NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

CENTRE FOR HEALTH TECHNOLOGY EVALUATION
Technology Appraisals

Consultation on Batch 32 draft remits and draft scopes and summary of comments and discussions at scoping workshops

5.1	Paclitaxel formulated as albumin-bound nanoparticles in combination with gemcitabine for previously untreated advanced pancreatic cancer
5.2	Pomalidomide for treating relapsed and refractory multiple myeloma previously treated with both lenalidomide and bortezomib
5.3	Nintedanib for previously treated locally advanced or metastatic non-small cell lung cancer
5.4	Vedolizumab for treating moderately to severely active ulcerative colitis
5.5	Obinutuzumab for previously untreated chronic lymphocytic leukaemia
5.6	Simeprevir in combination with peginterferon alfa and ribavirin for treating genotype 1 or 4 chronic hepatitis C
5.7	Serelaxin for treating acute heart failure

Provisional Title	**Paclitaxel formulated as albumin-bound nanoparticles in combination with gemcitabine for previously untreated advanced pancreatic cancer**		
Topic Selection ID Number	6645	**Wave / Round**	R64
TA ID Number	680		
Manufacturer	Celgene		
Anticipated licensing information	***CONFIDENDIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of paclitaxel formulated as albumin-bound nanoparticles in combination with gemcitabine within its licensed indication for previously untreated advanced pancreatic cancer.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of paclitaxel formulated as albumin-bound nanoparticles in combination with gemcitabine for previously untreated metastatic pancreatic cancer is appropriate. The proposed remit is not appropriate and should be amended in line with the wording of the marketing authorisation to specify that the treatment will only be for people with metastatic adenocarcinoma of the pancreas, and not those with locally advanced disease. The population should be amended to specify that patients should have metastatic adenocarcinoma of the pancreas that has not been previously treated with chemotherapy, in line with the marketing authorisation.		
Population size	Approximately 6400 - 7300 new diagnoses of pancreatic cancer in the UK each year will be for advanced disease that is not suitable for surgery (that is, locally advanced or metastatic disease).		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of paclitaxel formulated as albumin-bound nanoparticles in combination with gemcitabine within its licensed indication for previously untreated ~~advanced pancreatic cancer~~ **metastatic adenocarcinoma of the pancreas.**		
Costing implications of remit change	No changes proposed. Initial cost impact assessment was based on assumed number of people with metastatic disease. It is considered that this topic has potential to be high cost.		
Timeliness statement	Noting that paclitaxel formulated as albumin-bound nanoparticles is now licensed, issuing timely guidance for this technology will not be possible.		

Provisional Title	**Pomalidomide for treating relapsed and refractory multiple myeloma previously treated with both lenalidomide and bortezomib**		
Topic Selection ID Number	6521	**Wave / Round**	R54
TA ID Number	666		
Manufacturer	Celgene		
Anticipated licensing information	Pomalidomide received its UK marketing authorisation on 5th August 2013 for "the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least two prior treatment regimens, including both lenalidomide and bortezomib, and have demonstrated disease progression on last therapy."		
Draft remit	To appraise the clinical and cost effectiveness of pomalidomide within its licensed indication for treating relapsed and refractory multiple myeloma previously treated with both lenalidomide and bortezomib.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of pomalidomide for treating relapsed and refractory multiple myeloma previously treated with both lenalidomide and bortezomib is appropriate. The proposed remit is appropriate. No changes are required. Consultees commented that there is no recognised standard of care for treating relapsed and refractory multiple myeloma. Choice of treatment is usually guided by a patient's previous treatment history, their co-morbidities and the toxicity of previous treatments. It is recommended that the comparator in the scope is reworded from 'Standard clinical management' to 'Established clinical management without pomalidomide', to align the wording in line with the terminology used in the NICE Guide to the Methods of Technology Appraisal.		
Population size	Approximately 1500 patients per year		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	The indicative price to the NHS of pomalidomide is £8884 for a 21 day supply of 4mg capsules. Since pomalidomide is administered on days 1 to 21 of repeated 28 day cycles, assuming a progression free survival of 3.8 months (briefing note indication) the cost per patient could be around £35,500. Assuming an eligible population of around 1500 patients per year, this technology is likely to be high cost. Additional costs will also be incurred if administered in combination with dexamethasone and if any additional patient consultations are required as a result of the new technology. There may be some offsetting savings from other treatments		

