NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 55 draft remits and draft scopes and summary of comments and discussions at scoping workshops

Topic ID	Topic title
1197	Liraglutide for preventing cardiovascular events in people with type 2 diabetes
1158	Ertugliflozin for treating type 2 diabetes
1189	Naldemedine for treating opioid-induced constipation
1194	Ixekizumab for treating active psoriatic arthritis following inadequate response to disease-modifying anti-rheumatic drugs
1198	Eltrombopag for untreated severe aplastic anaemia
1186	Mepolizumab for treating eosinophilic granulomatosis with polyangiitis
1185	Caplacizumab for treating acute acquired thrombotic thrombocytopenic purpura
1188	Erenumab for preventing migraine
1060	Tildrakizumab for treating moderate to severe plaque psoriasis

Provisional Title	Liraglutide for preventing cardiovascular events in people with type 2 diabetes		
Topic Selection ID Number	8967	**Wave / Round**	R227
TA ID Number	1197		
Company	Novo Nordisk		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of liraglutide within its marketing authorisation for preventing cardiovascular events in people with type 2 diabetes.		
Main points from consultation	Following the consultation exercise, NICE is of the opinion that an appraisal of liraglutide monotherapy for preventing cardiovascular events is appropriate. A new referral is not sought because the remit for TA203 also covers this indication. Some stakeholders highlighted that the appraisal is urgent as it would give more people at high risk of CVD another therapy to reduce their risk of CVD events. The company stated that liraglutide is currently the only licenced GLP-1 receptor agonist to demonstrate cardio-protective outcomes. Empagliflozin (a SGLT-2 inhibitor) has recently been referred for appraisal for the same indication (batch 52). Notwithstanding the importance of the additional evidence on cardiovascular endpoints, and the reflection of this in the updated SmPC, NICE is of the opinion that existing guidance published by it for liraglutide in dual and triple therapy is unlikely to change. The additional evidence has not led to a change in the licensed indication, and together with the fact that cardiovascular endpoints are already part of the case for cost effectiveness of liraglutide, NICE guidance already published covers this. The exception to this consideration is the use of liraglutide monotherapy as existing NICE guidance doesn't cover this.		
Population size	Up to 1.2 million people in England could be eligible for treatment with liraglutide monotherapy. Horizon scanning document suggests that around 56% of patients receiving pharmacological treatment for type 2 diabetes are receiving first-line treatment, which equates to approximately 1.2 million people in England. Only a proportion of these people would be unable to take metformin. With the availability of data on cardiovascular disease, it is also possible that the uptake of liraglutide in combination with other anti-diabetes drugs (as part of existing NICE) may increase but it is uncertain to what extent.		
Process (TA/HST)	TA		

Proposed changes to remit (in bold)	Not applicable – referral not sought
Costing implications	A 28 day cycle of liraglitude costs £110, therefore a year's course of treatment would be £1,434. Liraglutide is administered by subcutaneous injection. There may be offsetting savings from people transferring from current treatments for the prevention of cardiovascular events.
Timeliness statement	Not applicable

Provisional Title	Ertugliflozin monotherapy and combination therapy for treating type 2 diabetes		
Topic Selection ID Number	8771 and 8772	**Wave / Round**	R211
TA ID Number	1158		
Company	Merck Sharp & Dohme		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remits	• To appraise the clinical and cost effectiveness of ertugliflozin monotherapy within its marketing authorisation for treating type 2 diabetes • To appraise the clinical and cost effectiveness of combination therapy with ertugliflozin within its marketing authorisation for treating type 2 diabetes		
Main points from consultation	Following the consultation exercise, NICE is of the opinion that an appraisal of ertugliflozin for treating type 2 diabetes is appropriate. The proposed remits are not appropriate and should be amended into a single remit: 'To appraise the clinical and cost effectiveness of ertugliflozin within its marketing authorisation for treating type 2 diabetes'. The company confirmed that ertugliflozin is a potential candidate for a cost comparison approach for monotherapy and dual therapy because this is the fourth treatment in the same drug class (SGLT-2 inhibitors) to be appraised by NICE. The company considers that ertugliflozin fulfils the criteria for a cost comparison for these indications because it is likely to provide similar or greater health benefits at similar or lower cost than the other SGLT-2s already recommended in TA 390 (monotherapy) and TA288, TA315 and TA336 (dual therapy). The approach to the process for appraising ertugliflozin for triple therapy will be agreed with the company in due course.		
Population size	Up to 1.2 million people in England could be eligible for treatment with ertugliflozin monotherapy and up to 517,000 for ertugliflozin combination therapy. The horizon scanning document suggests that around 56% of patients receiving pharmacological treatment for type 2 diabetes are receiving first-line treatment, which equates to approximately 1.2 million people in England. Only a proportion of these people would be unable to take metformin. It is also estimated that 25% of patients receiving pharmacological treatment for type 2 diabetes are receiving second-line treatment, which equates to approximately 517,000 people in England.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of ertugliflozin ~~**monotherapy/ combination therapy with ertugliflozin**~~ within its marketing authorisation for treating type 2 diabetes		

