Providers: ***(Surrey & Sussex NHS Foundations Trust, Royal Surrey County NHS Foundation Trust, Epsom & St Helier University Hospital NHS Trust, Kingston Hospital NHS Foundation Trust, Ashford & St Peter NHS Foundation Trust)*** **Commissioners** ***(East Surrey CCG, Guildford & Waverley CCG, North West Surrey CCG, Surrey Downs CCG, Surrey Heath CCG, Crawley CCG, Horsham & Mid-Sussex CCG)***

Evidence review for consideration

This template should be completed when applying to either:

- Add a treatment onto a provider formulary OR
- Request consideration by the Prescribing Clinical Network for use where the treatment could potentially impact on primary and secondary care

Please ensure that all fields are completed and use the guidance notes within the template to formulate your review.

Please be aware that this consolidated review template is to ensure that any evidence review can be discussed at provider and commissioner level. This will ensure that there are minimal delays in any potential implementation.

Please ensure that you follow your organisations individual standard operating procedure for ensuring this evidence review is discussed at local level

Intervention details	
Name, brand name	Infliximab (Inflectra, or other biosimilar)
Manufacturer	Inflectra = Hospira; Remsima = Napp
Proposed indication	Management of immune checkpoint inhibitor-associated colitis which is refractory to steroids Notes: 1. Immune checkpoint inhibitors include: **Ipilimumab** (currently NHSE-funded for melanoma) and **Pembrolizumab** (currently NHSE-funded for melanoma and non-small cell lung cancer) and **Nivolumab** (currently funded for renal cell carcinoma, melanoma, NSCLC, Hodgkin's disease and Head & Neck cancer) and **Ipilimumab and Nivolumab concurrently** (NICE approved for melanoma) - this combination carries the highest risk of adverse events including colitis. 2. Ulcerative colitis is a long term, idiopathic condition, managed by gastroenterologists. However, **immune checkpoint inhibitor-associated** colitis is a very different presentation, which is more aggressive than seen in most patients with IBD. The time course can be rapid, colonic perforation is a significant risk (up to 6% with ipilimumab-related colitis) and management is therefore significantly more aggressive and rapid than in conventional inflammatory bowel disease. Medical oncologists with experience in immunotherapy are the relevant specialists to prescribe infliximab in this setting, and not gastroenterologists.
Licensed status?	Infliximab is indicated for treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies.

Requested by	Dr Mazhar Ajaz, on behalf of all oncology consultants who are now using immune checkpoint inhibitors in the treatment of cancer.

SUMMARY

Clinical Effectiveness

Summarise results from trials, or evidence reviews, or if available include summary of evidence review from Trusted source where it exists.

Immunotherapy with MABs targeting CTLA-4 (e.g. ipilimumab), PD-1 (e.g. pembrolizumab, nivolumab) and PD-L1 is becoming the standard of care for an increasing number of indications within cancer.
Therefore an increasing number of patients will be exposed to these drugs, with a chance of developing toxicities from these treatments.
Any organ or tissue can be involved in an immune-related adverse event, with the colon being one of the more frequently affected.

European Society for Medical Oncology(ESMO) published clinical practice guidelines, for management of immunotherapy-related toxicities, this year:
Haanen, J et al; Management of Toxicities from Immunotherapy; ESMO Clinical practice Guidelines for diagnosis, treatment and follow-up;
Annals of Oncology 2017; 28 (Supplement 4): iv119–iv142, 2017

Below is a summary of the evidence for infliximab, under the section for management of colitis:

Published evidence for the use of infliximab in steroid-refractory colitis is mainly for ipilimumab-induced colitis.

There are no published clinical trials for management of this adverse event; the publications are mainly retrospective reviews or reports.

Where infliximab is used for steroid-refractory ipilimumab induced colitis, the published response rate is high; 83-100%.

There is only one case report in the literature for nivolumab-induced colitis requiring infliximab. This resolved promptly after a single dose of infliximab.

