ANNEX B. SUMMARY OF RECOMMENDATIONS FROM THE PHILIPPINE COVID-19 LIVING CPG

	Philippine COVID-19 Living CPG review (Feb 2021) **[Reference for the May 2021 HTAC recommendation]**	Philippine COVID-19 Living CPG review (Oct 2021) **[Latest version of the review]**
Recommended indication of tocilizumab	We recommend the addition of tocilizumab to systemic steroids in patients showing rapid respiratory deterioration and/or requiring high doses of oxygen (high-flow nasal cannula, noninvasive or invasive mechanical ventilation) and with elevated markers of inflammation (CRP > 75 mg/L). *(Moderate quality of evidence; Strong recommendation)*	We recommend the addition of tocilizumab to systemic steroids in patients showing rapid respiratory deterioration and/or requiring high doses of oxygen (high-flow nasal cannula, noninvasive or invasive mechanical ventilation) and with the elevated biomarkers of inflammation (CRP). *(Moderate certainty of evidence; Strong recommendation)*
Against the use of tocilizumab in specific population/s	Among patients with COVID-19 infection who do not require oxygen supplementation. *(Very low quality of evidence; Strong recommendation)*	Among patients with COVID-19 infection who do not require oxygen supplementation. *(Very low certainty of evidence; Strong recommendation)*
Reference studies of the recommendation	Total number: 8 studies	Total number: 14 studies

ANNEX C. SUMMARY OF NEW STUDIES ON TOCILIZUMAB FROM THE UPDATED REVIEW OF THE PHILIPPINE COVID-19 LIVING CPG (OCT 2021)

	Population (P)	**Intervention (I)**	**Comparator (C)**	**Outcome (O)**	**SD**	
HTAC Research question	Among confirmed hospitalized COVID-19 patients	Tocilizumab	Placebo and/or standard of care	Clinical improvement, mortality reduction, initiation of mechanical ventilation		
Author, Year	***Study Characteristics***					**Summary of Results**	
	Population (P)	**Intervention (I)**	**Comparator (C)**	**Outcome (O)**	**Study Design**	**Efficacy**	**Safety**
Derde, 2021 *preprint*	ICU-admitted critically ill hospitalized patients with COVID-19 patient and receiving respiratory support (n=2274)	Tocilizumab 8 mg/kg (IV) Sarilumab400 mg Anakinra 300 mg loading dose, 100mg q6h x 14 days Interferon β1a	Standard care	Respiratory and cardiovascular organ support-free days, Survival, In-hospital mortality 90 days, Time to ICU discharge, Time to hospital discharge	Open label, Adaptive RCT	In critically ill patients with COVID-19, tocilizumab (and other IL-6 inhibitors) is effective in improving survival and reducing duration of respiratory and cardiovascular organ support	All treatments in the study appeared safe
Hamed, 2021 *published*	Hospitalized COVID-19 patients AND	Methylpredniso lone + tocilizumab	Historical control group	Day 45 all-cause mortality, rate of admission to the	Open label RCT	In patients with severe COVID-19 pneumonia on oxygen support,	N/A (Not Evaluated)

