NATIONAL COVID-19 CLINICAL EVIDENCE TASKFORCE

NC19CET - Comparison of clinical and non-clinical factors for recommended immunomodulators.

	Baricitinib	Sarilumab	Tocilizumab
Drug class	Janus Kinase (JAK) inhibitor	Interleukin 6 (IL-6) receptor antagonist	Interleukin 6 (IL-6) receptor antagonist
Prescribed use	Severe active rheumatoid arthritis in adult patients who have responded inadequately, or who are intolerant, to one or more DMARDs[+].	Moderate to severe rheumatoid arthritis in adult patients who have responded inadequately, or who are intolerant, to one or more DMARDs[#].	Moderate to severe rheumatoid arthritis in adult patients who have responded inadequately, or who are intolerant, to one or more DMARDs[^].
TGA approved?	**Yes**	**No**	**Yes**
Analysis and Results			
Number of studies (patients)	2 (2558) (see study characteristics)	3 (2303) (see study characteristics)	10 (6570) (see study characteristics)
ICEMAN analysis	No	Yes	Yes
Subgrouping appropriate	No	No	No
Conditional recommended for….	adults hospitalised with COVID-19 who require supplemental oxygen, high-flow oxygen and/or non-invasive ventilation.	adults who require high-flow oxygen, non-invasive ventilation or invasive mechanical ventilation.	adults who require supplemental oxygen, particularly where there is evidence of systemic inflammation.
All-cause mortality	40 fewer per 1000 (56 fewer to 20 fewer) (RR 0.63, CI 95% 0.48-0.81) 2558 patients, 2 studies Certainty: Moderate	29 fewer per 1000 (79 fewer to 29 more) (RR 0.90, CI 95% 0.73-1.10) 2303 patients, 3 studies Certainty: Moderate	32 fewer per 1000 (52 fewer – 6 fewer) (RR 0.89, CI 95% 0.82-0.98) 6481 patients, 9 studies Certainty: Moderate
Mechanical ventilation and/or ECMO	52 fewer per 1000 (RR 0.66, CI 95% 0.46-0.93) 922 patients, 1 study	NR	30 fewer per 1000 (RR 0.81, CI 95% 0.70-0.93) 4248 patients, 4 studies
Serious adverse events	40 fewer per 1000 (RR 0.79 CI 95% 0.67-0.94) 2518 patients, 2 studies	4 more per 1000 (RR 1.02, CI 95% 0.89-1.18) 2315 patients, 3 studies	18 fewer per 1000 (RR 0.89, CI 95% 0.75-1.05) 2309 patients, 8 studies
Adverse events	23 fewer per 1000 (RR 0.95, 0.87-1.04) 2535 patients, 2 studies	43 more per 1000 (RR 1.08, CI 95% 0.98-1.19) 1865 patients, 2 studies	28 more per 1000 (RR 1.06, 0.86-1.30) 1562 patients, 7 studies
Dosage and pharmacokinetics			
Dose*	4 mg	200 mg - 400 mg	8 mg/kg, up to 800 mg
Dose frequency	Daily for 14 - 28 days	Single dose	Single dose
Route of administration	Oral	Intravenous	Intravenous
Systemic half life	12.5 hours (rheumatoid arthritis), 12.9 hours (atopic dermatitis)[+]	8 to 10 days, terminal concentration-dependent half life of 2-4 days; non-	Up to 13 days for 8 mg/kg every 4 weeks in patients with RA at steady-state[^].

		detectable concentration at 49 days (200 mg dose)[#].	
Frequent side effects	Risk of serious infections, gastrointestinal disorders, thrombosis, headache[+]	Upper respiratory tract infections, neutropenia, increased alanine aminotransferase[#].	Headache, dizziness, infections, injection site reactions[^].
Cost and availability			
Cost (full course)	~AUD $1271 per 4 mg x 28 pack (PBS DPMQ)	N/A	~AUD $429 per 400 mg vial (PBS DPMQ)
Availability	Moderate/high	N/A	Very low
Use in pregnancy	Category D (may increase incidence of human fetal malformations or irreversible damage)[+]	Category C (May cause harmful effects on the human fetus or neonate without causing malformations)[#].	Category C (May cause harmful effects on the human fetus or neonate without causing malformations)[^].
Use in children	Safety and efficacy not established[+].	Safety and efficacy not established[#].	Safety and efficacy not established for conditions other than juvenile idiopathic arthritis[^].

* Most frequently used dose provided to patients within included studies

[^] Therapeutic Goods Administration: Australian Product Information, Actemra (tocilizumab) http://www.guildlink.com.au/gc/ws/ro/pi.cfm?product=ropactem11014

[#] Therapeutic Goods Administration: Australian Product Information, Kevzara (sarilumab) pre-filled pen and pre-filled syringe https://www.tga.gov.au/sites/default/files/auspar-sarilumab-rch-190408-pi.pdf

[+] Therapeutic Goods Administration: Australian Product Information, Olumiant (baricitinib) https://www.ebs.tga.gov.au/ebs/picmi/picmirepository.nsf/pdf?OpenAgent&id=CP-2018-PI-01225-1

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