How much improvement in quality and/or length of life is the intervention likely to produce? i.e. what are the improvements in patient orientated outcomes

Complete resolution of symptoms can occur, including resolution of diarrhoea, abdominal pain, nausea, and weight loss.
Can avoid need for subtotal colectomy.

How likely is it that the improvement will happen? Include ARR and number needed to treat (NNT) if possible

Ipilimumab-induced colitis:
one third to two thirds of patients treated with high dose IV steroids either do not respond to steroids, or relapse during the steroid taper.
A single dose of infliximab usually provides an excellent response. Some patients may need a 2nd dose 2 weeks after the first.
Marthey et al report an 83% response rate to infliximab.

Note that ipilimumab is permanently discontinued in the event of any Grade 3 or 4 colitis.

PD-1/PD-L1 (e.g. pembrolizumab or nivolumab) induced colitis:
87.5% of patients respond to corticosteroids.
No published data on response rate to infliximab.

This is because the incidence of severe colitis is lower with PD-L1 antibodies, compared to ipilimumab; combined with the high response rate to corticosteroids, this results in a very low need for infliximab in this group.

Note that PD-1/PD-L1 antibodies should be discontinued permanently in the event of Grade 4, or any recurrent Grade 3, colitis.

What is the strength of the evidence? Use NICE / SIGN levels of evidence grading criteria to describe level of evidence and SORT criteria to describe strength of evidence
SORT criteria – see http://www.aafp.org/dam/AAFP/documents/journals/afp/sortdef07.pdf
(Note GRADE criteria is preferred, but more complex than SORT)
SORT Level 3

Safety

Summarise safety issues.
What are the safety issues, how serious are they?
What is the risk of harm from the intervention? Include ARI and number needed to harm (NNH) if possible
Are there any other risk considerations?

The most common side effect of infliximab is increased risk of infections.

Another common side effect is infusion-related reactions;

- The incidence is reduced with the use of standard pre-medication with hydrocortisone, chlorphenamine and paracetamol
- Any reactions which do develop are managed according to an agreed pathway

The most serious adverse reactions that have been reported with use of infliximab include HBV reactivation, congestive heart failure, serious infections (including sepsis, opportunistic infections and TB), serum sickness (delayed hypersensitivity reactions), haematologic reactions, systemic lupus erythematosus/lupus-like syndrome, demyelinating disorders, hepatobiliary events, sarcoidosis/sarcoid-like reaction, serious infusion reactions.
There is also an increased risk of various malignancies reported with chronic use – however, these adverse events are not relevant to this application for short-term use.

Patient impact

PRIMARY CARE – N/A	Will it be easy for the people who need this intervention to actually use it? Yes, as infliximab is already stocked in acute hospital Trusts, for the treatment of patients with ulcerative colitis. Staff are also experienced in using and administering it. To what extent does this intervention reflect the wishes or preferences of the public, the people at whom it is aimed or other stakeholders? Definitely reflects the wishes of the people at whom it is aimed Are there any commissioning or service implications to enable the intervention to be given to patients? We were led to believe by NHSE that infliximab for this indication is agreed as CCG commissioned, falling under NICE TA163.
SECONDARY CARE – YES	

Cost implications

PRIMARY CARE	Is there any cost-effectiveness data? Not to our knowledge What is the overall budgetary impact? Low patient numbers

SECONDARY CARE	How much does the intervention cost, £624 approx per dose (dose is patient weight dependent) what are the costs of comparative treatments? Methylpred 200mg IV = approx £5 drug costs What is population cost per 100,000 population? ? Are there additional health costs related to use of the intervention? No Are there any savings from using the intervention? For patients with Grade 2 refractory colitis, it is possible to treat as an out-patient and potentially prevent a hospital admission, which would occur if the colitis continues to fail to respond to steroids and worsens to Grade 3. For patients with Grade 3 or 4 colitis, the use of infliximab in patients who do not respond after up to 3 days of IV methylprednisolone may result in a shorter duration for their in-patient admission. Infliximab will save on potential cost of surgery (colectomy) for colitis; in the publication by Marthey et al, 6 out of 39 patients required a colectomy.