	avoided.
Timeliness statement	Noting that pomalidomide is now licensed, issuing timely guidance for this topic will not be possible.

Provisional Title	**Nintedanib for previously treated locally advanced or metastatic non-small cell lung cancer**		
Topic Selection ID Number	3379	**Wave / Round**	25
TA ID Number	438		
Manufacturer	Boehringer Ingleheim		
Anticipated licensing information	***CONFIDENDIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of nintedanib within its licensed indication for previously treated locally advanced or metastatic non-small cell lung cancer.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of nintedanib for previously treated locally advanced or metastatic non-small cell lung cancer is appropriate. The proposed remit is appropriate. No changes are required. During the scoping workshop, the manufacturer commented that the licence submitted to the EMA would focus on ***CONFIDENDIAL INFORMATION REMOVED***, as this was the subgroup which showed a statistically significant overall survival improvement in the LUME-LUNG 1 pivotal study. However, as this information was shared as commercial-in-confidence, the consultees agreed that the population included in the scope as well as the remit should remain broad, in line with the wording in the draft scope. ***CONFIDENDIAL INFORMATION REMOVED*** Comments received during consultation indicated that best supportive care should not be included as a comparator as only those people who cannot tolerate chemotherapy should be receiving best supportive care. Because nintedanib will be administered in combination with chemotherapy, only those who are able to tolerate chemotherapy would receive treatment.		
Population size	Approximately 7600 - 9500 people in the UK are diagnosed with adenocarcinoma each year. Only a small proportion of patients are fit enough to receive second-line treatment.		
Process (MTA/STA)	STA		
Proposed changes to remit (in bold)	None		
Costing implications of remit change	The cost of nintedanib has yet to be determined and therefore it is not possible to determine the cost impact of this topic. The target population is unlikely to exceed 1900, based on the upper limit of the range of those likely to be eligible for second-line therapy. ***CONFIDENDIAL INFORMATION REMOVED*** If nintedanib is administered in combination with docetaxel, any costs will be in addition to current costs of treatment with docetaxel, although offsetting savings will occur if this treatment		

	replaces treatment with pemetrexed.
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	**Vedolizumab for treating moderately to severely active ulcerative colitis**		
Topic Selection ID Number	6666	**Wave / Round**	R67
TA ID Number	691		
Manufacturer	Takeda		
Anticipated licensing information	***CONFIDENDIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of vedolizumab within its licensed indication for treating moderately to severely active ulcerative colitis in adults who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of vedolizumab for treating moderately to severely active ulcerative colitis is appropriate. It should be noted that this topic has substantial overlap with an MTA in the same disease area (infliximab, adalimumab and golimumab for treating moderately to severely active ulcerative colitis after the failure of conventional therapy [including a review of TA140 and TA262]). At the time of the scoping workshop, the MTA had received a referral and was ongoing (anticipated publication February 2015); an additional (post-referral) scoping workshop for the MTA was conducted immediately after the vedolizumab scoping workshop. Several of the proposed changes to the scope for vedolizumab have been made to ensure the scopes for these two topics are consistent. The proposed remit is appropriate but should be amended to indicate that treatment can be given after either conventional therapy or a TNF-alpha antagonist, in line with the anticipated marketing authorisation. Consultees considered that the population in the scope should be restricted to people with moderately to severely active ulcerative colitis, excluding those with acute severe disease (that is a medical emergency and requires inpatient treatment), in line with the trial populations in the pivotal clinical studies. In addition, the therapies that patients should have tried should be more clearly defined, that is, conventional therapy should be defined as immunomodulators or corticosteroids, and the prior therapies should be expanded to include TNFα antagonists. Therefore the wording of the population in the scope should be amended to “adults with moderately to severely active ulcerative colitis (excluding those with acute severe ulcerative colitis that is a medical emergency and requires inpatient treatment) who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy (immunosuppressants and/or corticosteroids) or a TNFα antagonist”.		

