2-year surveillance 2015 – Ulcerative colitis (2013) NICE guideline CG166

Appendix A: decision matrix

Summary of new evidence from 2-year surveillance	Summary of new intelligence from 2 year surveillance	Impact
Inducing remission in people with ulcerative colitis		
166 – 01. In adults, children and young people with mild to moderate ulcerative colitis, what is the clinical and cost-effectiveness of corticosteroids, aminosalicylates and immunomodulators (mercaptopurine, azathioprine, methotrexate and tacrolimus) for the induction of remission compared to themselves (different preparations and doses), each other, combinations of preparations (oral and topical) and placebo? (1.1.1-1.1.3, 1.2.1-1.2.12)		
Mesalazine/mesalamine/5-aminosalicylates in children *Dose comparison* One RCT[1] was identified that compared the efficacy of 6 weeks of low or high body weight dependent doses of oral, delayed-release mesalamine on children and young people aged five to seventeen years with mild-to-moderately active ulcerative colitis. The study reported no differences between the two treatment groups for treatment success. **Mesalazine/mesalamine/5-aminosalicylates in adults** Three RCTs[2,3,4] on mesalazine in adult patients with mild to moderate ulcerative colitis were identified. **Oral mesalazine compared to placebo** One RCT[2] on the PINCE study compared 8 weeks of oral mesalazine (5-aminosalicylic acid) 4 g/day combined with 4 weeks of daily active enema (1g mesalazine) to placebo in patients with mild to moderate ulcerative colitis. The study reported significantly higher remission, early response to treatment, mucosal healing and rectal bleeding cessation in the intervention group compared to the control group. The study also reported that quality of life	**Mesalazine/mesalamine/5-aminosalicylates** The topic experts noted the importance of the role of creatinine in deteriorating renal function and 5ASA treatment, however no studies were identified that were relevant to this. **Vedolizumab** The topic experts noted technology appraisal 342: Vedolizumab for treating moderately to severely active ulcerative colitis (June 2015). **Tacrolimus** The topic experts noted their clinical view that there may be potential uncertainty on safety and duration for best use of tacrolimus.	**Mesalazine/mesalamine/5-aminosalicylates in children** New evidence is consistent with guideline recommendations. The new evidence comes from one study that reported no differences between low or high body weight dependent doses. CG166 currently recommends that an oral aminosalicylate should be offered to induce remission in children and young people with mild to moderate first presentation or inflammatory exacerbation of left-sided or extensive ulcerative colitis. In the full guideline, the Guideline Development Group also noted that the dosage should depend on body weight. **Mesalazine/mesalamine/5-aminosalicylates in adults** Overall, the new evidence is consistent with guideline recommendations.

Summary of new evidence from 2-year surveillance	Summary of new intelligence from 2 year surveillance	Impact
improved in both the intervention and control group, with four multiple domains significantly higher in the intervention group compared to the control group. *Mesalazine suppository compared to placebo* One RCT[3] compared the efficacy of 4 weeks daily dose of 1g mesalazine suppository or placebo in patients with mild to moderate ulcerative colitis. The population included 56% in each group with proctitis. Endoscopic remission for ulcerative colitis patients and ulcerative colitis patients with proctitis was significantly higher in the intervention group than placebo. Rectal bleeding cessation was also significantly higher in the intervention group than placebo. **Mesalazine preparation comparison** One RCT[4] compared the efficacy and safety of 8 weeks of either oral once daily (4g in the morning) or oral twice daily (2g in the morning and 2g in the evening) prolonged release mesalazine in two hundred patients with mild to moderate ulcerative colitis. All patients also received 4 weeks of mesalazine enema 1 g/day. The study reported no significant difference in clinical and endoscopic remission or difference in safety between the two groups. The study reported that once daily had a significantly higher UC-DAI score and mucosal healing and a significantly lower time to remission, compared to twice daily. **Budesonide MMX** There is NICE advice on budesonide MMX: Ulcerative colitis: budesonide multimatrix (Cortiment) [ESNM58] (June 2015). This evidence summary focuses on two RCTs[5,6] that compared budesonide MMX with placebo and found budesonide MMX was safe and more effective than placebo in inducing clinical and endoscopic remission in patients with active, mild to moderate ulcerative colitis, however the effect size was small. There was no significant difference between budesonide MMX and placebo for clinical improvement or endoscopic improvement		*Oral mesalazine compared to placebo* New evidence is consistent with guideline recommendations. One RCT reported that those receiving oral mesalazine had higher remission rates, earlier response to treatment, higher mucosal healing and higher rectal bleeding cessation compared to placebo. CG166 recommends oral aminosalicylate to induce remission in people with mild to moderate ulcerative colitis. **Mesalazine suppository compared to placebo** New evidence is consistent with guideline recommendations. New evidence found that endoscopic remission was higher in ulcerative colitis patients and ulcerative colitis patients with proctitis (56% of the population) receiving mesalazine suppository than placebo. CG166 recommends a topical aminosalicylate to induce remission in patients with proctitis. **Mesalazine preparation comparison** New evidence is consistent with guideline recommendations. New evidence found no difference in remission rates between different preparations of mesalazine. It is unclear from the abstract what specific population of ulcerative colitis, if any, the study is on. CG166 does not make any recommendations on preparations of

