

NZSG IBD Guidelines for Biologics

IBD Preventive Care

Inflammatory bowel disease (IBD) is a chronic disease. The Gastroenterology team has a long term therapeutic relationship with the patient, and is well placed to help guide long term health maintenance, in conjunction with the general practitioner^{1,2}.

Many IBD patients require long term immunosuppression and/or prolonged course of steroids. They are at increased risk of infections, some of which are preventable by vaccinations. Those with previous exposures to certain infections may also be at risk of reactivation and serious infections, which can be prevented by treatment prior to initiation of immunosuppression.

Pre-immunosuppression Screen³⁻⁵

A detailed vaccination history and previous infections should be taken at diagnosis.

Pre-immunosuppression screen should be done ideally at diagnosis for all IBD patients to allow time for treatment and/or vaccinations, but essential prior to commencing biologic therapy.

Consider repeat after changes in risks e.g. travelling, or exposure to contacts.

Significant immunosuppression includes corticosteroids (e.g. Prednisone $\geq 20\text{mg}$ daily) for >2 weeks

<i>All IBD patients</i>		
<i>Test</i>	<i>Significant result</i>	<i>Action</i>
TPMT (Thiopurine methyl transferase) genotype & phenotype ⁶ Thiopurine metabolism Increased risk of thiopurine related leukopenia, neutropenia, myelosuppression	Homozygous or compound heterozygous carriers of 2 inactivating TPMT alleles Poor metabolisers (1 in 300)	Azathioprine/Mercaptopurine 10% daily and dose 3x/week <i>or</i> Avoid Thioguanine 10% daily and dose 3x/week <i>or</i> Avoid
	Heterozygous carriers of 1 inactivating TPMT allele Intermediate metabolisers (10%)	Azathioprine/Mercaptopurine 30-80% of normal dose Thioguanine 50-80% of normal dose Monitor for myelosuppression Allow 2-4 weeks to reach steady state
Hepatitis B serology HBsAg, HBsAb, HbCAb	HBsAg +ve Chronic hepatitis B	Check HBV DNA For Hep B treatment if immunosuppression (including high dose steroids) planned
	HBsAb -ve or < 10 IU/L No immunity	Hepatitis B vaccinations (Funded if immunosuppression >28 days planned) 3 doses, to complete >4 weeks prior to starting immunosuppression. More dose may be required to achieve HBsAb >10 IU/L
	HbCAb +ve, HBsAg -ve Past infection	No treatment required Monitor HBsAg & HBV DNA every 3 months if on immunosuppression
Hepatitis C serology HCV antibody	HCV antibody +ve	Check HCV viral load, if +ve, for Hep C antiviral treatment

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HIV serology Needs pretest counselling	HIV +ve	Confirm results. Refer to Infectious Diseases for treatment
All IBD patients		
Test	Significant result	Action
Quantiferon Gold Exposure to tuberculosis	Positive Likely latent TB	CXR and refer to Infectious Diseases for treatment prior to commencing immunosuppression
	Indeterminate	Repeat testing when off high dose immunosuppression
Chest xray	Pulmonary tuberculosis	Refer to Infectious Diseases
Varicella serology	Negative	Varicella vaccination (Live) (Funded) 2 doses, to complete >4 weeks prior to commencing immunosuppression Zoster immunoglobulins if non-immune & exposed
MMR serology Measles, Mumps, Rubella	Negative	MMR vaccination (Live) (Funded) To complete >4 weeks prior to commencing immunosuppression Immunoglobulins if non-immune & exposed
Epstein Barr serology	EBV IgG -ve No past infection	Consider avoiding thiopurines due to ↑ risk of lymphoma ³
Consider in some IBD patients		
Test	Significant result	Action
NUDT-15 genotyping ⁶ Thiopurine metabolism East Asians (Chinese, Korean, Japanese, Vietnamese, Thai) Increased risk of thiopurine related leukopenia, neutropenia, myelosuppression Testing available through Canterbury Health Laboratory (NUDT15 genotyping - Canterbury Health Laboratories (chl.co.nz))	NUDT15:c.415C>T present in 2 alleles (NUDT15*2/*2, NUDT15*2/*3, NUDT15*3/*3) Two loss of function alleles (2% East Asians; <1% European/Africans) Poor metabolisers	Azathioprine/Mercaptopurine Avoid Thioguanine 25% of normal dose or avoid
	NUDT15:c.415C>T present in 1 allele (NUDT15*2 or NUDT15*3) One loss of function allele (21% East Asians) Intermediate metabolisers	Azathioprine/Mercaptopurine 30-80% of normal dose Thioguanine 50-80% of normal dose Monitor for myelosuppression Allow 2-4 weeks to reach steady state
Hepatitis A serology If high risk or planning travel	HAV IgG -ve No immunity	Hep A vaccination (Not funded) Consider if immunosuppressed or for travel overseas Hep A vaccination or immunoglobulins if non-immune & exposed
CMV serology	CMV IgG +ve	Consider CMV colitis in those with active colitis despite high dose immunosuppression (esp. steroids)