Costing implications	If licensed, ertugliflozin will offer an additional treatment option for patients with type 2 diabetes. The price of ertugliflozin is currently unknown. The likely resource impact of this drug would be limited because there are already SGLT2 inhibitors recommended by NICE.
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	Naldemedine for treating opioid-induced constipation		
Topic Selection ID Number	8370	**Wave / Round**	R190
TA ID Number	1189		
Company	Shionogi		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of naldemedine within its marketing authorisation for treating opioid-induced constipation.		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of naldemedine for treating opioid-induced constipation is <u>appropriate</u> The proposed remit is appropriate. No changes are required. A comparator company stated that their product (methylnaltrexone) will likely receive marketing authorisation for an oral formulation next year. Therefore they suggested having a multiple technology appraisal of naldemedine (also oral), methylnaltrexone and naloxegol for this indication. • Methylnaltrexone subcutaneous injection (TA468) was in the NICE schedule but was terminated in August 2017 because the company did not provide an evidence submission. • Naloxegol was recommended for this indication in TA345. Review date is listed as July 2018. The group considered that this topic should proceed as an STA if referred to avoid potential delays in publishing guidance. An MTA is not considered necessary at this time.		
Population size	The population with opioid-induced constipation is unknown. In England in 2015 there were over 23 million prescriptions for opioid items; therefore the population size is expected to be large. Around 45-57% and 90% of people with non-cancer pain and cancer pain respectively have OIC. • If the licence for naldemedine is restricted to after laxatives, then the population could reduce to 50-80% of the total OIC population.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	If licensed, naldemedine may offer an additional treatment option for adults with opioid-induced constipation. The cost of naldemedine is not yet known. There may be some off-setting drug and service savings if people transfer from current treatment options for managing the complications of opioid therapy.		
Timeliness	Assuming that the anticipated date of the marketing		

statement	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	Ixekizumab for treating active psoriatic arthritis following inadequate response to disease-modifying anti-rheumatic drugs		
Topic Selection ID Number	8808	**Wave / Round**	R281
TA ID Number	1194		
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 active psoriatic arthritis in adults whose disease has not responded adequately to previous disease-modifying anti-rheumatic drug therapy.		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of ixekizumab for treating psoriatic arthritis is appropriate. The proposed remit is not appropriate and should be amended to ***CONFIDENTIAL INFORMATION REMOVED***in line with the anticipated marketing authorisation. No other material issues raised during consultation. Issues relating to comparators and outcomes have been resolved in the scope.		
Population size	Approximately 6,700 people in England would be eligible for treatment with ixekizumab, based on the resource impact report for TA433 (apremilast).		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of ixekizumab within its marketing authorisation for treating active psoriatic arthritis in ~~**adults**~~ **people** whose disease has not responded adequately to previous disease-modifying anti-rheumatic drug **(DMARD)** therapy, **or for whom DMARDs are not tolerated or contraindicated**		
Costing implications	Ixekizumab would represent an additional treatment option for people with psoriatic arthritis after an inadequate response to disease-modifying anti-rheumatic drugs (DMARD) therapies. Treatment tends to start with DMARDs before proceeding to TNF-α inhibitors. It is estimated that around 6,700 people in England are eligible for treatment with ixekizumab. Comparator treatments range between £9,200 and £11,000 per annum. The cost of ixekizumab is £1,125 for 80mg and £2,250 for 160mg. It is approved by NICE for the treatment of plaque psoriasis and it is recommended in the guidance at the PAS price. The cost compared to comparator treatments is unknown. The annual cost of treatment with ixekizumab based on list price would be around £19,000.		
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.		

