Acute severe ulcerative colitis (ASUC) is a potentially life-threatening complication of ulcerative colitis (UC). The established principles of ASUC management combine a multidisciplinary approach, high dose parenteral corticosteroids, venous thromboembolism (VTE) prophylaxis, surgical co-management, and close observation. Rescue medical therapy includes infliximab or ciclosporin, which may obviate the need for urgent colectomy. Improved management paradigms have decreased mortality. However, short-term colectomy rates of approximately 30% have remained stable. Given this and the unmet need for serious care of ASUC patients, the GESA has reviewed its previous guidelines, focusing on improving patient outcomes and harmonizing medical practice. The authors have revised the Statements, research, and procedures to provide recommendations that are based on evidence-based medicine. The current document is a result of clinical discussions and the best practice recommendations of the GESA, as well as provide adequate quality assessments. The Australian National Health and Medical Research Council (NHMRC) grades of recommendation and levels of evidence were applied.

Statement 2: Aim
The immediate treatment aim in ASUC is to achieve clinical remission. The long-term aim should be clinical, endoscopic, and histological remission.

Statement 3: First presentation investigations - laboratory
On presentation with ASUC, tests required include FBC, EUC, CRP, ESR, LFT, Mg, lidope, lipids, abdominal x-ray, stool microscopy/culture/serology for intestinal infection.

Statement 4: First presentation investigations - endoscopy
A flexible sigmoidoscopy without any preparation should be performed, preferably within 24 hours of admission. Biopsies collected should be tested for CMV.

Statement 5: Clinical pathway
The management of patients with ASUC, where available, should be guided by a clinical pathway to aid treatment, identify variance, and to audit care.

Statement 6: Ongoing review
Ongoing assessment should include at least once daily review of haemodynamic status and abdominal examination by a medical officer, stool charts (frequency, consistency, presence of blood and estimated stool volume), FBC, EUC, CRP, albumin, and serial abdominal x-ray.

Statement 7: Management team
Patients with ASUC are best managed by a multidisciplinary team comprising gastroenterologists, infectious disease physicians, specialist nursing staff, dietitian, pharmacist, and social worker on a specialised gastrointestinal ward. If the above are not available, discussion with a specialist centre should be considered.

Statement 8: Nutrition
The nutritional status of the patient should be assessed by a dietitian. Enteral supplements should be introduced as required. There is no proven role for routine parenteral nutrition in ASUC. There is no role for intestinal prostaglandins.

Statement 9: Venous thromboembolism – inpatient
Venous thromboembolism prophylaxis should be administered to all hospitalised patients with ASUC, using subcutaneous heparin or low molecular weight heparin, and can be stopped at discharge when no longer contraindicated.

Statement 10: Venous thromboembolism – outpatients
Continuation of VTE prophylaxis for several days following discharge from hospital should be considered.

Statement 11: Corticosteroids
Intravenous hydrocortisone 100mg three to four times daily or equivalent is the standard initial treatment of ASUC and should not be delayed pending serum testing for infections.

Statement 12: Indicators for rescue therapy
A failure to improve after four doses of IV corticosteroids is defined by: i) >7, >8 stools per day or 3 stools per day with a CRP>45mg/L; ii) on day 7 >3, >3 stools per day or visible blood; or iii) a PCTA >65 (in patients <18 years old) on day 7. An emphasis should be placed on formal assessment of severity at day 3 to identify these patients.

Statement 13: Options of rescue therapy
Rescue therapies include infliximab, ciclosporin, or surgery, with the choice depending on the judgment of the treatment team, drug availability, and patient factors such as preference and prior thromboembolic failure.

Statement 14: Rescue therapy in thiopurine-experienced patients
Patients who have previously had an inadequate response to thiopurine monotherapy, which is to say intolerance or compliance (adherence or therapeutic levels of TGN for 3 months) should preferentially not receive ciclosporin. An alternative rescue therapy such as infliximab is recommended.