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Vaccinations

Follow the **NZ Immunisation schedule**^{5,7} for age appropriate vaccinations.

Some vaccinations are recommended (and some are funded) in those planning to receive or are receiving immunosuppression for >28 days⁸⁻¹⁰.

Vaccine	Target group & Dosing schedule	Type of vaccine	Funded
Influenza vaccine	Annually in all IBD patients Immunocompromised with <u>no previous</u> influenza vaccines may need a 2 nd dose at least 4 weeks later	Non-live (inactivated)	<ul style="list-style-type: none"> Immunocompromised Pregnant Aged ≥ 65 Aged ≥ 55 Maori /Pacific Children aged 6 m to 12 yrs <p>2nd dose unfunded</p>
Pneumococcal	Immunosuppressed (high dose steroids >2 weeks or >28 days immunosuppression) PCV13 Single dose, then 23PPV >8 weeks later Booster every 5 years	Non-live PCV13 (conjugated) 23PPV (polysaccharide)	<ul style="list-style-type: none"> Children (<18 years) <p>Recommended, not funded</p>
Meningococcal	Immunosuppressed MenC 2 doses > 8 weeks apart, & booster 5 yearly MenB 2 doses > 8 weeks apart & booster 5 yearly	Non-live MenACWY (conjugated) MenB (recombinant)	<p>MenC & MenB</p> <ul style="list-style-type: none"> Children Adults immunosuppressive therapy >28 days <p>MenC & MenB boosters</p> <ul style="list-style-type: none"> Recommended, not funded
Haemophilus influenza	Immunosuppressed Hib-PRP-T 1 dose for re-vaccination	Non-live (conjugated)	Immunosuppressive therapy >28 days
Measles, Mumps, Rubella (MMR)	MMR non-immune 2 doses >4 weeks apart	Live-attenuated	Immunosuppressive therapy >28 days
Varicella zoster	Varicella naïve 2 doses >4 weeks apart	Live-attenuated	Immunosuppressive therapy >28 days
Herpes Zoster	Age ≥ 50 years Two doses 2-6 months apart	Non-live (recombinant) (Shingrix)	Age 65 Not currently funded age 50-64 or age >65
Human papilloma virus (HPV)	All young IBD patients (<45 years) 3 doses	Non-live (recombinant)	Age 26 & under Not funded age >26
Tetanus, Diphtheria, Pertussis	Immunosuppressed 1 dose + every 10 years	Non-live (toxoid & other) Tdap (Boostrix)	<ul style="list-style-type: none"> Children Pregnant women Age 45 and age 65 Immunosuppressive therapy
Polio	Immunosuppressed IPV or DTaP-IPV or DTaP-IPV-HepB/Hib	Non-live (inactivated) IPV	Immunosuppressive therapy >28 days

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<i>Vaccine</i>	<i>Target group & Dosing schedule</i>	<i>Type of vaccine</i>	<i>Funded</i>
COVID-19	As per current MOH recommendations COVID-19: Vaccine policy statements and clinical guidance Ministry of Health NZ COVID-19 vaccines Unite against COVID-19 (covid19.govt.nz)	Non-live	Yes
Travel vaccines	Attend travel clinic At least 6-8 weeks prior to departure	Some are live e.g. Yellow fever	Not funded

Live vaccines

- Contraindicated for those who are immunosuppressed due to risk of disseminated disease
- Can be received at least 1 month prior to commencement of immunosuppression, and 1-4 months after cessation of immunosuppression

Guidelines for live vaccine administration for individuals receiving non-corticosteroid agents (Adapted from the NZ Immunisation Handbook 2020⁵)