Provisional Title	Eltrombopag for untreated severe aplastic anaemia		
Topic Selection ID Number	8966	**Wave / Round**	R226
TA ID Number	1198		
Company	Novartis		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of eltrombopag within its marketing authorisation for untreated severe aplastic anaemia		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of eltrombopag for treating aplastic anaemia is appropriate. The proposed remit is appropriate. No changes are required. The company indicated that it will have difficulty making a submission due to the limited data available and the small patient numbers from the trial. Therefore it does not think this topic should progress. However, other stakeholders considered an appraisal appropriate, although not urgent. Note: Eltrombopag for refractory severe aplastic anaemia was terminated (TA382) because the company did not submit evidence for the same reason.		
Population size	Approximately 110 people in England would be eligible for treatment with eltrombopag. Assuming an incidence of 2 people per million population per year, for a population of England of 55.2 million in 2016, 110 new cases of adult aplastic anaemia in England per annum can be expected.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	If licensed, eltrombopag will offer an additional first line treatment option for patients with severe aplastic anaemia. The annual cost of eltrombopag is estimated at around £20,000. If all 110 people who are eligible for treatment with eltrombopag received it, the total annual cost for England would be £2.2 million. There may be some offsetting savings from reduced transfusions and reduced morbidity.		
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	Mepolizumab for treating eosinophilic granulomatosis with polyangiitis		
Topic Selection ID Number	8368	**Wave / Round**	R190
TA ID Number	1186		
Company	GlaxoSmithKline		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of mepolizumab within its marketing authorisation for treating eosinophilic granulomatosis with polyangiitis.		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of mepolizumab for treating eosinophilic granulomatosis with polyangiitis is appropriate. The proposed remit is appropriate. No changes are required. The company commented that because of the rarity of EGPA, the current NICE appraisal process is not 'an appropriate assessment for a medicine that already has a NICE recommendation with an agreed PAS in a larger population for a different indication'. The company suggested that access arrangements via an NHS England specialised commissioning policy would be more appropriate. The clinical expert at the workshop stated that all people with EGPA have eosinophilic asthma and most of them have severe and refractory asthma and would be eligible for mepolizumab anyway. Further correspondence with another expert highlighted that the dose of mepolizumab used in pivotal trials was 3 times higher than the dose indicated for severe refractory eosinophilic asthma. This means that although all people with EGPA have access to mepolizumab for their co-existing asthma (as per NICE TA431), the dose would not be adequate to treat their EGPA. The clinical trial evidence is only in people with relapsing or refractory EGPA ***CONFIDENTIAL INFORMATION REMOVED***and the clinical expert commented that mepolizumab could be used earlier in the treatment pathway because outcome would be better if used before any organ damage occurs. Early use of mepolizumab could also prevent frequent escalated regimens of corticosteroid and associated long-term side effects.		
Population size	Based on clinical expert comments, between 530 and 2650 people in England would be eligible for treatment with mepolizumab (based on prevalence estimates of 10 to 50 per million in England). The relapsed/refractory population would account for 50% of patients, however the clinical expert commented that it could be used earlier in treatment pathway (see above for more details.		