Relevant guidance / reviews

NICE TA163:
Infliximab is recommended as an option for the treatment of acute exacerbations of severely active ulcerative colitis only in patients in whom ciclosporin is contraindicated or clinically inappropriate, based on a careful assessment of the risks and benefits of treatment in the individual patient.

We have been informed by NHSE / Malcom Qualie that infliximab for management of colitis in the immune checkpoint inhibitor setting should be covered by this NICE guidance.
However, we are aware that NICE did not consider any evidence for infliximab in immune checkpoint inhibitor-associated colitis when deciding on this TA.

Are there any local guidelines that are relevant?

St Luke's Cancer Alliance guidelines for management of immunotherapy-related adverse events have just been launched – available at:
http://stlukescanceralliance.co.uk/wp-content/uploads/2015/10/Management-of-Immunotherapy-Toxicities-V1-10.17.pdf

These guidelines will be followed at Ashford & St Peter's Hospital, Surrey & Sussex Healthcare Trust, and Frimley Park Hospital, as well as Royal Surrey County Hospital.

Likely place in therapy relative to current treatments and suggested protocol for use (Primary & Secondary Care)

Describe likely place in therapy and which patient's it should be used in.

1. For immunotherapy patients with Grade 3/4 colitis and who have been initiated on IV steroids (methylpred 1-2mg/kg/day), but no improvement seen after 72 hours, or worsening severity after 24 hours

2. For immunotherapy patients with Grade 2 colitis which has not responded to at least 3 days of oral steroids and also not responded to 3 days of IV steroids

Where does the intervention potentially fit in the context of national or local guidance

No national guidance.
As described above, within the newly-launched local guidelines

Is the intervention likely to be used more widely than intended?

Immune checkpoint inhibitor usage in cancer is continually increasing.
Therefore the number of patients at risk of immune-related colitis is also increasing.
However, the expertise and experience in managing these symptoms is also increasing, along with an increased awareness of the importance of initiating steroid therapy early.

Indicate potential prescribing status
RED
If the intervention is for an unlicensed use is there a licensed equivalent and if so why is this not being considered for use? N/A
Is the intervention likely to be suitable for shared care?
NO
Include advantages and disadvantages?

Disadvantages are cost, and IV administration, and risk of side effects

Advantages are:

- infliximab is considered the best therapeutic option in the group which is refractory to steroids.
- Prompt resolution of the colitis allows in-patients to be discharged; and may avoid admission in those with Grade 2 steroid refractory
- Patients may continue with their immunotherapy treatment for their cancer **only** once the adverse reaction remains at Grade ≤ 1 **and** corticosteroid dose has been reduced to ≤ 10 mg prednisone or equivalent per day if this occurs within **12** weeks of the previous dose.
- Note that re-starting immunotherapy would **not be considered** in the event of Grade 4 colitis, or recurrent Grade 3 colitis, or the 1st episode of Grade 3 colitis induced by ipilimumab.

Any capacity issues for the service if this intervention is added to formulary at provider level and has there been any dialogue with commissioners already?
Yes, dialogue with commissioners.
No capacity issues – low usage

Recommendation to Prescribing Clinical Network/Drugs & Therapeutics Committee/ New Drugs & Interface Groups

Recommend to add to formulary, for management of immune checkpoint inhibitor-associated colitis refractory to steroids.