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Infliximab, Adalimumab and Golimumab Four relevant RCTs[7 8 9 10] were identified evaluating the use of infliximab, one RCT[11] was identified evaluating the use of golimumab and three RCTs (Suzuki 2014, ULTRA 1 and ULTRA 2 trials) [12,13 14] were identified evaluating the use of adalimumab in people with ulcerative colitis. However, guidance on infliximab, adalimumab and golimumab can be found in the technology appraisal 329: 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) (February 2015). CG166 does not review anti-TNF agents and for guidance on the use of anti-TNF agents CG166 cross refers to TA140. TA140 has now been replaced by TA329. **Vedolizumab** Four RCTs[15,16,17,18] were identified evaluating the use of vedolizumab in people with ulcerative colitis. However, guidance on vedolizumab can be found in the technology appraisal 342: Vedolizumab for treating moderately to severely active ulcerative colitis (June 2015). **Tacrolimus compared to placebo** One RCT[19] was identified that compared the efficacy and safety of tacrolimus to placebo at two weeks in sixty two patients with steroid-refractory, moderate to severe ulcerative colitis. The study reported that the clinical response rate and mucosal healing was significantly higher in the intervention group than the placebo group. There was no significant difference reported in rates of clinical remission between the two groups. The study reported the treatments were well tolerated, with minor side effects. **Etrolixumab dose comparison and compared to placebo**		aminosalicylate. **Budesonide MMX** The guideline should be read in conjunction with the NICE evidence summary on Ulcerative colitis: budesonide multimatrix (Cortiment) [ESNM58] (June 2015). This evidence summary focused on two RCTs [5,6] that found budesonide MMX had a significantly higher rate of clinical and endoscopic remission compared with placebo but the effect size was small and the clinical relevance is unclear. There was no significant difference between budesonide MMX and placebo for clinical improvement and endoscopic improvement. The evidence summary noted that the results from the Contribute trial, have not yet been fully published. Once published these results would be of relevance to the guideline. Progress of this trial will be evaluated again at the next surveillance review of the guideline. **Infliximab, Adalimumab and Golimumab** CG166 cross-refers to TA140 in recommendation 1.2.9 for the use of anti-TNF agents but TA140 has been replaced by TA329: 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). CG166 does not

