent for people who require interruption of antiplatelet therapy prior to

	cardiac surgery. The number of people admitted to hospital in 2011/12 for stable angina or acute coronary syndrome (ACS) was around 137,000 and it is estimated that around 12.5% (17,000) are referred for surgery. Administration of cangrelor is by IV infusion for up to 7 hours until an hour before surgery. The number of people eligible to receive cangrelor and the cost of the drug is unknown. The cost impact cannot currently be estimated from the information available. **4379:** It is estimated that around 55,000 people are admitted to hospital for acute coronary syndromes requiring percutaneous coronary interventions (PCI) each year. The cost of the cangrelor is unknown. The drug is intended to be used in addition to standard current care. There may be some additional costs relating to drug administration since cangrelor is administered by intravenous infusion. As there is a large eligible population, although the number who would choose this particular option is unknown, it is considered that this topic has potential to be high 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 will be possible.

Provisional Title	**TK cell therapy following haploidentical haematopoietic stem cell transplant for adults with acute leukaemia**		
Topic Selection ID Number	6679	**Wave / Round**	R68
TA ID Number	701		
Manufacturer	MolMed S.p.A.		
Anticipated licensing information	***confidential information removed*** The manufacturer has not engaged with NICE during the consultation process		
Draft remit	To appraise the clinical and cost effectiveness of TK cell therapy within its licensed indication in haematopoietic stem cell transplantation from a haploidentical family donor for adults with acute leukaemia.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of TK cell therapy following haploidentical haematopoietic stem cell transplant (HSCT) for adults with acute leukaemia is not appropriate. Attendees agreed that there is potentially little value to the NHS in for NICE to produce guidance on this topic as the number of patients likely to be eligible to receive TK cell therapy treated donor lymphocyte infusions is expected to only be approximately 10 people over a 3 year period. In addition, the clinical specialists highlighted that the clinical trials do not follow the UK protocol for haploidentical HSCT and therefore if the marketing authorisation is in line with these trials (in particular if the marketing authorisation specifies the time between the initial transplant and post-transplant donor lymphocyte infusion), it would be unlikely that TK cell therapy would be used in the UK, as the marketing authorisation would not permit its use for people who are being treated using the UK approach to HSCT. If an appraisal is considered appropriate, the proposed remit is considered appropriate. The comparator in the scope should be amended in line with clinical practice to “The attendees agreed the comparator in the scope should be amended to ‘T-lymphocyte replete haploidentical HSCT using standard management of GvHD (for example cyclophosphamide, ciclosporin with methotrexate and corticosteroids)’.		
Population size	10 people over 3 year period would be eligible for this treatment.		
Process (MTA/STA/HST)	N/A – referral not sought		
Proposed changes to remit (in bold)	N/A – referral not sought		
Costing implications of remit change	Updated due to clarification of population size provided above: The cost of TK cell therapy is not yet known. As it is an adjuvant therapy, all the drug costs will be incremental.		

	However, it may result in post-transplant immunosuppressant treatment not being needed which will give offsetting savings. From the information available the cost impact cannot be estimated. However, since it is estimated that only around 10 people over a 3 year period would be eligible for this treatment, to be classed as high cost incremental costs per person would have to be around £4.5 million.
Timeliness statement	N/A – referral not sought

Provisional Title	**Thymosin beta-4 and ciclosporin for treating dry eye syndrome**		
Topic Selection ID Number	6152 and 6153	**Wave / Round**	R29
TA ID Number	665		
Manufacturer	RegeneRx Biopharmaceuticals (thymosin beta-4) Santen (ciclosporin)		
Anticipated licensing information	<u>thymosin beta-4</u> Unknown. The manufacturer has not engaged with NICE during the consultation process <u>Ciclosporin</u> ***confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of thymosin beta-4 and ciclosporin within their licensed indications for treating dry eye syndrome.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of thymosin beta-4 and ciclosporin for dry eye syndrome is not appropriate. The manufacturer of thymosin beta-4 has not engaged with NICE, and the regulatory timings for both technologies are likely to be very different (phase III trials for thymosin beta-4 have not begun yet); therefore it is recommended that an STA to consider ciclosporin only is undertaken at this time. The proposed remit is not appropriate and should be changed to: “To appraise the clinical and cost effectiveness of ciclosporin within its licensed indication for treating dry eye disease”. Consultees considered that the condition should be referred to as ‘dry eye disease’ rather than ‘dry eye syndrome’ in line with current clinical terminology. The title of the appraisal will also be updated to reflect this change. The population in the scope should be amended in line with the clinical trial population and anticipated marketing authorisation for ciclosporin to ‘people with severe dry eye disease (DEWS 3 or 4) whose disease has not adequately responded to tear substitutes’. Clinical specialists at the scoping workshop confirmed that off-label veterinary ocular preparations of ciclosporin (0.2%) have routinely been used for the last 10-12 years to treat severe dry eye disease; and that if a licenced ciclosporin product became available, it would replace the use of the existing ciclosporin preparations. The clinical specialists also confirmed that punctual plugging is used to treat patients with aqueous-deficient dry eye disease, but it was agreed that this procedure would be undertaken in addition to ciclosporin use, and therefore it should not be included as a comparator for these patients. Consutlees acknowledged that there is a preparation of ciclosporin licenced for human use (0.05%) available in the US		

	but that it is not yet available in the UK. ***confidential information removed***
Population size	Approximately 500,000 people in England have dry eye disease. It is estimated that up to 20% of patients have severe (DEWS 3-4) disease and about 5% of these patients will need treatment with ciclosporin.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of **~~thymosin beta-4 and~~** ciclosporin within **~~their~~ its** licensed indication**~~s~~** for treating dry eye **~~syndrome~~ disease.**
Costing implications of remit change	Updated for ciclosporin (6152) only to take into account clarification of population. 6153 excluded due to exclusion from remit **6152:** It is estimated that the number of people eligible for the new technology may be around 5000. If licensed, ciclosporin would offer an additional treatment option compared with existing (unlicensed) ciclosporin A preparations. As the cost of ciclosporin for this indication is currently unknown, it is not possible to estimate the cost impact for this topic. Assuming an eligible population of 5000, incremental annual costs would need to be around 3000 per person for this technology to be classed as high 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 will be possible.