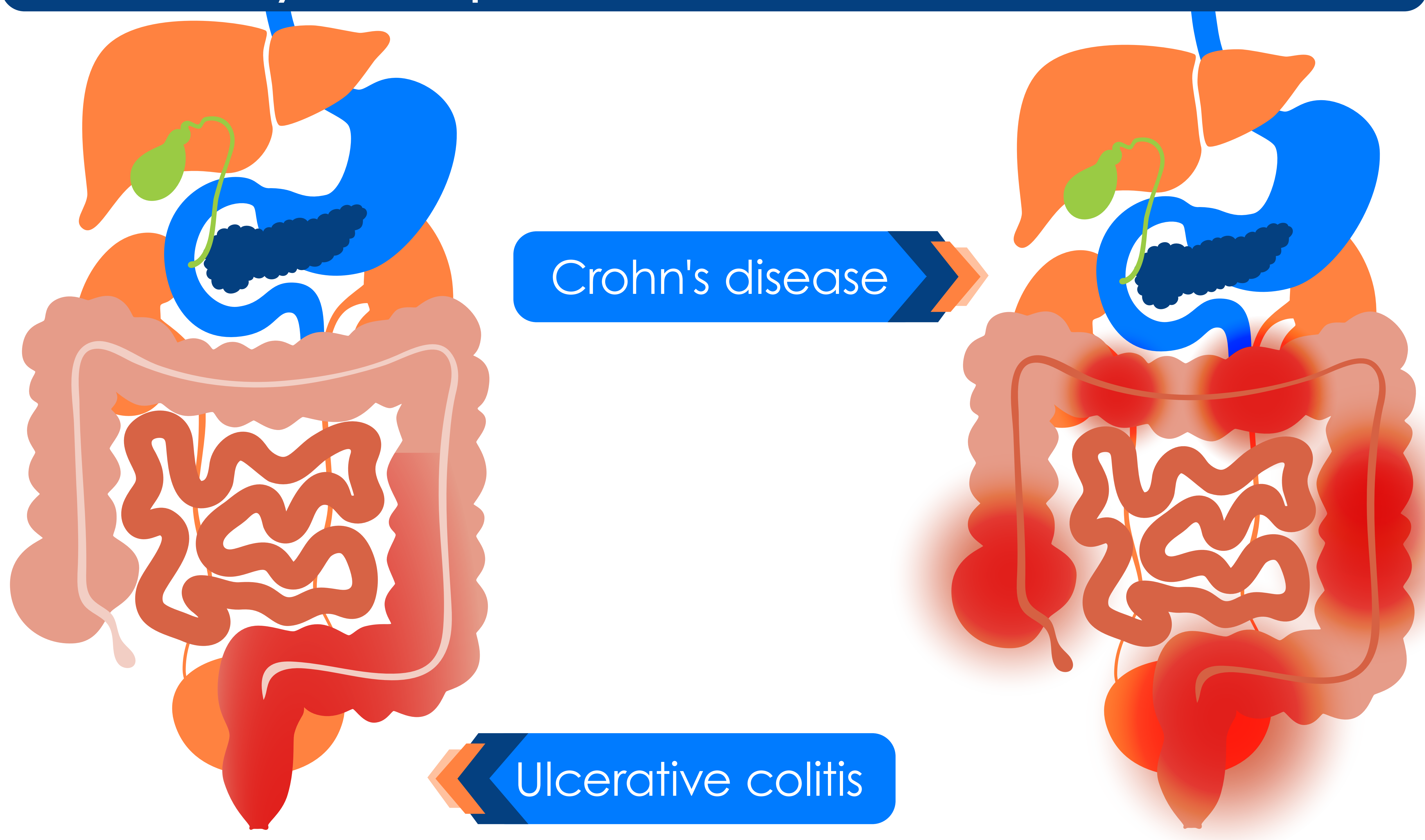


# Management of non-response and loss of response to anti-tumor necrosis factor therapy in inflammatory bowel disease

Marsal J, et al. Front Med (Lausanne). 2022 Jun 15;9:897936

Broadly, IBD comprises Crohn's disease and ulcerative colitis



## Anti-tumour necrosis factor (anti-TNF) therapy in inflammatory bowel disease (IBD)

- Is first-line biologic treatment for moderate-to-severe IBD
- Improves clinical symptoms
- Promotes endoscopic healing
- Improves quality of life
- Reduces hospitalisations and surgeries