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One RCT[20] was identified on Etrolixumab in patients with moderate to severely active ulcerative colitis who had not responded to conventional therapy. Participants were randomised to one of three groups, the first group received 100 mg subcutaneous etrolizumab at weeks 0, 4, and 8, and placebo at week 2; the second group received 420 mg at week 0 then 300 mg at weeks 2, 4, and 8 and the control group received placebo. The study reported that clinical remission at week 10 was significantly higher in both intervention groups compared to placebo. The study did not report any significant differences in adverse events. **Dersalazine sodium compared to mesalazine and placebo** One RCT[21] was identified on dersalazine sodium in patients with mild to moderately active ulcerative colitis. Participants were randomised to one of three groups. The first group received dersalazine sodium 1200 mg/12 h (13 patients), the second group received mesalazine 1200 mg/12 h (10 patients) and the third group received placebo (11 patients), for four weeks. The study reported significantly decreased expression of inflammatory genes in the colon biopsies of people receiving dersalazine sodium, compared to placebo or mesalazine. The study reported higher clinical remission in people receiving dersalazine sodium, compared to placebo or mesalazine. Higher adverse events were reported in the study in people receiving dersalazine sodium, compared to placebo or mesalazine. **Phosphatidylcholine "LT-02" compared to placebo** One RCT[22] was identified on phosphatidylcholine "LT-02" one hundred and fifty five patients who had not responded to mesalazine therapy, diarrhoea with blood and a simple Clinical Colitis Activity Index greater than five. Participants were randomised to receive 0g, 0.8g, 1.6g, or 3.2 g of LT-02. The study reported remission rates were higher in the 3.2g dosage group compared to placebo, however this difference was not statistically significant. The study		mention adalimumab and golimumab in recommendation 1.2.15 regarding documenting local safety monitoring policies and procedures. However, this related guideline has been included in the ulcerative colitis NICE pathway. **Vedolizumab** Topic expert feedback highlighted that vedolizumab is now available for ulcerative colitis. CG166 does not mention vedolizumab in recommendation 1.2.15 regarding documenting local safety monitoring policies and procedures. However, guidance on vedolizumab can be found in the technology appraisal 342: Vedolizumab for treating moderately to severely active ulcerative colitis (June 2015), which is not mentioned in the guideline but included in the ulcerative colitis NICE pathway. **Tacrolimus** New evidence is unlikely to impact on guideline recommendations. The new evidence comes from one study that reports findings for clinical response rate and mucosal healing that are significantly higher in the tacrolimus group than the placebo group however there was no significant difference reported in rates of clinical remission. The new evidence also reported the treatments were well tolerated, with minor side effects. CG166 also reported evidence from some

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also reported significantly higher histologic remission in groups that received LT-02 compared to placebo. The study reported mucosal healing was higher in groups that received LT-02 compared to placebo, however this difference was not significant. The study reported higher adverse events in the 3.2g dosage group compared to placebo. **BMS-936557 compared to placebo** One RCT[23] was identified on BMS-936557 compared to placebo in people with active ulcerative colitis. Patients received either intravenous BMS-936557(10 mg/kg) every two weeks for eight weeks (55 patients) or placebo (54 patients). The study reported no significant differences between the intervention or control group for clinical remission and mucosal healing rates. The study reported that the clinical response rate at Day 57 was higher in the BMS-936557 group compared to placebo, however this difference was not significant. The study reported that the clinical response and histological improvements were associated with a BMS-936557 steady-state trough concentration 108-235 mug/ml compared to placebo). The study therefore recommends further dose comparison studies. **Tofacitinib dose comparison and compared to placebo** One RCT[24] was identified on Tofacitinib dosages compared to placebo in people with moderately to severely active ulcerative colitis. For 8 weeks, patients received twice daily tofacitinib of 0.5 mg, 3 mg, 10 mg, or 15 mg or placebo. The study reported clinical response at eight weeks was not significantly difference between patients who received twice daily tofacitinib of 0.5 mg, 3 mg or 10 mg compared to placebo and a significant difference between patients who received twice daily tofacitinib of 15mg compared to placebo. Clinical remission at 8 weeks was not significantly different between patients who received twice daily tofacitinib of 0.5 mg compared to placebo however, there was a significant difference between patients who received		studies that also showed no clinically important difference between placebo and tacrolimus. However, the GDG note in the guideline that two studies did show a benefit and despite the limited evidence the GDG decided to make the recommendation to consider adding oral tacrolimus to oral prednisolone to induce remission. **Etrolixumab** New evidence is unlikely to impact on guideline recommendations. CG166 does not refer to etrolixumab. Etrolixumab does not currently have marketing authorisation in the UK and its development and regulatory status in the UK is currently: Phase III Clinical Trials for ulcerative colitis. **Dersalazine sodium compared to mesalazine and placebo** New evidence is unlikely to impact on guideline recommendations. CG166 does not refer to dersalazine sodium. Dersalazine sodium does not currently have marketing authorisation in the UK. **Phosphatidylcholine "LT-02" compared to placebo** New evidence is unlikely to impact on guideline recommendations. CG166 does not refer to phosphatidylcholine "LT-02". Phosphatidylcholine