RED = specialist only drug

Equality Impact Assessment

Consider impact of the recommendations being made on the 9 protected characteristics (Equality Act 2010)

Protected Characteristic	No impact? (mark X against each characteristic that applies)	Positive impact? (mark X against each characteristic that applies)	Adverse (negative) impact? (mark X against each characteristic that applies)	If adverse (negative) impact, how can this be mitigated? (please add comments below)
Age	x			
Disability	x			
Gender reassignment	x			
Marriage & civil partnership	x			
Pregnancy & maternity	x			
Race	x			
Religion & belief	x			
Sex	x			
Sexual orientation	x			

Impact to primary care

No impact to primary care

Impact to secondary care

Consider availability/supply
Supply already
Likelihood of need prescribing/monitoring in secondary care
All patients will be treated in secondary care
Are local Trusts commissioned to provide this service?
Yes
Consider if non-drug related activity is required i.e. additional resource / clinic capacities.
No
Any saving on drug costs / non-drug activity anticipated
Save on cost of extended courses of high dose steroids
Save on number of days of in-patient admissions
Can we be sure that the intervention will be delivered to the right people, at the right time, in the right place, by the right personnel? i.e. are there any service delivery or commissioning considerations

Impact to CCGs

Consider if non-drug related activity is required i.e. further commissioning needs
Any saving on drug costs / non-drug activity anticipated

Intervention details

Name and brand name	Infliximab (Inflectra, or other biosimilar)
Licensed indication, formulation and	Licensed indication: Infliximab is indicated for treatment of moderately to severely active ulcerative colitis in adult patients who have had an inadequate response to

usual dosage	conventional therapy including corticosteroids and 6-mercaptopurine (6-MP) or azathioprine (AZA), or who are intolerant to or have medical contraindications for such therapies. Dosage = 5mg/kg Administered in 250ml sodium chloride 0.9%, according to Trust guidelines
Complex calculation	Prepared in aseptic unit, using worksheet already in place for infliximab for UC patients. Or pre-filled 250ml bags may be purchased.
Summary of mechanism of action, and relevant pharmacokinetics	Include brief summary of pharmacology, and relevant pharmacokinetics Infliximab is an immunosuppressant; a tumour necrosis factor alpha inhibitor. At single doses of 3, 5, or 10 mg/kg, the median C_{max} values were 77, 118 and 277 micrograms/mL, respectively. The median terminal half-life at these doses ranged from 8 to 9.5 days. In most patients, infliximab could be detected in the serum for at least 8 weeks after the recommended single dose of 5 mg/kg for Crohn's disease
Therapeutic risk	There is a significant risk of patient harm if the intervention is not used as intended.
Total number of product risk factors (For injectable products only)	Six or more risk factors = high-risk product (Red). Risk reduction strategies are required to minimise these risks. Three to five risk factors = moderate-risk product (Amber). Risk reduction strategies are recommended. One or two risk factors = lower-risk product (Green). Risk reduction strategies should be considered. Any trust/clinical governance issues that need to be raised? At RSCH, all doses would be prepared in aseptics, as already set up for current infliximab use outside of cancer. At the other Trusts, standard practice is for infliximab to be supplied as vials, for nurses to prepare dose at the bedside, according to local Trust procedures. This would be the same for this indication.
Important drug interactions	Corticosteroids do not appear to affect the pharmacokinetics of infliximab to a clinically relevant extent.
Side effects	See Infliximab SPC The most common side effect of infliximab is increased risk of infections. The most serious adverse reactions that have been reported with use of infliximab include HBV reactivation, congestive heart failure, serious infections (including sepsis, opportunistic infections and TB), serum sickness (delayed hypersensitivity reactions), haematologic reactions, systemic lupus erythematosus/lupus-like syndrome, demyelinating disorders, hepatobiliary events, sarcoidosis/sarcoid-like reaction, serious infusion reactions. There is also an increased risk of various malignancies reported with chronic use – however, these adverse events are not relevant to this application for short-term use.
Precautions	See Infliximab SPC
Contraindications	See Infliximab SPC