Process (TA/HST)	TA
Proposed changes to remit (in bold)	None
Costing implications	Mepolizumab is administered by subcutaneous injection. The cost of mepolizumab is not yet known and therefore the cost impact is unknown
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	Caplacizumab for treating acute acquired thrombotic thrombocytopenic purpura		
Topic Selection ID Number	8306	**Wave / Round**	R183
TA ID Number	1185		
Company	Ablynx		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of caplacizumab with its marketing authorisation for treating acute acquired thrombotic thrombocytopenic purpura.		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of caplacizumab for treating acute acquired thrombotic thrombocytopenic purpura is appropriate. Stakeholders were in support of the HST process rather than a STA. However, caplacizumab is not associated with lifelong use or lifelong effect. The disease is punctuated by periods of treatment, stabilisation and relapse. During the periods of stabilisation caplacizumab is not used. The benefits are not maintained when off treatment, and patients can experience recurrent episodes of aTTP. This does not align with the interpretation of the criterion of 'potential for life long use', which relates to continuous use across the population being treated. The table in the scope has been updated: • The population specifies *adults* • The intervention specifies *caplacizumab in addition to plasma exchange therapy (with or without spun apheresis, steroids or rituximab),* because it is expected to be an adjunct to current treatment • The comparator has been clarified *Plasma exchange therapy (with or without spun apheresis, steroids or rituximab), without caplacizumab*		
Population size	Approximately 100-150 people in England would be eligible for treatment with caplacizumab (estimation from clinicians and TTP registry).		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	Caplacizumab is administered as one IV dose then suncutaneous injections (10mg dose) during the duration of the plasma exchange and for thirty days subsequently. The unit cost of Caplacizumab is unknown and therefore the resource impact cannot be calculated.		
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	Erenumab for preventing migraine		
Topic Selection ID Number	8434	**Wave / Round**	R195
TA ID Number	1188		
Company	Novartis		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of erenumab within its marketing authorisation for preventing migraine.		
Main points from consultation	Following the consultation exercise, NICE is of the opinion that an appraisal of erenumab for preventing migraine is appropriate. The proposed remit is appropriate. No changes are required. The population was originally defined to include only people with episodic migraine. The company clarified that the population studied within the erenumab clinical trial programme includes both chronic and episodic migraine, and that the license is not anticipated to differentiate between episodic and chronic migraine. The population in the scope has been amended in response to this comment.		
Population size	It is estimated that there are 190,000 migraine attacks experienced every day in England.		
Process (TA/HST)	TA		
Proposed changes to remit (in bold)	None		
Costing implications	Erenumab will offer an additional prophylactic treatment option for adult patients with migraine. It is administered as a monthly injection in doses of either 70mg or 140mg. The cost of erenumab is not currently known. The population likely to be eligible to receive erenumab could not easily be estimated from available routine published sources. There may be offsetting savings from people transferring from current treatment options.		
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	Tildrakizumab for treating moderate to severe plaque psoriasis		
Topic Selection ID Number	7633	**Wave / Round**	R129
TA ID Number	1060		
Company	Almirall		
Anticipated licensing information	***CONFIDENTIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of tildrakizumab within its marketing authorisation for treating adults with moderate to severe plaque psoriasis who are candidates for systemic therapy.		
Main points from consultation	Following the consultation exercise and the scoping workshop, NICE is of the opinion that an appraisal of tildrakizumab for treating moderate to severe plaque psoriasis is appropriate. It was noted that the wording of the remit was different compared with previous NICE scopes for plaque psoriasis. In response, the remit has been amended in line with previous NICE scopes for plaque psoriaris (see below). This did not affect the population eligible for treatment. The possibility of tildrakizumab being suitable for cost comparison has been considered. Tildrakizumab and ustekinumab are both interleukin 23 inhibitors, although ustekinumab also inhibits the activity of interleukin 12. It is not clear to what extent this difference has implications on relative effectiveness. The following feedback has been received on this issue: • The company did not anticipate that tildrakizumab will be appropriate for consideration using cost comparison methodology. • A comparator company stated that tildrakizumab may be suitable for cost comparison provided there is evidence to support health benefits that are similar or greater to the other biologic therapies. NICE is not aware of any evidence on the efficacy of tildrakizumab relative to ustekinumab. Therefore, it is proposed that this topic proceeds as a Single Technology Appraisal. It has been suggested that the comparators should include systemic non-biological therapies and phototherapy, in line with previous scopes in this therapy area. However, tildrakizumab is expected to be an alternative treatment in the systemic biological therapy part of the psoriasis treatment pathway. Therefore, comparisons with non-biologic treatment were not considered relevant.		
Population size	It is estimated that approximately 190,000 people have moderate to severe psoriasis in England. About 90% of people with the condition have plaque psoriasis.		

Process (TA/HST)	TA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of tildrakizumab within its marketing authorisation for treating ~~**adults with**~~ moderate to severe plaque psoriasis ~~**who are candidates for systemic therapy**~~.
Costing implications	Around 1.75% (754,000) of the general population in England have psoriasis. 90% (679,000) of these people have plaque psoriasis and around 2.55% (17,300) are eligible for biological treatment. Therefore it is estimated that 17,300 people are eligible for treatment with tildrakizumab each year. The cost of tildrakizumab is not yet known. Alternative biological treatment options cost between £10,000 and £13,000 per annum, so the cost impact will depend on the treatment cost in relation to the alternative options (NICE TA 442).
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.