NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 41 draft remits and draft scopes and summary of comments and discussions at scoping workshops

ID	Batch 41
719	Secukinumab for treating ankylosing spondylitis after inadequate response to non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors
815	Cobimetinib in combination with vemurafenib for treating advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma
824	Certolizumab pegol for treating rheumatoid arthritis after inadequate response to a TNF inhibitor
720	Secukinumab for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs
579	Certolizumab pegol for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs
798	Mepolizumab for treating severe eosinophilic asthma
812	Adalimumab for treating moderate to severe hidradenitis suppurativa
845	Nivolumab for previously treated advanced (unresectable or metastatic) melanoma
846	Nivolumab for previously untreated advanced (unresectable or metastatic) melanoma without a BRAF mutation
847	Nivolumab for previously untreated advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma
848	Nivolumab in combination with ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma
822	LCZ696 for treating chronic heart failure

Provisional Title	**Secukinumab for treating ankylosing spondylitis after inadequate response to non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors**		
Topic Selection ID Number	6442	**Wave / Round**	R49
TA ID Number	719		
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 ankylosing spondylitis after inadequate response to non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of secukinumab for treating ankylosing spondylitis after inadequate response to non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors is appropriate. The proposed remit is appropriate. No changes are required <u>Population</u> Updated to state: 'adults with **severe** active ankylosing spondylitis…' • The clinical trials supporting the marketing authorisation application included people who had moderate to severe ankylosing spondylitis. The company confirmed that although the trial inclusion criterion is described this way, patients eligible for inclusion were those with a BASDAI of at least 4 which is defined as severe disease activity rather than moderate, and this definition is consistent across other trials of ankylosing spondylitis. It also confirmed that the anticipated license is for severe disease. Therefore, the scoping workshop attendees agreed that the term 'moderate' be removed from the population in the scope. <u>Comparators</u> Amended to include certolizumab pegol. • Attendees at the workshop agreed that certolizumab pegol is used in current clinical practice in England in people whose disease has responded inadequately to, or is intolerant to non-steroidal anti-inflammatory drugs and should therefore be concluded as a comparator. Certolizumab pegol is currently included in the ongoing MTA review of TA143 and TA233. <u>Subgroups</u> The following subgroups have been included in the scope: - people who have had at least 2 NSAIDs - people who have had NSAIDs and TNF-alpha inhibitors. • Clinical trials supporting the proposed marketing authorisation included people who had responded		