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twice daily tofacitinib of 3 mg, 10 mg or 15mg compared to placebo. **Atorvastatin combined with standard therapy compared to placebo** One RCT[25] was identified on the efficacy and safety of atorvastatin combined with standard therapy compared to placebo, in patients with mild to moderately severe acute exacerbations of ulcerative colitis. For eight weeks patients received either once daily oral atorvastatin (20 mg) or placebo combined with standard therapy. Partial Mayo score was reported to increase significantly in the atorvastatin group compared to a decrease in the control group. There was no reported significant difference in clinical improvement between the two groups. **Basiliximab combined with prednisone compared to placebo** One RCT[26] was identified on the efficacy and safety of basiliximab used as a corticosteroid sensitising agent in patients with corticosteroid-refractory ulcerative colitis with moderate to severe ulcerative colitis. Patients were treated for a minimum of 14 days with oral prednisone (40-50 mg/day). One hundred and forty nine people received 30mg a day of prednisone until week 2, then 25mg a day in week 3, then 20 a mg/day in weeks 4 to 8. Patients were then randomly assigned to either 20 mg basiliximab or 40 mg basiliximab or placebo at weeks 0, 2, and 4. The study reported that clinical remission and adverse events were not significantly different between the intervention groups and the control groups. **Dexamethasone 21-phosphate compared to placebo during reduction of corticosteroids** One RCT[27] was identified on the efficacy of dexamethasone 21-phosphate in patients with steroid dependent ulcerative colitis. Nineteen patients were randomised to receive 9.8 +/- 4.6 mg dexamethasone 21-phosphate each month for six months and eighteen patients received placebo. The study		"LT-02" does not currently have marketing authorisation in the UK and its development and regulatory status in the UK is currently: Phase II Clinical Trials for ulcerative colitis. **BMS-936557** New evidence is unlikely to impact on guideline recommendations. CG166 does not refer to BMS-936557. BMS-936557 does not currently have marketing authorisation in the UK. **Tofacitinib** New evidence is unlikely to impact on guideline recommendations. CG166 does not refer to Tofacitinib. Tofacitinib was confirmed refusal of the marketing authorisation on 25 July 2013. However, it is currently in Phase III clinical trials for ulcerative colitis. **Atorvastatin** New evidence is unlikely to impact on guideline recommendations. The new evidence comes from one RCT that suggests that atorvastatin may not be an appropriate therapy for patients with mild to moderately severe acute exacerbations of ulcerative colitis compared to placebo. CG166 does not refer to atorvastatin which does not currently have UK marketing authorisation for use in ulcerative colitis.

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reported a significant difference for maintenance of clinical remission/maintenance of the dexamethasone 21-phosphate group and the placebo group. All patients reduced use of oral corticosteroids during the study. However, six patients in the dexamethasone 21-phosphate group and fifteen in the placebo group withdrew from the study due to clinical deterioration. In the remaining participants, the study reported a significantly higher maintenance of clinical remission or stable disease while discontinuing oral corticosteroids in the dexamethasone 21-phosphate compared the placebo group. The study also reported a significant decrease in steroid-related adverse events in the dexamethasone 21-phosphate group compared with the placebo group. **Abatacept compared to placebo** One study[28] was identified on the efficacy of abatacept in patients with moderate to severely active ulcerative colitis. One RCT (UC-IP1) in this study had a primary outcome of induction of remission. Four hundred and ninety patients were randomised to receive abatacept 30 mg/kg, 10 mg/kg, or 3 mg/kg or placebo at weeks 0, 2, 4, and 8. The study reported no significant difference in clinical response in the 30 mg/kg and 3 mg/kg compared to placebo, but a significantly higher clinical response (for 10 mg/kg compared to placebo.		**Basiliximab** New evidence is unlikely to impact on guideline recommendations. The study's findings suggest that basiliximab is not more effective than placebo at inducing remissions in people with corticosteroid-refractory moderate to severe ulcerative colitis. CG166 does not refer basiliximab and further consistent evidence demonstrating the benefits and harms of this treatment are needed before considering for inclusion in the guideline. **Dexamethasone 21-phosphate** New evidence is unlikely to impact on guideline recommendations. The evidence comes from one study with a small sample size that reported a significantly higher maintenance of clinical remission or stable disease while discontinuing oral corticosteroids in the dexamethasone 21-phosphate group compared the placebo group. CG166 does not refer to dexamethasone 21-phosphate and further consistent evidence demonstrating the benefits and harms of this treatment are needed before considering for inclusion in the guideline. **Abatacept** New evidence is unlikely to impact on guideline recommendations. The new evidence comes from

