Biologics Sequencing

Ulcerative Colitis

	Preferred	*Second line*	*Third line*
Bio-naïve UC	IFX / VDZ	UST	ADA
PNR to 1 anti-TNF	UST	VDZ	2nd anti-TNF
LOR to IFX	UST / VDZ	ADA	
LOR to ADA	IFX	UST / VDZ	
Age>65yo or safety concerns	VDZ	UST	Anti-TNF
Pregnancy or breastfeeding	Anti-TNF	UST / VDZ	
Extra-intestinal manifestations	Anti-TNF	UST	VDZ
ASUC	IFX		

Consider discussing challenging cases with a local or regional expert, or at a MDM for collaborative decision-making.

Consider suitability of clinical trials or referral to a trial centre to increase

Crohn's Disease

	Preferred	*Second line*	*Third line*	*Fourth line*
Bio-naïve CD	Anti-TNF	*UST	VDZ	
PNR to 1 anti-TNF	UST	VDZ	2nd anti-TNF	
LOR to 1 anti-TNF	2nd anti-TNF	UST	VDZ	
Age>65yo or safety concerns	*UST	VDZ	ADA	IFX
Pregnancy or breastfeeding	Anti-TNF	UST / VDZ		
Extra-intestinal manifestations	Anti-TNF	UST	VDZ	
Perianal and Fistulising disease	IFX	ADA	UST	VDZ

PNR = Primary Non-Response – patient failed to respond to induction therapy, 'never responded' to treatment
LOR = Loss of Response or Secondary Non-Response – patient initially responded to induction therapy, treatment became less effective over time, frequently caused by immunogenicity

Bio-naive UC:

- Infliximab is preferred as the 1st line steroid-sparing biologic if rapid response is required
- Vedolizumab is a good first line agent especially if the patient is co-morbid or age >65yo
- Consider steroids at induction given slower speed of onset
- Adalimumab may be considered as the first line biologic in milder phenotypes given subcutaneous formulation and low cost

Anti-TNF experienced UC:

- Ustekinumab is the preferred biologic if there is PNR to either anti-TNFs
- Patients with LOR to Adalimumab could switch to Infliximab if there was excellent initial response; or switch out of class (to UST/VDZ) if there was partial initial response
- Patients with LOR to Infliximab should *probably* preferentially switch out of class (to UST/VDZ)
- 2nd TNF must be co-prescribed with an immunomodulator (IMM) if LOR to 1st TNF
- Patients who are intolerant to 1 anti-TNF should consider switching out of class
- There are unfunded advanced therapies (eg upadacitinib) which has excellent efficacy in biologic-experienced patients with rapid speed of onset. This is under Pharmac review, and if funded will likely be ranked highly within the above algorithm.

Other UC Considerations:

- Infliximab is the only approved biologic for acute severe ulcerative colitis (ASUC)
- Steroids and Infliximab (consider accelerated regimen) remain the mainstay of treatment for ASUC
- Cyclosporin induction for ASUC should only be used in select cases under expert guidance
- *Consider* stopping immunomodulator co-prescription with Ustekinumab or Vedolizumab especially in the elderly patient or those with safety concerns
- Anti-TNF is the preferred biologic for EIMs including cutaneous, ocular, and articular manifestations
- Ustekinumab can be considered if there is co-existing peripheral spondyloarthropathies or anti-TNF induced paradoxical reactions
- Colectomy should be considered as a valid treatment in biologic- refractory patients

Bio-naive CD:

- Adalimumab should be considered as the first line biologic given subcutaneous formulation and low cost
- Anti-TNF is preferred for fistulising disease especially Infliximab for complex fistulising/perianal disease
- *Ustekinumab is not currently funded as first line therapy however this may change in the future, in which case it should be considered as first line therapy for luminal Crohn's, especially if age >65yo or safety concerns
- Consider vedolizumab if age >65yo or safety concerns, especially if milder disease phenotype

Anti-TNF experienced CD:

- Ustekinumab is the preferred biologic if there is PNR to either anti-TNFs
- Patients with LOR to 1 anti-TNF could consider switching to a 2nd anti-TNF if there was excellent initial response or if LOR is driven by immunogenicity; or switch to Ustekinumab if there was only partial initial response
- 2nd TNF must be co-prescribed with an immunomodulator (IMM) if LOR to 1st TNF
- Patients who are intolerant to 1 anti-TNF should consider switching out of class
- Efficacy of Vedolizumab drops in patients with previous anti-TNF/biologic failure
- There should be a low threshold for considering week 10 dose in this context – compassionate access via Takeda
- There are unfunded advanced therapies (eg upadacitinib) which has excellent efficacy in biologic-experienced patients with rapid speed of onset. This is under Pharmac review, and if funded will likely be ranked highly within the above algorithm.

Other CD Considerations:

- Both EEN and biologics should be considered as steroid sparing induction agents
- Of the biologics, Infliximab probably has the fastest speed of onset
- *Consider* stopping immunomodulator co-prescription with Ustekinumab or Vedolizumab especially in the elderly patient or those with safety concerns
- Anti-TNF is the preferred biologic for EIMs including cutaneous, ocular, and articular manifestations
- Ustekinumab can be considered if there is co-existing peripheral spondyloarthropathies or anti-TNF induced paradoxical reactions
- Ileocaecal resection should be considered as a valid treatment in short segment terminal ileal disease and an alternative to biologic therapy