	inadequately to NSAIDs and those who had responded inadequately to no more than 1 TNF-alpha inhibitor. The majority of patients included in the trials were naïve to treatment with TNF-alpha inhibitors (62%-73%). Attendees agreed that these groups should be considered separately if the evidence allows. <u>Other considerations:</u> updated to state that the availability and cost of biosimilars will be taken into account. • Attendees at the workshop noted that biosimilar versions of infliximab (Inflectra [Hospira UK] and Remsima [Celltrion Healthcare]) now have marketing authorisations for ankylosing spondylitis as well as the reference product (Remicade). Attendees agreed that this should be captured in the scope.
Population size	Around 200,000 people have been diagnosed as having ankylosing spondylitis in the UK. There are thought to be approximately 2,300 new diagnoses each year in England and Wales. Ankylosing spondylitis is about 3 times more common in men than in women. Approximately 1 in 10 people with ankylosing spondylitis have a severe form of the disease.
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of secukinumab within its marketing authorisation for treating ankylosing spondylitis after inadequate response to non-steroidal anti-inflammatory drugs or TNF-alpha inhibitors.
Costing implications of remit change	The estimated number of people in England with clinically significant ankylosing spondylitis is around 72,000 people (0.14%). It is estimated that around 7,200 (10%) of these people have a severe form of the disease and may be eligible for treatment. Since secukinumab could potentially be a treatment option alongside tumour necrosis factor (TNF) inhibitors (etanercept, adalimumab and golimumab), the cost impact of this guidance will be dependent on the cost of secukinumab in comparison to the other treatment options. If the drug cost is comparable, the topic has potential to be cost neutral.
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	**Cobimetinib in combination with vemurafenib for treating advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma**		
Topic Selection ID Number	7416	**Wave / Round**	R113
TA ID Number	815		
Company	Roche Products		
Anticipated licensing information	*****Confidential information removed*****		
Draft remit	To appraise the clinical and cost effectiveness of cobimetinib in combination with vemurafenib within its marketing authorisation for treating advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of cobimetinib in combination with vemurafenib for treating advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma is appropriate. The proposed remit is appropriate. No changes are required. No changes to the scope were requested by the stakeholders.		
Population size	Incidence of melanoma is increasing in England with rates doubling approximately every 10-20 years. There were 11,121 people diagnosed with melanoma and 1871 related deaths in England in 2011.		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	No change		
Costing implications of remit change	The number of people that would be eligible to receive vemurafenib and cobimetinib is around 500. Malignant melanoma affects approximately 11,100 people each year in England of which 1,100 are diagnosed with stage IIIc or IV malignant melanoma. Of these about 560 have melanomas that harbor activating BRAF mutations of which 500 will have BRAFV600 mutations. The cost of combination treatment with vemurafenib and cobimetinib for this indication is estimated at £83,000 per person per course of treatment. Vemurafenib is already recommended as monotherapy treatment at a list price of £53,000 but available to the NHS with an agreed patient access scheme. Therefore only cobimetinib would represent an additional cost of about £30,000. It is not known how many people would receive the combination treatment.		
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	**Certolizumab pegol for treating rheumatoid arthritis after inadequate response to a TNF inhibitor**		
Topic Selection ID Number	7637	**Wave / Round**	N/A from RPP
TA ID Number	824		
Company	UCB Pharma		
Anticipated licensing information	Marketing authorisation: Already granted. Marketing authorisation wording: Certolizumab pegol, in combination with methotrexate (MTX), is indicated for the treatment of moderate to severe, active rheumatoid arthritis (RA) in adult patients when the response to disease-modifying antirheumatic drugs (DMARDs) including methotrexate, has been inadequate. Certolizumab pegol can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.		
Draft remit	To appraise the clinical and cost effectiveness of certolizumab pegol within its marketing authorisation for treating rheumatoid arthritis after failure of a TNF inhibitor.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that although an appraisal of certolizumab pegol for treating rheumatoid arthritis after an inadequate response to a TNF inhibitoris appropriate, the timing of the appraisals requires further consideration. The proposed remit should be revised for clarity. A second TNF-alpha inhibitor may be prescribed because of a lack of response to the first TNF inhibitor or a loss of response to the first TNF inhibitor. Scoping workshop attendees suggested that the remit should be amended as follows: To appraise the clinical and cost effectiveness of certolizumab pegol within its marketing authorisation for treating rheumatoid arthritis after inadequate response to a TNF inhibitor. <u>Comparators</u> Updated to include: • Tocilizumab in combination with methotrexate for people for whom rituximab in contraindicated or withdrawn • Best supportive care for people whose disease has not responded adequately to the biological DMARDs • Tocilizumab monotherapy for people for whom rituximab cannot be given because methotrexate is contraindicated or withdrawn Biosimilar infliximab should be included as a comparator and the 'economic analysis' section has been updated to state that the availability and cost of biosimilars of infliximab should be taken into account. <u>Timing and STA/MTA</u> Stakeholders had differing views about the timing of the appraisal. The company (UCB Pharma) would like an STA of certolizumab pegol because it considers that the lack of NICE guidance means that some trusts refuse to fund certolizumab pegol as a second-line biological which places the company at		

	a competitive disadvantage. The other stakeholders would prefer to wait until the ongoing MTA (ID537) of first-line biologicals is completed. The Institute could then review whether a further MTA is needed to update the guidance on biologicals for patients with an inadequate response to a TNF-alpha inhibitor. At the Decision Point 4 meeting it was agreed that the Institute would seek a referral from the DH and the topic would be scheduled into the work programme as an STA once the ongoing review of TNF-a inhibitors has been completed.
Population size	About 10,900 people in England have severe rheumatoid arthritis and have had an inadequate response to TNF-alpha inhibitors (estimated based on the costing statement for TA195).
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of certolizumab pegol within its marketing authorisation for treating rheumatoid arthritis **after inadequate response to** a TNF inhibitor.
Costing implications of remit change	It is estimated that around 10,900 people in England have severe rheumatoid arthritis and have had an inadequate response to TNF-alpha inhibitors. Since certolizumab pegol is similar in cost to other treatments recommended by NICE for the treatment of rheumatoid arthritis after inadequate response to a TNF inhibitor, we do not anticipate that it's use within the NHS will result in a significant incremental impact on NHS resources.
Timeliness statement	As the technology has received a marketing authorisation, issuing timely guidance will not be possible.