Pregnancy & Lactation	See Infliximab SPC
Monitoring requirements	Include any relevant information on monitoring requirements either for efficacy or toxicity Close monitoring of colitis symptoms, as already ongoing before infliximab administered Monitor for development of atypical infections, as discussed above
Prescribing considerations	• Likely traffic light status (see attached guidelines) **RED**
Other considerations	How does this treatment link to documents already on the prescribing advisory database? Will there need to be other documents reviewed and if so how do they need to be updated? Consider timescales (within 3 months,6 months etc.?) N/A Does the intervention need to be available in the out of hours period? Yes, could be administered out of hours as an in-patient in severe cases. If out of aseptics opening hours, some batch bags of infliximab are held as stock in the RSCH pharmacy. At ASPH, FPH and SASH, it is standard practice for nurses to prepare the dose on the ward, using vials provided by pharmacy. For out of hours supply in this scenario, the usual Trust procedures could be followed, as necessary.

Potential patient group (if appropriate to include)	
Brief description of disease	Include disease severity, morbidity and mortality, prognosis Immunotherapy-induced colitis, refractory to high dose steroids. Currently, cancers with NHSE or CDF funding for immunotherapy include melanoma, NSCLC, renal cell carcinoma, Head & Neck cancer, and Hodgkin's disease.
Potential patient numbers per 100,000	Describe number of patients affected and potential number of patients likely to receive the treatment The number of patients across the catchment for the St Luke's Cancer Centre who might develop steroid-refractory colitis after treatment with immunotherapy for cancer is difficult to accurately predict per 100,000. In the last 12 months, across the St Luke's Alliance, about 130 patients have received 1 or more doses of pembrolizumab, nivolumab or ipilimumab - breakdown as follows: Pembrolizumab 92 patients Ipilimumab + Nivolumab regimen 22 patients (of which most go / will go on to have Nivolumab monotherapy) Nivolumab 18 patients (of which 8 previously had ipi/nivo) Ipilimumab only 2 patients However, the number of patients receiving immunotherapy is rising, particularly pembrolizumab and nivolumab.

	It is those receiving Ipilimumab + Nivolumab concurrently, or Ipilimumab, who are most at risk of developing steroid-refractory colitis. Historically, usage of infliximab has been very low, with < 5 doses ever used at RSCH, to memory, since 2012, when we started using immunotherapy in cancer. So, historically, that is approximately 1 patient per year. All immunotherapy patients used to be asked to come to the RSCH A&E, if they experienced any toxicity. But this is not the case now, and they go to their nearest A&E. We don't have any information on infliximab potentially administered at any of the other Trusts, following an acute admission via their A&E. Looking at the available literature, Beck et al quote an incidence of 2% of **ipilimumab** patients requiring infliximab to manage colitis. The overall requirement for infliximab for colitis, for all immunotherapy patients being treated within the St Luke's Alliance, would be predicted to be significantly less than the 2% of patients quoted in the Beck paper, as: - only a minority (< 18%) of patients in the St Luke's catchment are being treated with ipilimumab-based immunotherapy - the majority only receive PD-1 antibodies, which are associated with a lower incidence of steroid-refractory colitis, with only one published case report regarding use of infliximab in that setting.
Patient outcomes required	Describe desired treatment benefits, and what outcomes/benefits, and size of effect are considered clinically significant Resolution of colitis. Avoidance of colectomy. A secondary outcome is that resolution of colitis may allow resumption of anti-cancer immunotherapy, if considered appropriate. Note that: a) in all cases, further immunotherapy treatment is withheld until colitis resolved to Grade ≤ 1 and the corticosteroid dose has been reduced to ≤ 10 mg prednisone or equivalent per day. b) Ipilimumab should be permanently discontinued in the event of any Grade 3 or 4 colitis c) Pembrolizumab or nivolumab should be permanently discontinued in the event of any Grade 4 colitis. d) further immunotherapy may not necessarily be clinically required

Summary of current treatment pathway

Include treatment options, relevant national or local guidance, and place in care pathway

Local pathway/guidelines now available at (see page 3 for management of colitis):
http://stlukescanceralliance.co.uk/wp-content/uploads/2015/10/Management-of-Immunotherapy-Toxicities-V1-10.17.pdf

G3/4 colitis

- immediately initiate IV methylpred 1-2mg/kg/day.
- If no improvement within 72 hours, or worsening after 24 hours, consider a dose of infliximab 5mg/kg. A repeat dose after 2 weeks may occasionally be required.