	lung infiltrates >50% of lung fields within 48 hrs admission, O2 saturation <93%at rest on room air (N=76)	(IV) Methylprednisolone only		intensive care unit (ICU), length of ICU stay, invasive ventilation, days on ventilators, and length of hospital stay.		adding tocilizumab to methylprednisolone did not improve any of the studied outcomes significantly	
Hermine, 2021 *Preprint*	Patients hospitalized with moderate-to-severe COVID-19 patients requiring oxygen but without ventilation support, high flow or mechanical ventilator, WHO class 5 (n=453)	Tocilizumab 8 mg/kg PLUS Dexamethasone 10 mg/day (IV) for 5 days and tapering up to 10 days	Dexamethasone 10 mg/day for 5 days and tapering up to 10 days	Survival without mechanical ventilation, Progression based on WHO clinical progression scale, Time to oxygen supply independency, Time to hospital discharge, and adverse events	Open label RCT	There were no significant differences between those who received tocilizumab and those who did not on WHO-Clinical Progression Scale scores greater than 5 at day 4. No difference on day 28 mortality was found.	Good overall safety; no increase in adverse or serious adverse events in the tocilizumab group.
Rutgers, 2021 *Preprint*	Patients admitted to the general ward with proven Covid-19 and in need of supplemental oxygen (n=354)	Tocilizumab 8 mg/kg (IV) + standard of care	Standard of care	Thirty-day mortality, median stay in the ICU, mechanical ventilation, time to death	Open label RCT	Tocilizumab demonstrates a clinically meaningful efficacy when given early in the disease course in hospitalized patients who need oxygen support, even when concomitantly treated	The use of tocilizumab in COVID-19 infected patients is safe

						with dexamethasone.	
Soin, 2021 *Published*	Adults (aged ≥18 years) admitted to hospital with moderate to severe COVID-19 (n=183)	Tocilizumab 6 mg/kg (IV)	Standard of care	Progression of COVID-19, mortality, clinical improvement, time to clinical improvement, ventilator free days, organ failure free days, ICU admission, time to hospital discharge, time to negative result on PT-PCR, safety	Open label RCT	There was no significant difference between those who received tocilizumab plus standard of care compared to standard of care only, in terms of progression of COVID-19.	Safety results were as expected on the basis of the known safety profile of tocilizumab and the disease manifestations of patients admitted to hospital with COVID-19.
Talaschian, 2021 *Published*	Severe hospitalization COVID-19 patients (n=40)	Tocilizumab 8 mg/kg (IV)	Standard care	Clinical improvement, 28-day mortality Time to improvement	Double blind RCT	The study results recommended that tocilizumab could not be a beneficial agent for treating severe cases of COVID-19 patients and have not significantly affected patients' clinical improvement.	No adverse events were found in the standard care arm while four adverse events were seen in the intervention arm. Of these four adverse events, 3 were considered to be related or possibly related and one was considered to be unrelated to intervention by the site investigators.

Simple Costing: https://docs.google.com/spreadsheets/d/1cDJzo1D5M19AKWsVQYgu1tI8t1ZEf-YJ80YEyPYqGwc/edit#gid=1218600655

ANNEX D: COSTING ANALYSIS

	400 mg/20 mL, 20 mL vial	200 mg/10 mL, 10 mL vial	80 mg/4 mL, 4 mL vial
Unit Cost (PHP) *(based on Median Procurement Price in Public Hospitals)*	₱9,050.00	₱10,290.70	₱4,116.25
Source	DOH Purchase Request Cost	Government List Price from the Manufacturer	Government List Price from the Manufacturer
Drug regimen used in the calculation	800 mg per single infusion		
Number of dosage units per treatment course	2	4	10
Source	*Number of ampule/vial used per treatment course as per US NIH (single IV dose not exceeding 800 mg)*	*Number of ampule/vial used per treatment course as per US NIH (single IV dose not exceeding 800 mg)*	*Number of ampule/vial used per treatment course as per US NIH (single IV dose not exceeding 800 mg)*
Duration of treatment	1	1	1
	day	*day*	*day*
Source	*US NIH*	*US NIH*	*US NIH*
Drug regimen cost per patient per treatment course (PHP)	**₱18,100.00**	**₱41,162.80**	**₱41,162.50**

Recommended treatment regimen per FDA: *Tocilizumab IV 8 mg/kg body weight for a single dose, not to exceed 800 mg per single infusion. If clinical signs or symptoms worsen or do not improve after the first dose, one additional infusion of tocilizumab 8mg/kg body weight (not to exceed 800 mg per single infusion) may be administered at least 8 hours after the initial infusion.*

Assumption for the Costing Analysis: *The HTAC used the maximum dose (800 mg) for a single infusion since the additional dose is dependent on the assessment of the healthcare provider.*