Provisional Title	**Secukinumab for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs**		
Topic Selection ID Number	6443	**Wave / Round**	R49
TA ID Number	720		
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 active psoriatic arthritis in adults 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 secukinumab for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs is appropriate. Key issues from the scoping workshop: Comparators: Updated to include 2 additional comparators; apremilast and certolizumab for those who have received at least 2 DMARDs and for people in whom DMARDs and biological therapies are not tolerated or contraindicated. In February 2015 2 biosimilar drugs for infliximab received a marketing authorisation for treating psoriatic arthritis (inflectra [Hospira UK] and remsima [Celltrion Healthcare]). The manufacturers are to be added to the matrix and a sentence noting that the 'the availability and cost of biosimilars should be taken into account will be included in the 'other considerations' section of the scope. Outcomes: Updated to remove 2 outcomes (effect on concomitant skin condition and other complications of psoriatic arthritis [skin, nail and scalp outcomes]) and addition of 1 outcome (periarticular disease for example enthesitis, tendonitis, dactylitis). Subgroups: The subgroup previous treatment (including previous treatment with DMARDs and TNF-alpha inhibitors) was removed because the population in the scope already was stratified by lines of treatment. The 2nd subgroup was amended to "reason for treatment failure (for example due to lack of efficacy, intolerance, or adverse events).		
Population size	The prevalence of psoriasis in the UK population is estimated at between 1.5-3%. An estimated 5–7% of all people with psoriasis, and approximately 40% of those with extensive skin disease, have psoriatic arthritis. The prevalence of psoriatic arthritis in England in 2013 was estimated to be around 53,900 to 161,600 people.		
Process (MTA/STA/HST)	At DP4 it was agreed that secukinumab should be referred onto the work programme as an MTA with certolizumab pegol. The appraisals team will explore combining this with a review of		

	existing guidance for the treatment of arthritis following inadequate response to disease modifying anti-rheumatic drugs (TA's 199, 220 and 313).
Proposed changes to remit (in bold)	*(Same as topic ID579)* To appraise the clinical and cost effectiveness **of certolizumab pegol and** secukinumab within their marketing authorisations for treating active psoriatic arthritis in adults for whom disease-modifying anti-rheumatic drugs have been inadequately effective, not tolerated or contraindicated
Costing implications of remit change	The cost of secukinumab is not yet known, however it is estimated that the topic would be low cost or cost neutral. There are around 60,000 people in England with progressive psoriatic arthritis of which approximately 2.4% (1,450) are anticipated to be eligible to receive secukinumab. The estimated population who may switch to secukinumab from the comparator TNF-α inhibitor drug treatments is unknown. Most of the TNF-α inhibitors cost between £9,000 and £11,000 per year. If the cost of secukinumab is similar to this, the cost impact will be minimal. However, there may be future savings associated with less joint surgery and fewer hospital admissions if improved disease control for people with progressive psoriatic arthritis is achieved with this new technology.
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	**Certolizumab pegol for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs**		
Topic Selection ID Number	5694	**Wave / Round**	N/A from RPP
TA ID Number	579		
Company	UCB Pharma		
Anticipated licensing information	Marketing authorisation: Already granted. Marketing authorisation wording: Cimzia, in combination with MTX, is indicated for the treatment of active psoriatic arthritis in adults when the response to previous DMARD therapy has been inadequate. Cimzia can be given as monotherapy in case of intolerance to methotrexate or when continued treatment with methotrexate is inappropriate.		
Draft remit	To appraise the clinical and cost effectiveness of certolizumab pegol within its marketing authorisation for treating active psoriatic arthritis in adults 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 certolizumab pegol for treating active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs is appropriate. Key issues following scoping workshop: <u>Appropriateness</u> The majority of scoping workshop attendees agreed that it was appropriate for this topic to proceed. However, the manufacturer of certolizumab pegol no longer wants this topic to proceed to appraisal because it already has a marketing authorisation and is currently being used in clinical practice. <u>Comparators</u> Updated to include 2 additional comparators; apremilast and secukinumab for those who have received at least 2 DMARDs, and both DMARDs and biological therapies. In February 2015 2 biosimilar drugs for infliximab received a marketing authorisation for treating psoriatic arthritis (inflectra [Hospira UK] and remsima [Celltrion Healthcare]). The manufacturers are to be added to the matrix and a sentence noting that the 'the availability and cost of biosimilars should be taken into account will be included in the 'other considerations' section of the scope. <u>Outcomes</u> Updated to remove 2 outcomes ('effect on concomitant skin condition' and 'other complications of psoriatic arthritis [including skin, nail and scalp outcomes]') and addition of 1 outcome ('periarticular disease [for example tendonitis, enthesitis, dactylitis'] Subgroups: The subgroup 'previous treatment (including		

