

Practical guide to therapeutic drug monitoring (TDM) in inflammatory bowel disease

Thiopurines (azathioprine (AZA), 6-mercaptopurine (6MP), thioquanine (TG))

- Check TPMT (+/- NUDT15 in Asian patients) prior to commencement.

When to check metabolites:

- 4 weeks after commencement or dose change
- Periodically during maintenance
- In the event of loss of response

6- TGN target range:

- 235-450 pmol/8x10⁸ RBC (AZA/6MP)
- 800-1200 pmol/ 8x10⁸ RBC. (TG)
- Lower targets may be appropriate for patients in remission on combination therapy

Interpretation:

6-TGN	6-MMP	Action
Low/sub-therapeutic	Low/sub-therapeutic	Check adherence/Dose escalate
Low/sub-therapeutic	High (>10-20x)	If AZA/6MP consider switch to TG, split dose of AZA/6MP or add allopurinol and reduce AZA/6MP dose to 25-33%
Therapeutic		Continue current dose
High	High/Normal	Reduce dose

Anti-TNF inhibitors (infliximab (IFX) and adalimumab (ADA))

When to check:

- In the event of non-response or loss of response.
- At end of induction (Week 14 IFX and Week 8-12 ADA)
- Annually during maintenance if in remission.
- Consider checking during induction at times in the tables

Infliximab target concentrations (dose escalate if below target)

Induction	Maintenance	Specific situations
20-25 mg/L at week 2 15-20 mg/L at week 6	5-10 mg/L (7-10 mg/L at week 14)	>10 µg/mL maintenance in perianal fistulizing Crohn's disease & acute severe ulcerative colitis
		If >15 mg/L and in remission; Consider dose reduction

Adalimumab target concentrations (dose escalate if below target)

Induction	Maintenance	Specific situations
>10-14mg/L at week 4	>7 mg/L	>10 µg/mL maintenance in perianal fistulizing Crohn's disease & acute severe ulcerative colitis
		If >15 mg/L and in remission; Consider dose reduction

- All changes should be considered as part of a treat to target strategy.
- If patients have active disease (clinical, or objective markers) despite therapeutic drug levels, switch of therapy should be considered.

Antidrug Antibodies with infliximab and adalimumab

Assays for antidrug antibodies are performed automatically when the drug concentration is <2mg/L.

Interpretation of antidrug antibody result

- Negative – dose increase may successfully increase the drug concentration
- Weak positive – dose increase may possibly overcome the antibody and increase drug concentration
- Strong positive – dose increase unlikely to be successful. Consider switching drug.