Summary of new evidence from 2-year surveillance	Summary of new intelligence from 2 year surveillance	Impact
		one study that reported no significant difference in the abatacept group compared to placebo for induction of remission. CG166 does not refer to abatacept which does not currently have UK marketing authorisation for use in ulcerative colitis.
166 – 02. In adults, children and young people with acute severe ulcerative colitis, what is the clinical and cost-effectiveness of corticosteroids and ciclosporin compared to each other and their combination (corticosteroids and ciclosporin) for the induction of remission? (1.2.13-1.2.15)		
No relevant evidence identified.	The topic experts noted that an endoscopic severity scoring has been developed by the Mayo Clinic.	No new evidence was identified that would affect recommendations.
166 – 03. Which validated tools are the most predictive of the likelihood of surgery in people with acute severe ulcerative colitis? (1.2.16-1.2.17)		
No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
Information about treatment options for people who are considering surgery		
166 – 04. For adults, children and young people with ulcerative colitis considering surgery, what information on short and long term outcomes should be offered to patients and their carers by healthcare professionals? (1.3.1-1.3.6)		
No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
Maintaining remission in people with ulcerative colitis		
166 – 05. In adults, children and young people with ulcerative colitis in remission, what is the clinical and cost-effectiveness of corticosteroids, aminosalicylates, immunomodulators (mercaptopurine, azathioprine, methotrexate and tacrolimus) for the maintenance of remission compared to themselves (different preparations and doses), each other, combinations of preparations (oral and topical) and placebo? (1.4.1-1.4.6)		
Corticosteroids	**Corticosteroids:**	**Corticosteroids**

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No relevant evidence identified. **MMX mesalamine compared to delayed-release mesalamine** One RCT[29] was identified that compared the efficacy and safety of once-daily (2.4 g) MMX mesalamine to twice-daily (1.6 g daily) delayed-release mesalamine in maintenance of endoscopic remission in 826 patients with ulcerative colitis. The study reported no significant differences in endoscopic remission, time to relapse or adverse events between the two treatment groups. **Oral mesalazine regimen comparison** One RCT[30] on the PODIUM study was identified that compared the efficacy of 12 months once daily (2g once) or twice daily (1g twice) slow-release oral mesalazine (Pentasa) in patients with left-sided ulcerative colitis. The study reported no significant difference between the intervention group and control group for clinical and endoscopic remission, mucosal healing and adverse events. **Mesalazine granules compared to placebo** One study[31] with a subgroup analysis of data from two RCTs was identified that evaluated the efficacy of mesalamine granules compared to placebo in patients with ulcerative colitis in remission who switched from other 5-aminosalicylic acid (5-ASA) formulations. The study reported that at 6 months, remission was significantly higher in the mesalamine granules group compared to the placebo group. The study also reported that maintenance of similar rectal bleeding, physician's rating of disease activity rating and stool frequency at 6 months compared to baseline was higher in the mesalamine granules group compared to the placebo group. **Immunomodulators**	**Budesonide MMX** The topic experts noted there may be potential new evidence on the use of Budesonide MMX however, no specific evidence was provided. Mesalazine/mesalamine/5-aminosalicylates CG166 notes information from the British National Formulary that was current at the time: The delivery characteristics of oral mesalazine preparations may vary; these preparations should not be considered interchangeable." Clinical feedback indicated that, in 2014, the BNF wording was changed to "there is no evidence to show that any one oral preparation of mesalazine is more effective than the other; however the delivery characteristics or oral mesalazine preparation may vary. If it is necessary to switch to different brand patients should be advised to report any changes in symptoms." The topic experts noted that there may potentially be some evidence that switching between different brands can lead to relapse and potentially an increased cost related to relapse, for example from hospital readmissions or surgery. It is noted that there are financial differences between "branded" and "branded generics" and perhaps there may therefore be a tendency to prescribe the cheaper version, despite the potential increased costs related to relapse. There may be a need for primary and secondary care specialists to discuss mesalazine	No relevant evidence identified. **Mesalamine MMX compared to delayed-release mesalamine** New evidence is unlikely to impact on guideline recommendations. The new evidence comes from one RCT that found no difference between MMX mesalamine and delayed-release mesalamine for maintenance of endoscopic remission. CG166 does not recommend a specific aminosalicylate. **Mesalazine granules compared to placebo** New evidence is unlikely to impact on guideline recommendations. The new evidence comes from one RCT that compared mesalamine granules to placebo and reported maintenance related outcomes were higher in the mesalamine granules group. Evidence included in CG166 found that oral aminosalicylates were more effective than placebo at maintaining remission. As such, CG166 recommends oral aminosalicylate for maintenance of remission, however does not recommend a specific type or preparation of aminosalicylate. **Oral mesalazine regimen comparison** New evidence is unlikely to impact on guideline recommendations. The new evidence comes from one study that reported no significant difference in once daily (2g once) versus twice daily (1g twice)

