

Immune-Related Adverse Event: Diarrhoea/Colitis

Gastrointestinal (GI) irAEs are common and although they are typically mild to moderate in severity, if they are left unrecognised or untreated, they can become life-threatening.

Grading of irAE diarrhoea needs to be accurately assessed to determine treatment. Patients should be fully screened for other irAEs which can occur simultaneously. Side effects can occur many months after stopping treatment

Loperamide should be used with caution as this can mask the true severity of the symptoms and can precipitate toxic megacolon.

Patients often complain of 'watery' diarrhoea, often need to get up in the night and may have associated frequency and tenesmus.

Mild (Grade 1)

- < 4 stools/day over baseline
- or mild increase in ostomy output

in the absence of abdominal pain, mucous/blood in stools

If abdominal pain, mucous/blood in stool treat as grade 2-4

Investigations:

- Baseline bloods (FBC, U&E, LFTs, TFTs, cortisol & CRP)
- Stool microscopy and culture
- C Diff toxin
- Ask patient to complete stool chart
- Faecal calprotectin

Treatment:

- Encourage fluids
- Avoid high fibre and lactose
- Consider loperamide- use with caution- can mask symptoms and precipitate toxic megacolon

Actions:

- Telephone assessment within 3 days
- Consider holding immunotherapy (if on combination anti-PD1/CTLA4 withhold immunotherapy)
- Ensure amber pathway is followed if symptoms are persistent.

Symptoms: PERSIST (>5 days) or WORSEN or associated with dehydration/deranged U & E/ nausea/vomiting

Moderate (Grade 2)

If any of the following symptoms are present:

- 4-6 stools/day over baseline or moderate increase in ostomy output
- Moderate abdominal pain/cramps/discomfort
- Mucous in stool

Clinical Assessment

Investigations:

- As per mild (grade 1)
- Abdominal X-Ray (consider CT abdo/pelvis)
- Infliximab screen as per Grade 3/4

Treatment:

- Prednisolone 60mg/day + PPI cover and taper
- Encourage oral fluids
- If associated nausea/vomiting consider admission for iv steroids

Actions:

- Omit next dose of immunotherapy
- Daily telephone monitoring until resolving
- Consider flexible sigmoidoscopy + biopsies

Assess response to treatment within 72 hours

Symptoms Resolve or improve to mild- continue steroid taper with telephone review at least weekly

Symptoms PERSIST, WORSEN or RELAPSE

Severe or Life-Threatening (Grade 3 + 4)

If any of the following symptoms are present:

≥7 stools/day over baseline or significant increase in ostomy output

- Severe abdominal pain
- Fever
- Dehydration
- Blood in stool
- Incontinence
- Limiting ADL's

Admit patient

Investigations on day 1:

- As per moderate (grade 2)
- Screen for Infliximab administration suitability on admission (to include- TB Quantiferon test, hepatitis screen, HIV, varicella zoster anti-bodies (IGG antibody), chest X-Ray (if chest CT not already performed))
- Refer for IP sigmoidoscopy with biopsies
- Daily bloods (FBC, U&E, LFTs & CRP)
- CT Abdomen/pelvis
- Regular stool chart

Treatment:

- IV hydration and fluid balance
- IV Methylprednisolone 1 mg/kg/day + PPI cover and continue for a minimum of 3 days (iv hydrocortisone 200mg tds as an alternative if methyl pred not available)
- Antibiotics are not required as standard
- Consider dietetics referral- There is no evidence for bowel rest/NMB

Use analgesia with CAUTION

Actions:

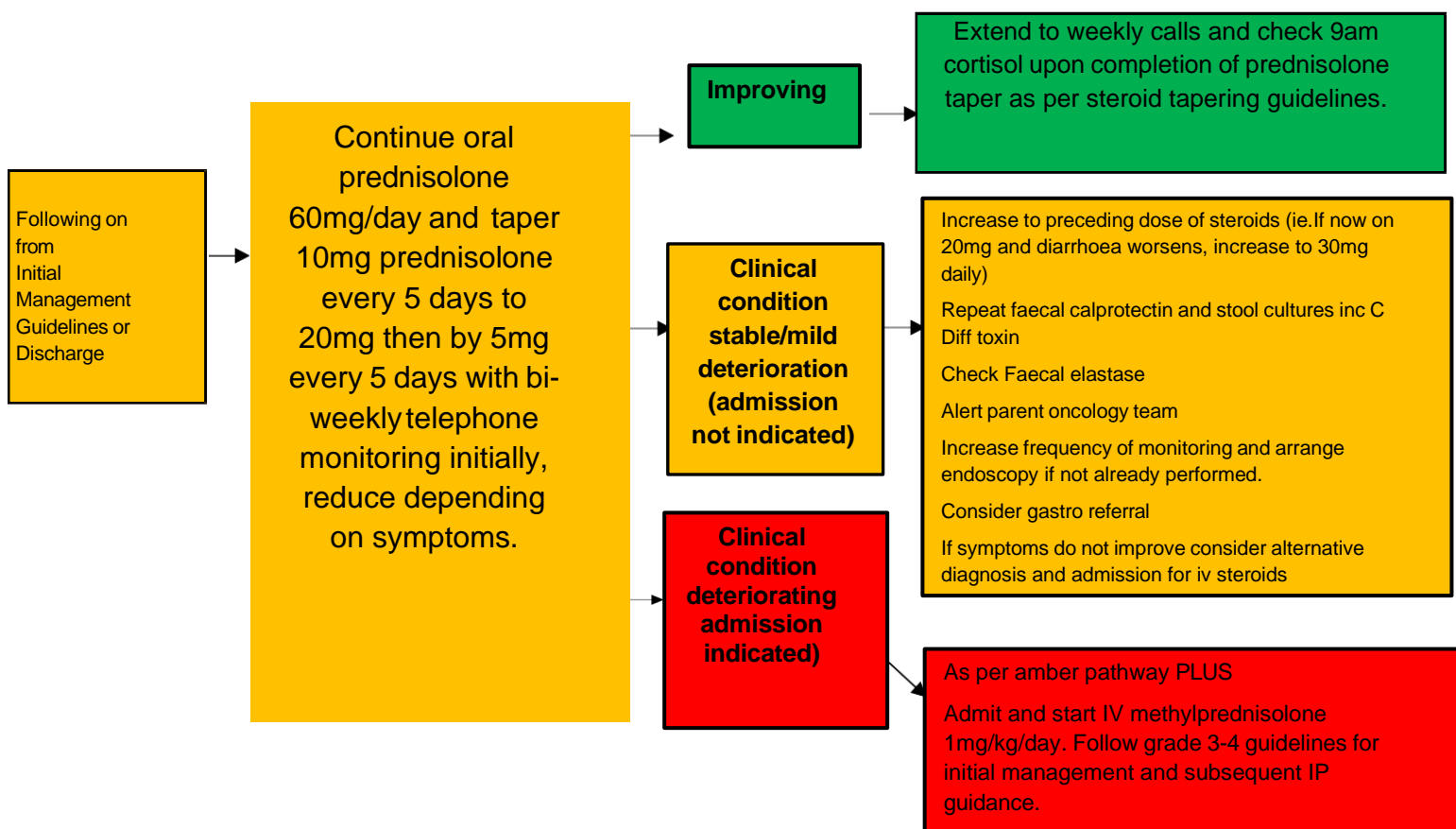
- Daily stool chart
- Consider discontinuation of immunotherapy
- Assess after 72 hours, if no improvement will need infliximab
- IP referral to gastroenterology