	previous treatment with DMARDs and TNF-α inhibitors') was removed because the population in the scope already been stratified by lines of treatment. The 2nd subgroup was amended to "reason for treatment failure (for example due to lack of efficacy, intolerance, or adverse events)"
Population size	The prevalence of psoriasis in the UK population is estimated at between 1.5-3%. An estimated 5–7% of all people with psoriasis, and approximately 40% of those with extensive skin disease, have psoriatic arthritis. The prevalence of psoriatic arthritis in England in 2013 was estimated to be around 53,900 to 161,600 people.
Process (MTA/STA/HST)	At DP4 it was agreed that certolizumab pegol should be referred onto the work programme as an MTA with secukinumab. The appraisals team will explore combining this with a review of existing guidance for the treatment of arthritis following inadequate response to disease modifying anti-rheumatic drugs (TA's 199, 220 and 313).
Proposed changes to remit (in bold)	*(Same as topic ID720)* To appraise the clinical and cost effectiveness of certolizumab pegol **and secukinumab** within their marketing authorisations for treating active psoriatic arthritis in adults for whom disease-modifying anti-rheumatic drugs have been inadequately effective, not tolerated or contraindicated.
Costing implications of remit change	There are around 60,000 people in England with progressive psoriatic arthritis of which approximately 2.4% (1,450) are anticipated to be eligible to receive certolizumab pegol. Since certolizumab pegol is similar in cost to other treatments currently recommended by NICE for the treatment of active psoriatic arthritis following inadequate response to disease modifying anti-rheumatic drugs, we do not anticipate that it's use within the NHS will result in a significant incremental impact on NHS resources. However, there may be future savings associated with less joint surgery and fewer hospital admissions if improved disease control for people with progressive psoriatic arthritis is achieved with this new technology.
Timeliness statement	As the technology has received a marketing authorisation, issuing timely guidance will not be possible.