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No relevant evidence identified. **Golimumab** One RCT[32] compared golimumab to placebo for maintenance of clinical remission in patients with moderate-to-severe active ulcerative colitis, despite conventional therapy. However, guidance on golimumab can be found in the technology appraisal 329: 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) (February 2015). CG166 does not review anti-TNF agents and for use of anti-TNF agents CG166 cross refers to TA140 which has now been replaced by TA329. **Faecal calprotectin to guide pharmacological treatment** One RCT[33] was identified on the use of faecal calprotectin to guide pharmacological treatment in people with ulcerative colitis in remission. The intervention group received monthly faecal calprotectin analysis and received a dose escalation of oral 5-aminosalicylate (5-ASA) at 300micro g/g. The study reported that relapse at 18 months was not significantly different between the intervention and control group. However, the study reported a significant difference between faecal calprotectin >300micro g/g and relapse. **Abatacept compared to placebo** One study[28] was identified on the efficacy of abatacept in patients with ulcerative colitis in remission. One RCT (UC-MP) in this study had a primary outcome of maintenance of remission. The study included patients who had responded in the induction trial to abatacept at week 12 for induction of remission (please see 'abatacept compared to placebo' in 166-01). One hundred and thirty one patients were randomized to receive either abatacept 10 mg/kg or placebo every 4 weeks for 52 weeks. The study reported not significant differences in the abatacept group compared to placebo for	choice and good patient education to report deterioration in symptoms. No new evidence on switching between different mesalazine brands was identified. **Faecal calprotectin to guide pharmacological treatment** The topic experts noted that faecal calprotectin is clinically being used to detect relapse and monitor treatment.	slow-release oral mesalazine (Pentasa) for clinical and endoscopic remission, mucosal healing and adverse events. CG166 recommends once-daily dosing and recommends to "explain that once-daily dosing can be more effective, but may result in more side effects." However, the evidence in CG166 also reported no differences between different dose regimens. The GDG acknowledged in the guideline that people may prefer a once daily dosing regimen, and given the limited evidence, decided to make the recommendation for once per day. **Immunomodulators** No relevant evidence identified. **Golimumab** CG166 does not make any reference to the use of golimumab for maintenance of remission. However, CG166 cross-refers to TA140 for the use of anti-TNF agents for induction of remission but TA140 has been replaced by TA329: 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). This related guideline has been included in the ulcerative colitis NICE pathway. Currently, the use of golimumab is only recommended for the induction of remission.

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remission rates at week 52.		**Faecal calprotectin to guide pharmacological treatment** New evidence is unlikely to impact on guideline recommendations. There is a NICE diagnostic guidance (DG11) Faecal calprotectin diagnostic tests for inflammatory diseases of the bowel (October 2013) that addresses the use of faecal calprotectin tests to help differentiate non-inflammatory bowel disorders from inflammatory disorders, such as ulcerative colitis. CG166 does not cover diagnosis and faecal calprotectin was not reviewed in CG166, however it does relate to guiding treatment for the maintenance of remission. The evidence from one RCT does not show a significant difference in relapse rates between treatment guided by faecal calprotectin and the control group. Further evidence is needed before considering for inclusion in the guideline. **Abatacept compared to placebo** New evidence is unlikely to impact on guideline recommendations. The new evidence comes from one study that reported no significant differences in the abatacept group compared to placebo for maintenance of remission. CG166 does not refer abatacept. Further evidence reporting the benefits and harms of abatacept for maintaining remission in ulcerative colitis is needed before considering for inclusion in the guideline.