	Consultees considered that for clarity and consistency with the scope for the ongoing MTA in ulcerative colitis that the comparators in the scope should be amended to list individual agents as follows: 'Established clinical management without vedolizumab, which may include a combination of aminosalicylates (sulfasalazine, mesalazine, balsalazide or olsalazine), corticosteroids (beclomethasone, budesonide, hydrocortisone or prednisolone), thiopurines (mercaptopurine or azathioprine), calcineurin inhibitors (tacrolimus), TNFα antagonists (infliximab, adalimumab or golimumab) and surgical intervention'. 'Rate of hospitalisation' should be added to the outcome measures in the scope to maintain consistency with the ongoing MTA in ulcerative colitis. Following the proposed change to the population to exclude patients with acute severe ulcerative colitis, the subgroups in the scope are no longer required. Consultees agreed that subgroups based on prior exposure to TNFα antagonists would be relevant and important to include, as vedolizumab showed different clinical effectiveness in these groups in the clinical trials. Therefore, the subgroups should be changed to: 'People who have been previously treated with one or more TNFα antagonists and people who have not received prior TNFα antagonist therapy'.
Population size	132,600 people in England and Wales have ulcerative colitis.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of vedolizumab within its licensed indication for treating moderately to severely active ulcerative colitis in adults who are intolerant of, or whose disease has had an inadequate response or loss of response to conventional therapy **or a tumour necrosis factor-alpha antagonist**.
Costing implications of remit change	No changes anticipated. Expanding the prior therapies to include TNFα antagonists should not increase the eligible population since this group is likely to have already tried conventional therapy. The population eligible to receive vedolizumab could not be estimated from available published sources, as it is not known what proportion are moderate to severe and resistant or intolerant to alternative treatments. The unit cost of vedolizumab is also 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	**Obinutuzumab for previously untreated chronic lymphocytic leukaemia**		
Topic Selection ID Number	5915	**Wave / Round**	R40
TA ID Number	650		
Manufacturer	Roche Products		
Anticipated licensing information	***CONFIDENDIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of obinutuzumab within its licensed indication for previously untreated chronic lymphocytic leukaemia.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of obinutuzumab for previously untreated chronic lymphocytic leukaemia is appropriate. The proposed remit is appropriate. The clinical specialists advised that obinutuzumab would be used to treat patients who are unable to receive fludarabine combination chemotherapy, in line with the trial population. Therefore, the population in the scope should be changed to: 'People with previously untreated chronic lymphocytic leukaemia for whom fludarabine combination chemotherapy is not appropriate.' Considering that the population for this appraisal will be people for whom fludarabine combination chemotherapy is not appropriate, 'fludarabine and cyclophosphamide (with or without rituximab)' should be removed as a comparator from the scope. Clinical specialists advised that alemtuzumab is not widely used in clinical practice for people with chronic lymphocytic leukaemia for whom fludarabine combination chemotherapy is not appropriate; therefore it should not be included as a comparator. Consultees noted that minimal residual disease negativity is a common outcome measure in clinical trials of chronic lymphocytic leukaemia and advised that it is a predictor of progression-free survival and overall survival. Consultees therefore agreed that minimal residual disease negativity would be a useful addition to the outcome measures in the scope.		
Population size	Approximately 2800 people are diagnosed in the UK each year. About 67% will need treatment, of whom half will be unsuitable for fludarabine combination chemotherapy, which equates to approximately 900 patients, who may receive treatment with obinutuzumab.		
Process (MTA/STA)	STA		