Provisional Title	**Mepolizumab for treating severe eosinophilic asthma**		
Topic Selection ID Number	7411	**Wave / Round**	R112
TA ID Number	798		
Company	GlaxoSmithKline		
Anticipated licensing information	***Confidential information removed***.		
Draft remit	To appraise the clinical and cost effectiveness of mepilozumab within its marketing authorisation for treating severe eosinophilic asthma		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of mepolizumab for treating severe eosinophilic asthma is appropriate. Key issues from scoping workshop: <u>Comparators</u> Updated to include omalizumab as a comparator for people with severe persistent IgE-mediated eosinophilic asthma. <u>Outcomes</u> Updated to include patient and clinician evaluation of response and lung function to the list of outcomes in the draft scope. 'Clinically significant acute exacerbations' and 'asthma symptoms' has been changed to 'clinically significant exacerbations' and 'asthma control' respectively. <u>Subgroups</u> The draft scope should be amended to state that, if evidence allows, the following four subgroups should be considered separately: 1) people who do not adhere to their current treatment; 2) people who have severe allergic IgE-mediated eosinophilic asthma; 3) people who require maintenance oral corticosteroid treatment and 4) people who require frequent oral corticosteroid treatment.		
Population size	Severe difficult to control asthma has an estimated prevalence of 140 patients/million population with an annual incidence of approximately 14 patients/million		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	No change		
Costing implications of remit change	Mepolizumab offers an additional first-line treatment option for severe refractory eosinophilic asthma. If mepolizumab is prescribed to people with severe difficult to control asthma, the eligible population will be around 7,400 for England. Since the cost of mepolizumab is unknown the potential cost impact of this technology is also unknown. In addition to the drug costs there are also likely to be additional costs associated with attending a specialist centre to receive treatment.		
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	**Adalimumab for treating moderate to severe hidradenitis suppurativa**		
Topic Selection ID Number	5714	**Wave / Round**	R121
TA ID Number	812		
Company	AbbVie		
Anticipated licensing information	*****Confidential information removed*****		
Draft remit	To appraise the clinical and cost effectiveness of adalimumab within its marketing authorisation for treating moderate to severe hidradenitis suppurativa		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of adalimumab for treating moderate to severe hidradenitis suppurativa is appropriate The key issue from the scoping workshop was the comparators to be included in the final scope. The list of comparators has been updated. High-dose oral steroids and intralesional corticosteroid injection have been removed as comparators. • Consultees were in agreement that the following comparators should be included:Combination antibiotics: clindamycin plus rifampicine, tetracyclines • Retinoids (acitretin but not isotretinoin) • Dapsone • Ciclosporin • Metfomin • Surgery • Infliximab plus methotrexate Following DP4 it was agreed that the background section of the scope be updated to reflect current clinical practice for the management of hidradenitis suppurativa (as above) and the comparator box of the PICO be reworded to 'established clinical management without adalimumab'.		
Population size	Approximately 90,000 people		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	No changes		
Costing implications of remit change	The prevalence of hidradentitis suppurativa is subject to uncertainty, though there may be around 90,000 people in England with the condition. The number of these people that would have a contraindication, intolerance or adequate response to oral antibiotics is not known and therefore the uptake of adalimumab cannot be estimated. The annual cost of treatment with adalimumab may be around £6,700. There are potential savings from reduced number of surgeries and associated wound care if hidradentitis		

	suppurativa was better managed, as there are currently no licensed treatments.
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	**Nivolumab for previously treated advanced (unresectable or metastatic) melanoma**		
Topic Selection ID Number	7618	**Wave / Round**	R127
TA ID Number	845		
Company	Bristol-Myers Squibb		
Anticipated licensing information	**CHMP positive opinion received 23 April 2015:** Opdivo as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults *****Confidential information removed*****		
Draft remit	To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating advanced, unresectable melanoma after progression following anti-CTLA-4 therapy.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of nivolumab for previously treated advanced (unresectable or metastatic) melanoma is appropriate. After the scoping workshop, nivolumab received a positive CHMP opinion as monotherapy for the treatment of advanced (unresectable or metastatic) melanoma in adults. Therefore the remit and population were updated as follows: <u>Remit:</u> To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating advanced (unresectable or metastatic) melanoma <u>Population:</u> Adults with previously treated advanced (unresectable or metastatic) melanoma <u>Comparators:</u> Scoping workshop attendees confirmed that chemotherapy, particularly dacarbazine, is used in clinical practice when targeted therapies have failed or are inappropriate, and therefore should be included as a comparator. They also stated that vemurafenib and dabrafenib should be included as comparators for the BRAF mutation-positive group if the marketing authorisation does not specify previous treatment with BRAF inhibitors in addition to anti-CTLA-4 therapy. Given that the CHMP positive opinion does not specify any details of previous treatment, the comparators are therefore defined as follows: For BRAF mutation-positive disease • Dabrafenib and vemurafenib (for people who have not previously received BRAF inhibitors • Ipilimumab (for people who have not previously received ipilimumab • Dacarbazine and BSC (for people who have received both a BRAF inhibitor and ipilimumab or for whom either of these is unsuitable For BRAF mutation-negative disease		