<i>Non-biologic agent</i>				
	<i>Dose regime</i>	<i>Administration of live vaccines</i>	<i>Dose regime</i>	<i>Administration of live vaccines</i>
Mesalazine Olsalazine Sulfasalazine	Any dose	Any time before, during, or after treatment		
Azathioprine	≤3 mg/kg per day	Any time before, during, or after treatment	>3 mg/kg per day	Give at least 1 month prior to commencement of medication
6-mercaptopurine	≤1.5 mg/kg per day		>1.5 mg/kg per day	
Methotrexate	≤0.4 mg/kg per week		>0.4 mg/kg per week	Delay for 3 months after discontinuation
Cyclosporine Tacrolimus			Any dose	Give at least 1 month prior to commencement of medication
Tofacitinib				

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<i>Biologic agent</i>				
	<i>Dose regime</i>	<i>Administration of live vaccines</i>	<i>Dose regime</i>	<i>Administration of live vaccines</i>
Adalimumab Infliximab Ustekinumab*			Any dose	Give at least 1 month prior to commencement of medication Delay for 3 months after discontinuation [#]
Vedolizumab*			Any dose	Give at least 1 month prior to commencement of medication Delay for 3-4 months after discontinuation

*Addition to the original table.

[#]Modified based on the ECCO guidelines³

Other Preventive Care^{1,2}

- **Smoking cessation**¹ – Particularly important in those with Crohn’s disease
 - Smoking is associated with development of disease, disease progression, and poor medical and surgical outcomes
 - Also associated with increased cardiovascular risk and other chronic diseases
 - Offer smoking cessation advice. <https://www.health.govt.nz/your-health/healthy-living/addictions/quitting-smoking>
- **Bone health** – Increased risk of osteoporosis with steroid exposure, malnutrition, and small bowel involvement
 - Cornerstones recommendation⁴:
 - Steroid use > 3 months
 - Inactive disease but past chronic steroid use of at least 1 year within the past 2 years
 - Inactive disease but maternal history of osteoporosis
 - Inactive disease but malnourished or very thin
 - Inactive disease but amenorrhoeic
 - Post menopausal women
 - Screening DEXA scan at time of diagnosis and 5 yearly
 - Consider regular calcium and vitamin D, particularly while on steroids
- **Nutrition** – Particularly in those with small intestinal Crohn’s disease and/or post ileal resection
 - Annual iron studies, B12/folate, and vitamin D
- **Psychological** – Screening for depression and anxiety in all IBD patients is recommended
 - Funded counselling sessions may be available via GP

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- **Cardiovascular health** – Increased risk of cardiovascular disease compared with the general population
 - Screening and management of cardiovascular risk factors
- **Pneumocystis jirovecii (PJP)** – IBD patients on triple immunosuppressive therapy, should receive co-trimoxazole prophylaxis
- **DVT prophylaxis** – Increased risk of venous thromboembolism (VTE) in those with IBD, further increased with active disease (particularly with acute severe ulcerative colitis), surgery, hospitalisation, and pregnancy
 - Low molecular weight heparin (Enoxaparin) should be given to all IBD inpatients
 - Extended prophylaxis on discharge should be considered in those with strong risk factors for VTE (*not funded except peri-operatively*)

Cancer screening

- **Skin checks** – Increased risk in all IBD patients
 - Increased risk of melanoma compared with the general population (RR 1.37; 95% CI 1.10-1.70) independent of the use of a biologic
 - Increased risk of melanoma with anti-TNF therapy
 - Increased risk of non-melanoma skin cancers (SCC/BCC) with thiopurines
 - Regular skin check, particularly age >50 years (not funded) – annually
 - Advise sun protection
- **Cervical screening** – as per national guidelines ([National Cervical Screening Programme](#) | [National Screening Unit \(nsu.govt.nz\)](#))
 - Annual screening currently recommended on immunosuppressed female IBD patients
 - From 12th September 2023, the primary test for cervical screening will change to a human papillomavirus (HPV) test, with the option of self-testing
 - Australia (GESA)² recommends 3 yearly HPV based cervical screening
 - HPV vaccine as per National Immunisation Schedule for age 9-26
- **Colorectal cancer screening** – as per guidelines
 - IBD & PSC – Annually
 - UC (E2/E3) and Crohn's colitis – surveillance colonoscopy 8 years from diagnosis. Subsequent surveillance interval depends on risk factors and endoscopy finding.

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