Statement 15: Rescue therapy – other biologics
There are currently no data on the efficacy and safety of adalimumab, vedolizumab, and golimumab in ASUC.

Statement 16: Surgery
Following failure of one rescue medical treatment, surgery is recommended. Sequential rescue medical therapies risk sepsis and a delay in surgery.

Statement 17: Efficacy of rescue therapy
The efficacy of the rescue therapy should be assessed daily in the event of deterioration or failure to improve patients should proceed to surgery.

Statement 18: Colectomy in ASUC
Colectomy in ASUC should be performed by a surgeon experienced in emergency colectomy, who will discuss with the patient regarding surgical options, which may include proctocolectomy. Patients should be reviewed by a stomal therapist where available.

Statement 19: Pouchitis
The product information of infliximab recommends infusions at week 0, 2, and 6 at a dose of 5mg/kg. The value of shorter dosing intervals and/or higher doses of infliximab to be determined.

Statement 20: Combination of infliximab and thiopurine
If infliximab and thiopurine are still required, combination of thiopurine and infliximab is more efficacious than infliximab alone.

Statement 21: Thiopurine trough level
The maintenance dose of infliximab should be guided by the trough infliximab level.

Statement 22: Ciclosporin as rescue therapy
Ciclosporin should be administered as a continuous IV infusion at the initial dose of 2mg/kg/d adjusted to blood levels (target 150-250ng/ml). Thereafter dosing is converted to oral ciclosporin at a dose of 4mg/kg/d, and adjusted for approximately three months. The target trough ciclosporin level is 150-250ng/ml.

Statement 23: Pharmacy
All rescue medical therapies should be readily available into hospital pharmacies that manage ASUC, and have a mechanism for prompt dispensing.

Statement 24: Pharmacy
There is no evidence of occupational health and safety risks relating to occupational exposure to anti-TNF agents. Standard precautions are sufficient for drug preparation and administration.

Statement 25: Maintenance therapy - thiopurines
Patients who respond to rescue medical therapy but have not yet failed thiopurine maintenance therapy (such as thiopurine-naive patients) should be commenced on ongoing maintenance therapy as a rescue medication.

Statement 26: Maintenance therapy - thiopurines
PMT pharmacokinetics should be considered if available. However, thiopurine therapy can be commenced without PMT results. FBC and LFTs should be measured weekly for 4 weeks after commencement of thiopurine, then fortnightly for next 4 weeks, and then 5-monthly.

Statement 27: Maintenance therapy – thiopurine metabolites
Metabolic levels may be used to determine the management in patients with regard to the risk of response, metabolism, and adherence.

Statement 28: Maintenance therapy – allioprophylaxis
Thiopurine metabolites (those with inadquate TGN levels and MTHFR SNP ratio >1) or patients who are intolerant of an effective dose of thiopurine, can try allopurinol with dose-reduced azathioprine or mizoribine to a thiopurine equivalent original dose in conjunction with close monitoring of FBC and LFT, and outlined in Statement 14b, and thiopurine metabolites.

Statement 29: Pregnancy
The management of ASUC in pregnant patients should be no different from the management of non-pregnant patients. Thiopurines, ciclosporin, thiopurines, infliximab, and colectomy should be used as needed in all stages of pregnancy and during breastfeeding.

Statement 30: Opportunistic infections – pneumocystis jiroveci pneumonia (PP)
Pneumocystis carinii, ciclosporin, and either a calcineurin inhibitor or infliximab require prophylaxis against PJP using cotrimoxazole 1600mg/600mg three times weekly. VZV and toxoplasma 1500mg daily are options for patients with sulphur allergy.

Statement 31: Opportunistic infections – Cytomeglovirus (CMV) disease
CMV colitis should be considered in all patients with ASUC. The diagnosis of CMV colitis, which is made on the basis of the classical of a single stool, histology, and immunohistochemistry. Additional supportive information is provided by colonic biopsy PCR and plasma PCR.