Proposed changes to remit (in bold)	None
Costing implications of remit change	No changes anticipated. The manufacturer estimates the cost of treatment with obinutuzumab to be in the range of £10,000-£15,000 per patient for 6-8 cycles of treatment. Treatment with obinutuzumab would need to cost around an additional £15,000 per patient per year for this topic to be high cost. Since there is no recognised standard treatment any potential offsetting savings cannot be calculated reliably.
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	**Simeprevir in combination with peginterferon alfa and ribavirin for treating genotype 1 or 4 chronic hepatitis C**		
Topic Selection ID Number	6381 & 6382	**Wave / Round**	R42
TA ID Number	668		
Manufacturer	Janssen		
Anticipated licensing information	***CONFIDENDIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of simeprevir within its licensed indication for treating chronic hepatitis C.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of simeprevir in combination with peginterferon alfa and ribavirin for treating chronic hepatitis C is appropriate. The proposed remit should be amended to specify that treatment is only for people with genotype 1 or 4 chronic hepatitis C. Clinical specialists acknowledged the possibility of shortened treatment courses with simeprevir if a rapid virological response to treatment is achieved. It is unclear however, whether shortened treatment duration will be stipulated in the SPC. It was agreed that duration of treatment is an important outcome and therefore 'rapid virological response (leading to shortened treatment duration)' should be added as an outcome in the scope. Consultees discussed the subgroup 'IL28b polymorphism'. The clinical specialists explained that although it can be useful to understand the polymorphism status of a patient, especially when managing other treatments (and determining the risk of stopping other important treatments that react with treatment for hepatitis C), it was not a key driver of treatment decision making. In addition, IL28b polymorphism testing is not routine and there is unequal access across the UK. Consultees therefore agreed that IL28b polymorphism should not be included as a subgroup. Consultees acknowledged that there are many pieces of existing guidance, in addition to a number of new topics for hepatitis C being considered by NICE soon. Consultees suggested that an MTA to bring all of the guidance together is needed, but for the time being, simprevir should be considered as part of the STA process to ensure timely guidance can be issued.		
Population size	There are approximately 216,000 people chronically infected with hepatitis C in the UK. Approximately 50% of these patients have genotype 1 disease.		
Process (MTA/STA)	STA		

Proposed changes to remit (in bold)	Simeprevir in combination with peginterferon alfa and ribavirin for treating **genotype 1 or 4** chronic hepatitis C.
Costing implications of remit change	No changes proposed. Since the cost of simprevir is unknown, the cost impact of this technology cannot be calculated. Other treatment options (for completed treatment) cost around £22,400 per person so any cost impact will depend on the relative cost of simprevir compared to this.
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	**Serelaxin for treating acute heart failure**		
Topic Selection ID Number	5665	**Wave / Round**	R47
TA ID Number	673		
Manufacturer	Novartis		
Anticipated licensing information	***CONFIDENDIAL INFORMATION REMOVED***		
Draft remit	To appraise the clinical and cost effectiveness of serelaxin within its licensed indication for treating acute decompensation of heart failure.		
Main points from consultation	Following the consultation exercise and the scoping workshop, the Institute is of the opinion that an appraisal of serelaxin for treating acute heart failure is appropriate. The proposed remit is not appropriate. Consultees noted that the pivotal clinical trial included people with new-onset and chronic heart failure. It was considered that describing the condition as 'acute decompensation of heart failure' in the remit would not fully capture all of these people. Therefore, the remit should be amended to remove the term 'decompensation'. Consultees noted that the trial included people with dyspnoea (breathlessness), mild-to-moderate renal dysfunction, normal to high blood pressure (>125 mm Hg) who were taking loop diuretics. Clinical specialists commented that the trial was set out to assess improvements in breathlessness; but that in practice only about 25% of people with acute heart failure would present with symptoms of breathlessness and because of the inclusion criteria in the supporting trial, the evidence base would only support the use of serelaxin, if licensed, to such people. Furthermore, since the trial included people with mild-to moderate renal dysfunction and with normal to high blood pressure, this further restricted who might be suitable for treatment with serelaxin. Consultees considered that the population in the scope should reflect the participants in the trial and therefore should specify that these people are presenting with breathlessness and have renal dysfunction. Consultees agreed that because 'normal to high blood pressure' is proposed to be specified in the licensed indication, as this is a safety issue, that this does not need to be explicitly stated in the population as any recommendation from NICE will be within the licensed indication for the technology. Therefore, the population in the scope should be amended to 'people with breathlessness due to acute heart failure who have associated renal dysfunction and are receiving loop diuretics'. Note: Decision makers at the DP4 meeting considered that the population should be broadened to remove the requirement for loop diuretics. The population in the scope has been updated accordingly to "people with breathlessness due to acute heart failure who have associated renal dysfunction". Consultees commented that inotropes are rarely used in the patient population considered for this technology and would		