G2 colitis, persisting for > 3 days despite loperamide and symptomatic management

- Initiate oral pred 0.5 – 1 mg/kg/day (non-enteric coated, max 60mg/day)
- If no improvement within 72 hours, or worsening, initiate IV methylpred 1-2mg/kg/day.
- If no improvement within 72 hours, or worsening, consider a dose of infliximab 5mg/kg. A repeat dose after 2 weeks may occasionally be required.

In all cases, further immunotherapy treatment is withheld until colitis resolved to Grade ≤ 1 and the corticosteroid dose has been reduced to ≤ 10 mg prednisone or equivalent per day.

Ipilimumab should be permanently discontinued in the event of any Grade 3 or 4 colitis.
Pembrolizumab or nivolumab should be permanently discontinued in the event of any Grade 4 colitis.

Evidence review

If there is an up to date summary of the evidence from a Trusted source e.g. NICE evidence summary new medicines (ESNM), MTRAC, SMC, AWMSG, London Medicines Evaluation Network attach the summary, it is unnecessary to do an evidence review
If an up to date summary of the evidence is not available – summarise the clinical evidence supporting the application for both efficacy and safety.
Outline and summarise the clinical literature reviewed. Include a brief explanation of the trials included and the rationale for focusing on specific studies (for example, active comparator RCTs only may be considered, or a recent meta-analysis). For included studies summarise key characteristics; for RCTs, for example:

- The trial design including the population
- The number of subjects and the allocation process
- The primary efficacy endpoint
- The key results and their statistical / clinical significance

Follow this with a summary of the strengths and limitations of the efficacy data, and key safety data identified in the studies.
Further tips are included in the SOP for writing evidence reviews

Up to date review provided in ESMO guidelines 2017

Equity / Stakeholder views (if relevant)

Decisions of local Trusts DTCs and neighbouring APCs	Include decisions from neighbouring APCs or DTCs if known None known
Recommendations from national /	Include conclusions or recommendations from NICE, SMC, AWMSG, MTRAC etc

regional decision making groups	None
Stakeholder views	Use the enclosed proforma to obtain views from clinicians Summarise who has been consulted e.g. secondary care consultants, what their views are and any declared conflict of interest Have views of patient groups been sought? I can confirm that the St Luke's oncology consultants who use immunotherapy want access to infliximab on the rare occasions when it is needed. This is very low usage – views of patient groups have not been sought and not considered appropriate to do so.
CCG priorities	Does this treatment fit with existing national, regional or local priorities, policies or activity?

Health economic considerations	
Cost per year per patient	Include annual cost per patient, and population cost per 100,000 people Usually a single dose of infliximab is all that is required This currently costs £624 approx, using a biosimilar infliximab (dose is patient weight dependent)
Alternative treatments cost per patient per year	Include comparable costs of alternative treatments at patient and per 100,000 population if relevant Not relevant
Other financial considerations (if relevant)	Include additional costs such as monitoring costs, and any potential off-set costs Potential off-set costs include reduction of in-patient admissions and reduced incidence of need for colectomy
Health economic data (if available)	Include information from relevant health economic analysis, indicate the level of robustness of the analysis

References

Include references written in Vancouver style

Haanen, J et al;
Management of Toxicities from Immunotherapy; ESMO Clinical practice Guidelines for diagnosis, treatment and follow-up;
Annals of Oncology 2017; 28 (Supplement 4): iv119–iv142, 2017
doi:10.1093/annonc/mdx225 (page iv 128-131)