Statement 32: Opportunistic infections – GMV treatment
Treatment of CMV colitis is intravenous ganciclovir 5mg/kg twice daily for 3-5 days followed by oral valganciclovir 900mg PO twice for 2-3 weeks. Early infectious disease physician consultation is recommended. Temporary withdrawal of immunosuppressive therapy should be considered on a case-by-case basis.

Statement 33: Opportunistic infections – EBV
Seronegative-status adolescents and young adults should avoid EBV and use alternative immunomodulators.

Statement 34: Opportunistic infections – Varicella zoster virus
Varicella zoster virus activity index
Consensus Statements on the Management of Acute Severe Ulcerative Colitis (ASUC)  
November 2017

Extract from “Review article: acute severe ulcerative colitis - evidence-based consensus statements.”, JH Chen et al, Wiley AP&T, 2016 (full article available on www.gesa.org.au)

Wall Chart Supplement

Table 1: Evidence hierarchy: designations of ‘levels of evidence’ according to type of research question

<table>
<thead>
<tr>
<th>Level</th>
<th>Intervention</th>
<th>Diagnosis accuracy</th>
<th>Prognosis</th>
<th>Aetiology</th>
<th>Screening intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>I*</td>
<td>A systematic review of level II studies</td>
<td>A systematic review of level II studies</td>
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<td>A systematic review of level II studies</td>
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</tr>
<tr>
<td>II</td>
<td>A randomised controlled trial</td>
<td>A study of test accuracy with an independent, blinded comparison with a valid reference standard; 1 among consecutive persons with a defined clinical presentation 2</td>
<td>A prospective cohort study 3</td>
<td>A prospective cohort study</td>
<td>A randomised controlled trial</td>
</tr>
<tr>
<td>III-1</td>
<td>A pseudorandomised controlled trial (i.e. alternative allocation or some other method)</td>
<td>A study of test accuracy with an independent, blinded comparison with a valid reference standard; 3 among non-consecutive persons with a defined clinical presentation 4</td>
<td>All or none 5</td>
<td>All or none 5</td>
<td>A pseudorandomised controlled trial (i.e. alternate allocation or some other method)</td>
</tr>
</tbody>
</table>
| III-2 | A comparative study with concurrent controls:  
- Non-randomised experimental trial 6  
- Cohort study  
- Case-control study  
- Interrupted time series with a control group | A comparison with reference standard that does not meet the criteria required for level II and III-1 evidence | Analysis of prognostic factors amongst persons in a single arm of a randomised controlled trial | A retrospective cohort study | A comparative study with concurrent controls:  
- Non-randomised experimental trial  
- Cohort study  
- Case-control study |
| III-3 | A comparative study without concurrent controls:  
- Historical control study  
- Two or more single arm study  
- Interrupted time series without a parallel control group | Diagnostic case-control study 7 | A retrospective cohort study | A case-control study | A comparative study without concurrent controls:  
- Historical control study  
- Two or more single arm study |
| IV    | Case series with either post-test or pre-test/post-test outcomes | Study or diagnostic yield (no reference standard) 8 | Case series, or cohort study | A cross-sectional study or case series | Case series |

Table 2: Definition of NHMRC grades of recommendations

<table>
<thead>
<tr>
<th>Grades of recommendation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Body of evidence can be trusted to guide practice</td>
</tr>
<tr>
<td>B</td>
<td>Body of evidence can be trusted to guide practice in most situations</td>
</tr>
<tr>
<td>C</td>
<td>Body of evidence provide some support for recommendation(s) but care should be taken in its application</td>
</tr>
<tr>
<td>D</td>
<td>Body of evidence is weak and recommendation must be applied with caution</td>
</tr>
</tbody>
</table>

Reference: NHMRC additional levels of evidence and grades for recommendations for developers of guidelines  