	• Dacarbazine • Best supportive care <u>Post scoping workshop</u> Following the CHMP positive opinion, the company met with the NICE team and proposed that the 3 scopes for nivolumab monotherapy (ID845, 846 and 847) could be combined into a single STA, with a second STA for nivolumab in combination with ipilimumab (ID 848) to follow in line with the proposed license extension. The company stated that although the clinical trial underpinning the evidence for the untreated BRAF positive population will not be available at the time of the first appraisal, there is published evidence showing that BRAF mutation status does not impact nivolumab efficacy. In addition available evidence also suggests that the line of therapy is not prognostic for overall survival outcome with nivolumab. At the DP4 meeting, it was decided that this topic (ID845) together with the other monotherapy topics (ID846 and 847) will be combined into 1 STA.
Population size	235 patients per year - (11,281 new cases of melanoma in 2012; 10% of cases are stage IIIc or IV, and 21% of stage IIIc/IV receive 2nd-line treatment)
Process (MTA/STA/HST)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating advanced (unresectable **or metastatic**) melanoma ~~**after progression following anti-CTLA-4 therapy.**~~
Costing implications of remit change	In 2012 there were around 11,300 new cases of malignant melanoma. It is thought that 10% of these people will have either advanced stage III or stage IV melanoma (NICE TA319). The proportion of people who relapse and are able to receive second line treatment is thought to be approximately 21% (around 235 people). The NHS cost of nivolumab is unknown but it is currently licensed in Japan where it costs £89,000 per year. This is more expensive than its comparators, ipilimumab (£76,000 before PAS discount), vemurafenib (£53,000 before PAS discount), dabrafenib (£73,000 before PAS discount) and dacarbazine (£680). Therefore it is anticipated that there may be increased costs for the NHS associated with the use of nivolumab.
Timeliness statement	Although this technology has already received a positive CHMP opinion, combining ID 845, 846 and 847 can provide the opportunity to publish timely guidance.

Provisional Title	**Nivolumab for previously untreated advanced (unresectable or metastatic) melanoma without a BRAF mutation**		
Topic Selection ID Number	7775	**Wave / Round**	R127
TA ID Number	846		
Company	Bristol-Myers Squibb		
Anticipated licensing information	**CHMP positive opinion received 23 April 2015:** Opdivo as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults *****Confidential information removed*****		
Draft remit	To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating previously untreated advanced, unresectable melanoma		
Main points from consultation	This topic, together with the next two (ID 847 and 848) were presented in one scope under the same remit (for previously untreated disease) for the purpose of consultation and the scoping workshop. Following the CHMP positive opinion, the remit will no longer cover ID848 (nivolumab in combination with ipilimumab). The remit has been updated, and population remains unchanged as follows: <u>Remit:</u> To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating advanced (unresectable or metastatic) melanoma <u>Population:</u> Adults with previously untreated advanced (unresectable or metastatic) melanoma without a BRAF mutation <u>Comparators:</u> Scoping workshop attendees stated that dacarbazine should be included because a small number of patients seen in clinical practice are unable to take ipilimumab for reasons including the presence of autoimmune diseases, co-morbidities, contra-indications or very poor performance status. Therefore the comparators have been updated to ipilimumab and dacarbazine. <u>Post scoping workshop</u> Please see item 5.9 for the company's proposal to combine the monotherapy topics (ID845, 846 and 847) together in a single STA, with a second STA for nivolumab in combination with ipilimumab (ID848) to follow. At the DP4 meeting, it was decided that this topic (ID846) together with the other monotherapy topics (ID845 and 847) will be combined into 1 STA.		
Population size	Approximately 590 patients per year – (11,281 new cases of melanoma in 2012; 10% of cases are stage IIIc or IV, 52% are BRAF mutation-negative)		
Process (MTA/STA/HST)	STA		

Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating ~~**previously untreated**~~ advanced (unresectable **or metastatic**) melanoma
Costing implications of remit change	In 2012 there were around 11,300 new cases of malignant melanoma. It is thought that 10% of these people will have either advanced stage III or stage IV melanoma (NICE TA319). The proportion that are BRAF mutation negative is 52% (around 590 people). The NHS cost of nivolumab is unknown but it is currently licensed in Japan where it costs £89,000 per year. This is more expensive than its comparators, ipilimumab (£76,000 before PAS discount) and dacarbazine (£680). Therefore it is anticipated that there may be increased costs for the NHS associated with the use of nivolumab.
Timeliness statement	Although this technology has already received a positive CHMP opinion, combining ID 845, 846 and 847 can provide the opportunity to publish timely guidance.