	therefore not be relevant comparators, and should be removed from the scope. Decision makers at DP4 considered that the comparators in the scope should be amended to 'Established clinical treatment without serelaxin (including intravenous nitrates and loop diuretics). Clinical specialists at the workshop highlighted that the proposed outcome 'signs and symptoms of heart failure' needs to be more specifically defined in the scope. Consultees agreed that breathlessness was the most relevant symptom and therefore the most relevant outcome to capture since this is the symptom that patients present with and the main clinical trial supporting the marketing authorisation application was designed primarily to capture improvements in dyspnoea (breathlessness). Consultees also heard from the manufacturer that signs such as 'crackles' and 'oedema' had also been assessed in the trial that these would be relevant signs of heart disease. Consultees agreed that 'renal function' was more relevant as a safety outcome since it has been shown to be affected by other treatments in clinical trials. Therefore, the outcome 'renal function' should be removed and 'adverse effects of treatment' should be amended to: 'adverse effects of treatment (including renal function)'. In addition, the outcome 'signs and symptoms of heart failure' should be removed and two outcomes 'breathlessness' and 'signs of heart failure' should be included in the scope instead.
Population size	There are around 60,000 acute heart failure admissions each year, however, the evidence base and the proposed wording for marketing authorisation may only allow use of the technology in a small fraction of people with acute heart failure. It was estimated by the clinical specialists that the number of patients who would be eligible for serelaxin in the UK could potentially be as low as 1-2% of people presenting with acute heart failure. This takes into account that only 25% of patients with acute heart failure present with breathlessness at rest and • of these approximately half would have a BP >125mm/Hg; • of those remaining approximately 50% would have mild to moderate renal failure; and • of these approximately 75% would not have the correct troponin level.
Process (MTA/STA)	STA
Proposed changes to remit (in bold)	To appraise the clinical and cost effectiveness of serelaxin within its licensed indication for treating acute **~~decompensation of~~** heart failure.
Costing implications of remit change	Since there are around 60,000 admissions for heart failure in England per year, using clinical specialist estimates that only 1-2% of people presenting with heart failure would be eligible for treatment with serelaxin, the actual eligible population may be around 900 people per year (1.5% of 60,000).

	The cost of the drug is unknown. The indicated use of the drug is as an alternative treatment option to be administered by intravenous infusion over a 48 hour period. Current practice is to administer vasodilators by intravenous infusion over a period of time which may vary for each person. It is anticipated that the administration of serelaxin will not extend hospital length of stay. There may however be offsetting savings arising from reduced length of hospital stay and reduced subsequent readmissions to hospital. Since the cost of serelaxin is unknown and the extent of the off-setting savings are unclear, the cost impact of this technology cannot be estimated.
Timeliness statement	***CONFIDENDIAL INFORMATION REMOVED***