Pregnant women		
166 – 06. What are the consequences of using drug treatments for the induction and maintenance of remission in pregnant women? (1.5.1)		
No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
Monitoring		
166 – 07. In children and young people with ulcerative colitis, are disease activity, systemic corticosteroid use, total vitamin D and malnutrition, risk factors for poor bone health? (1.6.1-1.6.2)		
No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
166 – 08. In children and young people with ulcerative colitis, what are the optimal strategies (timing, location) for monitoring growth? (1.6.3-1.6.7)		
No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
Research recommendations		
RR – 01 What is the clinical and cost effectiveness of prednisolone compared with aminosalicylates for the induction of remission for people with moderate ulcerative colitis?		
No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
RR – 02 What is the clinical and cost effectiveness of prednisolone plus an aminosalicylate compared with beclometasone plus an aminosalicylate for induction of remission for people with moderate ulcerative colitis?		
No relevant evidence identified.	None identified relevant to this question.	No new evidence was identified that would affect recommendations.
RR – 03 What are the benefits, risks and cost effectiveness of methotrexate, ciclosporin, tacrolimus, adalimumab and infliximab compared with each other and with placebo for induction of remission for people with subacute ulcerative colitis that is refractory to systemic corticosteroids?		
Methotrexate, tacrolimus and adalimumab No relevant evidence identified.	The topic experts also identified the CYSIF trial and COmparison of iNfliximab and ciclosporin in STeroid Resistant Ulcerative Colitis: a Trial	One relevant RCT was identified evaluating the use of infliximab compared with ciclosporin in people with ulcerative colitis. However, guidance on infliximab can be found in the technology

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Ciclosporin compared to infliximab One RCT [34] on the CYSIF trial was identified evaluating the use of infliximab compared with ciclosporin in people with ulcerative colitis. However, guidance on infliximab in people for whom ciclosporin is contraindicated or clinically inappropriate can be found in technology appraisal 163. It was determined that this TA will be updated upon publication of the CYSIF trial and COmparison of iNfliximab and ciclosporin in STeroid Resistant Ulcerative Colitis: a Trial (CONSTRUCT), which is due for publication in November 2015.	(CONSTRUCT). CONSTRUCT and the CYSIF trial both compare infliximab to ciclosporin in patients with acute severe ulcerative colitis who did not respond to intravenous steroids.	appraisal 163: Infliximab for acute exacerbations of ulcerative colitis (December 2008) which is included in the ulcerative colitis NICE pathway. TA163 will undergo an update to include data from the CYSIF trial and the COmparison of iNfliximab and ciclosporin in STeroid Resistant Ulcerative Colitis: (CONSTRUCT) trial, this trial is due for publication in November 2015.
RR – 04 What is the clinical and cost effectiveness of regular maintenance treatment compared with no regular treatment (but rapid standard treatment if a relapse occurs) in specific populations with mild to moderate ulcerative colitis?		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 05 To develop and validate a risk tool that predicts the likelihood of needing surgery for adults admitted to hospital with acute severe ulcerative colitis.		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 06 In children and young people with ulcerative colitis receiving steroid treatment, what are the clinical benefits of routine monitoring of bone density, what tests should be done and how frequently?		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 07 A registry to collect data to answer 'What are the potential harms or benefits of drug treatments in pregnant women with ulcerative colitis?'		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 08 What are the information needs of people with ulcerative colitis when they are considering surgery?		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 09 What is the clinical and cost effectiveness of sulphasalazine compared to high-dose branded mesalazine for induction of remission for people with mild moderate ulcerative colitis?		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.

RR – 10 What is the validity, reliability and accuracy of available adult risk tools as a predictor for the need for surgery in people admitted into hospital with acute severe ulcerative colitis?		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 11 What is the validity, reliability and accuracy of the paediatric ulcerative colitis activity index (PUCAI) as a predictor for surgery for children and young people admitted to hospital with acute severe colitis?		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 12 In people with mild to moderate ulcerative colitis, what are the best second-line treatment strategies for induction of remission after people have failed to respond to ASA mono or combination therapies?		
See clinical review question '166-01' above.	None identified relevant to this question.	See clinical review question '166-01' above.
RR – 13 In people with subacute ulcerative colitis, what are the best second-line treatment strategies for induction of remission after people have failed to respond to oral prednisolone?		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 14 In people with mild to moderate ulcerative colitis, what are the best strategies for the induction of remission after people have failed to respond to tacrolimus?		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.
RR – 15 Establish a national registry to identify the incidence of growth failure and/or pubertal delay in ulcerative colitis and the relationship with treatment (to record treatment [steroids, ASA, immunomodulators] and growth [z scores]).		
No relevant evidence identified.	None identified relevant to this question.	No relevant evidence identified.

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Appendix A: decision matrix 2-year surveillance 2015 – Ulcerative Colitis (2013) NICE guideline CG166

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