Provisional Title	**Nivolumab for previously untreated advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma**		
Topic Selection ID Number	7695	**Wave / Round**	R127
TA ID Number	847		
Manufacturer	Bristol-Myers Squibb		
Anticipated licensing information	**CHMP positive opinion received 23 April 2015:** Opdivo as monotherapy is indicated for the treatment of advanced (unresectable or metastatic) melanoma in adults *****Confidential information removed*****		
Draft remit	To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating previously untreated advanced, unresectable melanoma		
Main points from consultation	This topic, together with ID 846 and 848 were presented in one scope under the same remit (for previously untreated disease) for the purpose of consultation and the scoping workshop. Following the CHMP positive opinion, the remit will no longer cover ID848 (nivolumab in combination with ipilimumab). The remit has been updated, and the population remain unchanged as follows: <u>Remit:</u> To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating advanced (unresectable or metastatic) melanoma <u>Population:</u> Adults with previously untreated advanced (unresectable or metastatic) BRAF V600 mutation-positive melanoma <u>Comparators:</u> Scoping workshop attendees considered the comparators in the draft scope (dabrafenib, vemurafenib and ipilimumab) to be appropriate. <u>Post scoping workshop</u> Please see item 5.9 for the company's proposal to combine the monotherapy topics (ID845, 846 and 847) together in a single STA, with a second STA for nivolumab in combination with ipilimumab (ID 848) to follow. At the DP4 meeting, it was decided that this topic (ID847) together with the other monotherapy topics (ID845 and 846) will be combined into 1 STA.		
Population size	Approximately 540 patients per year – (11,281 new cases of melanoma in 2012; 10% of cases are stage IIIc or IV, 48% are BRAF mutation-positive)		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating ~~**previously untreated**~~ advanced (unresectable **or metastatic**) melanoma		

Costing implications of remit change	In 2012 there were around 11,300 new cases of malignant melanoma. It is thought that 10% of these people will have either advanced stage III or stage IV melanoma (NICE TA319). The proportion that are BRAF mutation positive is 48% (around 540 people). The NHS cost of nivolumab is unknown but it is currently licensed in Japan where it costs £89,000 per year. This is more expensive than its comparators, ipilimumab (£76,000 before PAS discount) and dacarbazine (£680). Therefore it is anticipated that there may be increased costs for the NHS associated with the use of nivolumab.
Timeliness statement	Although this technology has already received a positive CHMP opinion, combining ID 845, 846 and 847 can provide the opportunity to publish timely guidance.

Provisional Title	**Nivolumab in combination with ipilimumab for previously untreated advanced (unresectable or metastatic) melanoma**		
Topic Selection ID Number	7777	**Wave / Round**	R127
TA ID Number	848		
Manufacturer	Bristol-Myers Squibb		
Anticipated licensing information	*****Confidential information removed*****		
Draft remit	To appraise the clinical and cost effectiveness of nivolumab within its marketing authorisation for treating previously untreated advanced, unresectable melanoma		
Main points from consultation	This topic, together with ID 846 and 847 were presented in one scope under the same remit (for previously untreated disease) for the purpose of consultation and the scoping workshop. Following the CHMP positive opinion for nivolumab monotherapy, the previous remit will no longer cover this topic. Therefore remit for this topic was updated as follows: <u>Remit:</u> To appraise the clinical and cost effectiveness of nivolumab in combination with ipilimumab within its marketing authorisation for treating previously untreated advanced (unresectable or metastatic) melanoma <u>Population:</u> This will remain as 'adults with previously untreated advanced (unresectable or metastatic) melanoma' <u>Comparators:</u> Scoping workshop attendees considered the comparators in the draft scope (dabrafenib, vemurafenib and ipilimumab for BRAF mutation-positive; ipilimumab for BRAF mutation-negative) to be appropriate. <u>Post scoping workshop</u> Please see item 5.9 for the company's proposal to combine the monotherapy topics (ID845, 846 and 847) together in a single STA, with a second STA for nivolumab in combination with ipilimumab (ID 848) to follow.		
Population size	Approximately 1130 patients per year – (11,281 new cases of melanoma in 2012; 10% of cases are stage IIIc or IV)		
Process (MTA/STA/HST)	STA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of nivolumab **in combination with ipilimumab** within its marketing authorisation for treating previously untreated advanced (unresectable **or metastatic**) melanoma		