## Sub-optimal response to anti-TNFs in IBD

### Primary non-response (PNR)

No clinical response within 14 weeks of treatment initiation

Occurs in 10-40% of people with IBD

### Loss of response (LOR)

Progressive loss of response to anti-TNFs following initial treatment response

Occurs in up to 50% of patients, annual rate is ~5–20%

**Pharmacokinetic**  
increased drug clearance

**Pharmacodynamic**  
active drug persists despite biological therapeutic levels, suggesting mechanistic factors

**Low albumin levels**  
associated with diminished clinical response, particularly in severe IBD

### Primary factors

low trough serum drug concentrations  
anti-drug antibodies (ADABs)  
reduced TNF binding capacity or suboptimal drug concentrations

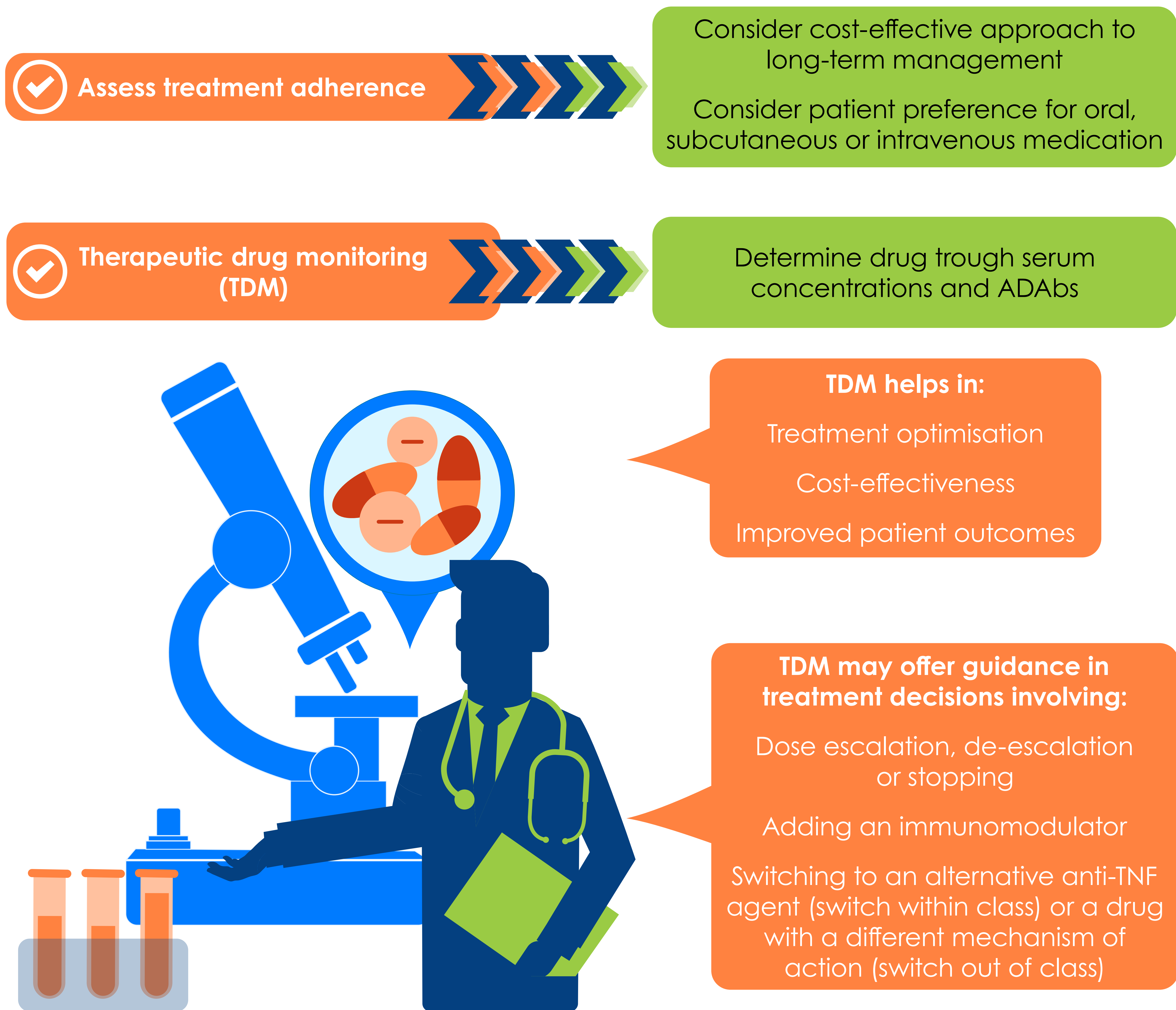