See subsequent IP management for next steps

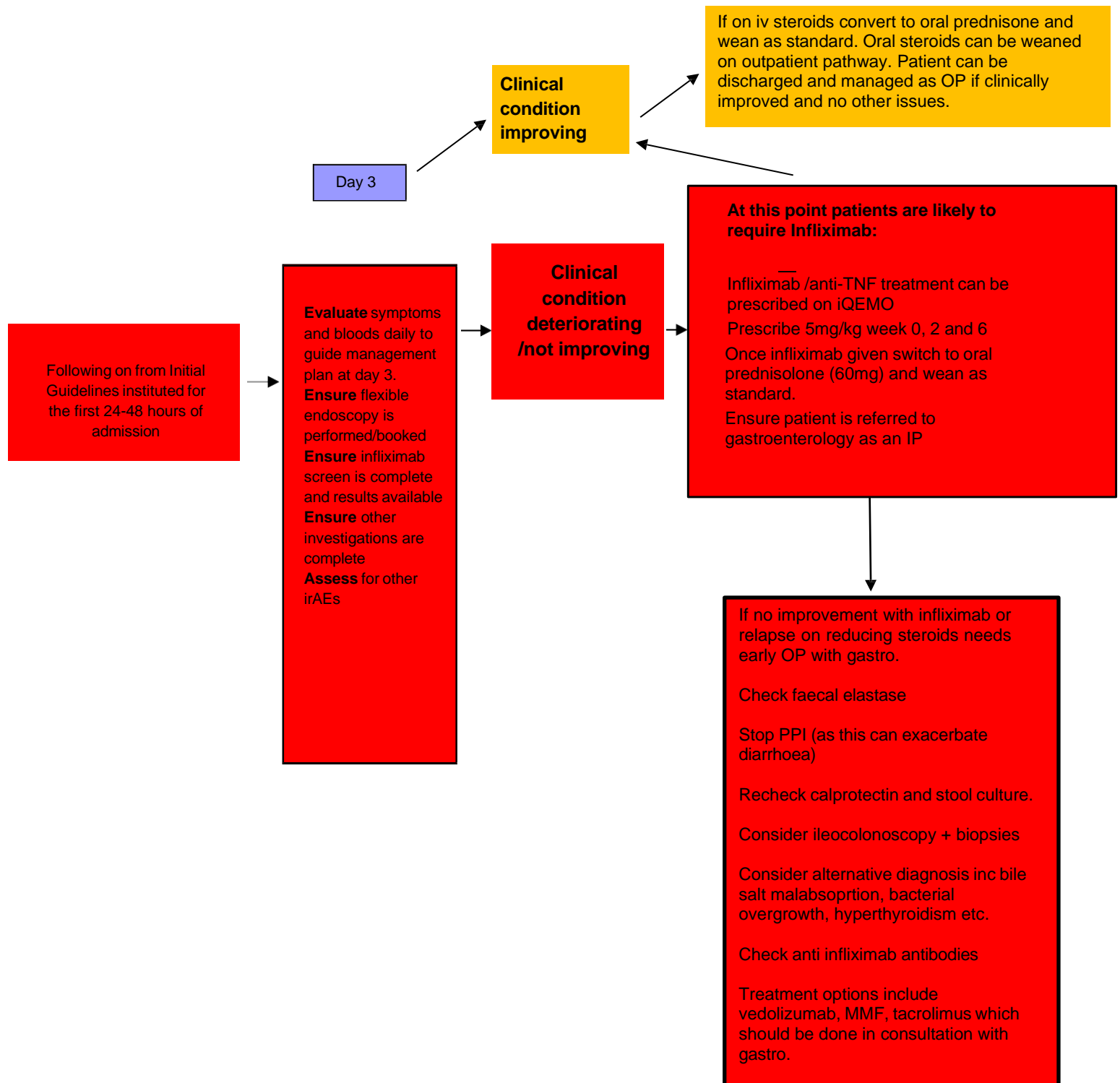
**** IMPORTANT ****Subsequent management of patients with colitis that is either not improving or worsening should always be discussed with a gastroenterologist and the patient's oncologist

Subsequent management– Diarrhoea/Colitis

Outpatient management



Inpatient Management



References:

British Society of Gastroenterology endorsed guidance for the management of immune checkpoint inhibitor-induced enterocolitis. Powell et al., Lancet Gastroenterol Hepatol 2020; 5: 679–97
 UKONS Acute Oncology Initial Management Guidance v2.0