Costing implications of remit change	In 2012 there were around 11,300 new cases of malignant melanoma; it is thought that 10% of these people will have either advanced stage III or stage IV melanoma (1,130 people). The NHS cost of nivolumab is unknown but it is currently licensed in Japan where it costs £89,000 per year. Ipilimumab costs £76,000 before PAS discount. The comparator treatments are vemurafenib (£53,000 before PAS discount) and dabrafenib (£73,000 before PAS discount). Therefore it is anticipated that there will be increased costs for the NHS associated with the use of nivolumab in combination with ipilimumab.
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	LCZ696 (sacubitril valsartan) for treating chronic heart failure		
Topic Selection ID Number	6929	**Wave / Round**	R80
TA ID Number	822		
Company	Novartis		
Anticipated licensing information	***Confidential information removed***		
Draft remit	To appraise the clinical and cost effectiveness of LCZ696 within its marketing authorisation for treating chronic heart failure (NYHA stage II-IV) with reduced left ventricular fraction.		
Main points from consultation	Following the consultation exercise, the Institute is of the opinion that an appraisal of LCZ696 (sacubitril valsartan) is appropriate. Stakeholders widely agreed that a Single Technology Appraisal of sacubitril valsartan would add value. This topic was originally planned to be scoped and referred as part of Batch 42. Consultation on the draft scope closed on Friday 07 May 2015 and comments received indicated that an appraisal of this topic is supported. The scoping workshop for this topic is scheduled to take place on Tuesday 02 June 2015. Following consideration of the consultation comments, the Technology Appraisals programme is seeking formal referral of the remit as part of Batch 41 in order to expedite the timing of the appraisal and publication of final guidance. Sacubitril valsartan has recently received a positive PIM designation from the MHRA. This is an early indication that this technology is a promising candidate for the Early Access to Medicines Scheme (EAMS). It is recognised that there is a need for guidance to be issued as quickly and timely as possible due to the forthcoming involvement in EAMS and the anticipated licensing dates for sacubitril valsartan. *****Confidential information removed***** During consultation, the company responsible for sacubitril valsartan indicated that the remit should be updated to reflect the anticipated wording of the marketing authorisation. No other requests to update the remit were received. Therefore the remit has been updated as follows: <u>Remit:</u> To appraise the clinical and cost effectiveness of sacubitril valsartan within its marketing authorisation for treating heart failure (NYHA class II-IV) with systolic dysfunction. The scoping workshop will still be held on 02 June 2015 in order to refine the scope, particularly the PICO table, following consultation comments.		
Population size	There are approximately 800,000 people living with heart failure in the UK. The proportion of people with systolic dysfunction, who would be suitable for treatment with sacubitril valsartan, will be explored at the scoping workshop.		
Process (MTA/STA/HST)	STA		

Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of **sacubitril valsartan** within its marketing authorisation for treating heart failure (NYHA class II-IV) with **systolic dysfunction.**
Costing implications of remit change	Using the costing template for NICE TA267 (Ivabradine for treating chronic heart failure) provides a possible estimate of the eligible population. It is estimated that there is a prevalence of heart failure due to left ventricular dysfunction of 0.41% of adults in England and that 80% of them have a class II to IV New York Heart Association score. This gives a population of around 133,000 people who may be eligible for LCZ696. The cost of the drug is not yet known. Existing other options are relatively inexpensive. The number of people who may choose LCZ696 rather than existing technologies is not known. However, due to the potentially large eligible population, the cost impact of this technology could be large, even with a relatively small incremental cost per person.
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 as part of Batch 41, issuing timely guidance for this technology will be possible.