The above ESMO guidelines include the following references for infliximab in colitis:

Horvat TZ, Adel NG, Dang TO et al. Immune-related adverse events, need for systemic immunosuppression, and effects on survival and time to treatment failure in patients with melanoma treated with ipilimumab at Memorial Sloan Kettering Cancer Center. J Clin Oncol 2015; 33: 3193–3198.
Retrospective review of 298 patients who had received ipilimumab.
35% required systemic corticosteroid treatment for an irAE (not necessarily colitis)
10% also required anti-TNFα therapy to manage the adverse event.
19% discontinued therapy because of an irAE, which was most commonly diarrhoea.

Gupta A, De Felice KM, Loftus EV, Jr, Khanna S. Systematic review: colitis associated with anti-CTLA-4 therapy. Aliment Pharmacol Ther 2015; 42: 406–417.
Review of studies published in PubMed before Nov 2014, and looking at CTLA-4 antibodies (ipilimumab or tremelimumab) and colitis.
Summary points:
Diarrhoea reported in 27-54% of patients on CTLA-4 therapy.

Diffuse acute and chronic colitis are the most common findings on endoscopy (8-22%).
Most cases may be successfully managed with discontinuation of anti-CTLA-4 and conservative therapy.
Those with persistent grade 2 and grade 3/4 diarrhoea should undergo endoscopic evaluation and require corticosteroid therapy.
Corticosteroid-resistant cases may respond to anti-tumour necrosis factor-alpha therapy such as infliximab.
Surgery is reserved for patients with bowel perforation or failure of medical therapy.

Beck KE, Blansfield JA, Tran KQ et al. Enterocolitis in patients with cancer after antibody blockade of cytotoxic T-lymphocyte-associated antigen 4. J Clin Oncol 2006; 24: 2283–2289.
A report of 198 patients treated with ipilimumab.
21% experienced Grade 3 or 4 colitis.
Most patients responded to high dose corticosteroids.
4 patients (2%) with steroid-refractory colitis responded promptly to infliximab.
5 patients developed perforation or required colectomy.

Marthey L, Mateus C, Mussini C et al. Cancer immunotherapy with anti-CTLA-4 monoclonal antibodies induces an inflammatory bowel disease. J Crohns Colitis 2016; 10: 395–401.
39 patients who had received anti-CTLA-4 therapy (37 ipilimumab; 2 tremelimumab) were included in this study. All had endoscopic signs of inflammation after anti-CTLA-4 therapy.
37% achieved complete remission of colitis with high dose steroids.
12 patients required infliximab, of whom 83% responded.

Gonzalez, R et al; PD-1 inhibitor gastroenterocolitis: case series and appraisal of immunomodulatory gastroenterocolitis; Histopathology 2017; 70: 558 – 567
Evaluation of 37 gastrointestinal tract biopsies from 20 patients taking a PD-1 or PD-L1 inhibitor.
Most patients responded to drug cessation and/or steroids, but follow-up endoscopies were not performed.
No reference made to the need for infliximab in any of these patients.

Also (not referenced in ESMO guidelines);

Yanai et al; Nivolumab induced colitis treated by Infliximab
Clinical Gastroenterology and Hepatology 2017; 15: e80 – e81
http://www.cghjournal.org/article/S1542-3565(16)30675-9/pdf
A case report of steroid-refractory colitis in a patient receiving nivolumab, and which resolved promptly after a single dose of infliximab.

Prepared by:

Susan Taylor, Pharmacy Dept, Royal Surrey County Hospital

Declaration of Interest:

None Date: 25.9.17

Reviewed by: Dr Mazhar Ajaz

Oncology Consultant, Royal Surrey County Hospital

Declaration of Interest: None Date: 12.10.17

Reviewed by: Carina Joanes

Lead Commissioning Pharmacist, Surrey Downs CCG

Declaration of Interest:

Date:

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
v.1				*Out for consultation*
v.2				

Comments on Evidence review