### Other mechanisms

disease transitioning to other cytokine pathways

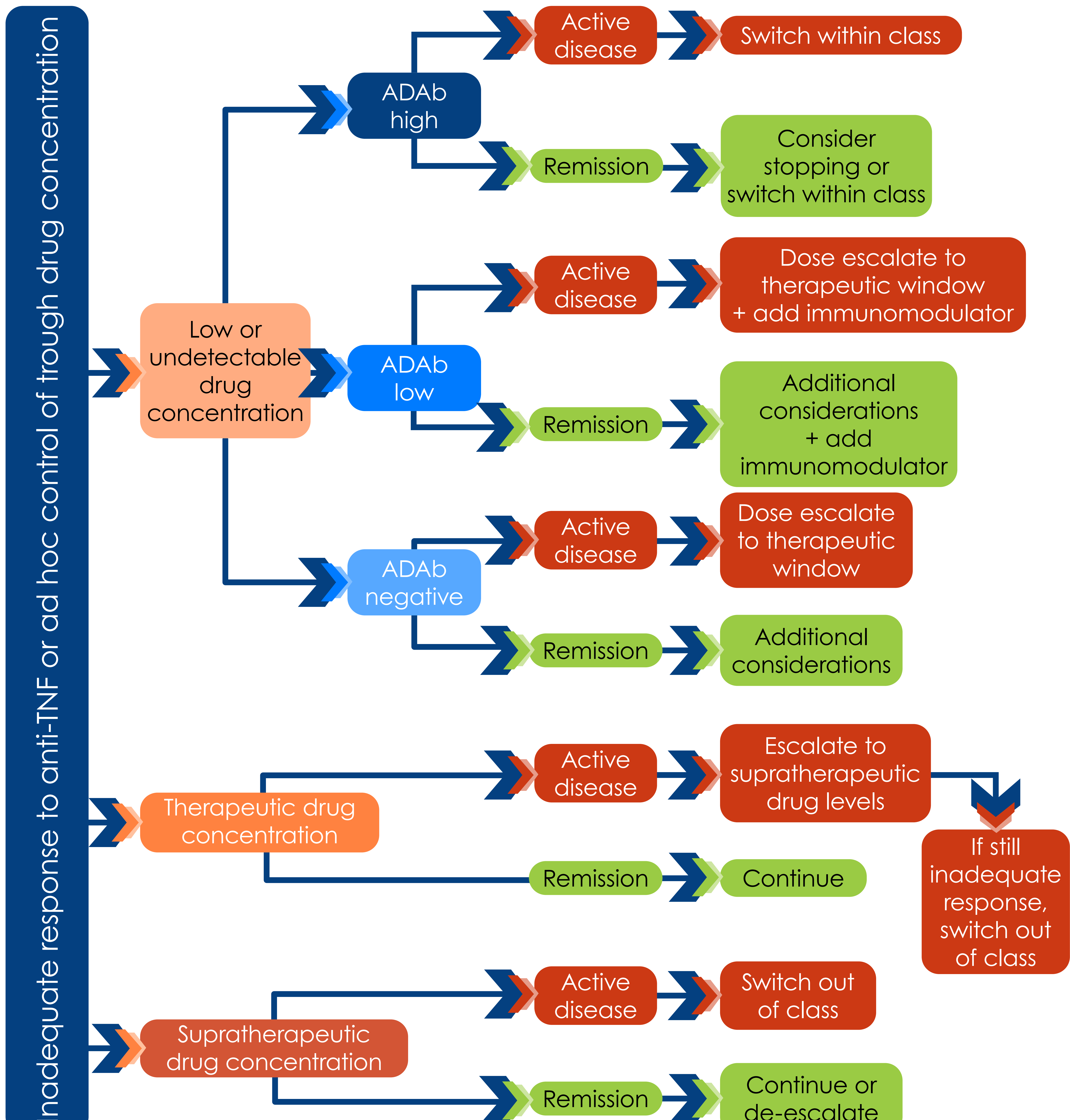
## Clinical assessment for PNR or LOR management

- Are symptoms due to an increase in IBD activity?**  
**Rule out**
  - Gastrointestinal infections
  - Bacterial overgrowth
  - Irritable bowel syndrome
  - Bile acid malabsorption
- Assess disease-associated inflammatory activity using:**
  - Blood inflammatory markers such as serum C-reactive protein and albumin
  - Faecal biomarkers such as faecal calprotectin
  - Endoscopic biopsies or resection specimens
  - Endoscopy
  - Cross-sectional imaging (MRI and computed tomography, bowel ultrasonography)

## Therapeutic management of non-response to anti-TNFs



## TDM-based algorithm for optimising anti-TNF therapy



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