Rationale for updating the HTAC recommendation on *COVID-19 Vaccine (ChAdOx1-S [recombinant]) (COVID-19 Vaccine AstraZeneca)*

In lieu of evolving evidence on COVID-19, the HTAC releases its updated recommendations on the emergency use of *COVID-19 Vaccine (ChAdOx1-S [recombinant]) (COVID-19 Vaccine AstraZeneca).*

Further, the updated *WHO Interim recommendations for use of the ChAdOx1-S [recombinant] vaccine against COVID-19* dated April 21, 2021 recommended an interval of 8 to 12 weeks between the two doses of the vaccine. This is based on the observation from the Phase 3 trials of the vaccine that two-dose efficacy and immunogenicity increases with a longer dosing interval. The previous HTAC recommendation was based on the dosing interval (i.e., 4-12 weeks) indicated in the Philippine FDA-approved EUA of *COVID-19 Vaccine AstraZeneca* last January 28, 2021.

AMENDMENTS

The following sections in the previous HTAC ES on *COVID-19 Vaccine Astrazeneca* are amended as follows:

HTAC Recommendation:

Version 1 *(as of 08 February 2021)*	Version 2 *(as of 25 June 2021)*
The HTAC **recommends the emergency use of *COVID-19 Vaccine AstraZeneca*** to reduce the burden of COVID-19 among eligible populations aged 18 years and older.	The HTAC **recommends the emergency use of *COVID-19 Vaccine AstraZeneca* with a dosing interval of 8-12 weeks** to reduce the burden of COVID-19 among eligible populations aged 18 years and older

Summary of HTAC judgement and considerations in formulating its recommendation for the vaccine:

Criterion	HTAC Judgment	
	Version 1 ***(as of 08 February 2021)***	**Version 2** ***(as of 25 June 2021)***
Can *COVID-19 Vaccine AstraZeneca* significantly reduce the magnitude and severity of COVID-19?	**Yes**. *COVID-19 Vaccine AstraZeneca*, with 62% efficacy has the potential to reduce the disease burden by averting a significant number of symptomatic infections and deaths assuming sufficient vaccine coverage.	**Yes**. *COVID-19 Vaccine AstraZeneca* has the potential to reduce the disease burden by averting a significant number of symptomatic infections and hospitalization due to COVID-19 assuming sufficient vaccine coverage.
Is *COVID-19 Vaccine AstraZeneca* efficacious and safe?	Based on the interim results of the Phase III trial on *COVID-19 Vaccine AstraZeneca* (Voysey et al, 2020) *[cut-off analysis: date: 04 November 2020]:* **Yes**, it is efficacious for preventing symptomatic	Based on the interim results of the Phase III trial on *COVID-19 Vaccine AstraZeneca* (Voysey et al, 2021) *[cut-off analysis: date: 07 December 2020]:* **Yes**, it is efficacious for preventing symptomatic

	COVID-19 based on moderate certainty of evidence. COVID-19 Vaccine AstraZeneca may also reduce hospitalization due to COVID-19 based on low certainty of evidence. However, we note that the vaccine efficacy precision is low for this outcome. Currently, the reported vaccine efficacy of *COVID-19 Vaccine AstraZeneca* on severe COVID-19 and asymptomatic COVID-19 is still inconclusive based on low certainty of evidence. The duration of protection cannot be assessed given the current data. **Yes**, it is safe in the known short-term safety outcomes, based on moderate certainty of evidence. Meanwhile, its long term safety outcomes are inconclusive based on low certainty of evidence. It should not be given to individuals below 18 years old and to those with a known history of severe allergic reaction to any component of the vaccine. While vaccination is not contraindicated in other special populations who were excluded in the analysis/trials (i.e., immunocompromised patients, pregnant and lactating women), close medical supervision will be required.	COVID-19, based on high certainty of evidence and reducing the risk of hospitalization due to COVID-19, based on real world evidence. Currently, the reported vaccine efficacy of *COVID-19 Vaccine AstraZeneca* against severe COVID-19 and asymptomatic COVID-19 is still inconclusive based on low and moderate certainty of evidence, respectively. The duration of protection cannot be assessed given the current data. **Yes**, it is safe in the known short-term safety outcomes, based on moderate certainty of evidence. Meanwhile, its long term safety outcomes are inconclusive based on low certainty of evidence. Although vaccination appears to be associated with an extremely rare but potentially fatal thrombosis with thrombocytopenia syndrome (TTS) and certain hematologic and vascular adverse events such as thrombocytopenia, idiopathic thrombocytopenic purpura, arterial thromboembolic events and hemorrhagic events, the HTAC deems the benefits far outweigh the risks. Pending stronger evidence of the association and consensus from stringent regulatory agencies, the HTAC finds no reason at this time not to recommend the use of the vaccine as approved by the FDA Philippines. However, measures against these adverse events must be included in all protocols for addressing adverse effects.

		On the other hand, based on the recent advisory (June 11, 2021) of EMA on the use of *COVID-19 Vaccine Astrazeneca* among people with history of capillary leak syndrome (CLS), the HTAC recommends against the use of this vaccine for the said population. Information on CLS as a side effect and history of CLS as a contraindication should both be included in the product information of the vaccine. Further, healthcare professionals should be aware of the signs and symptoms of capillary leak syndrome and of its risk of occurrence in people who had been diagnosed previously with the condition. Individuals who received *COVID-19 Vaccine AstraZeneca* are also advised to seek immediate medical attention if they experience symptoms associated with capillary leak syndrome such as rapid swelling of arms and legs, sudden weight gain or feeling faint due to low blood pressure. It should not be given to individuals below 18 years old and to those with a known history of severe allergic reaction to any component of the vaccine. While vaccination is not contraindicated in other special populations who were excluded in the analysis/trials (i.e., immunocompromised patients, pregnant and lactating women), close medical supervision will be required.
Is *COVID-19 Vaccine AstraZeneca* affordable and feasible to use in a national immunization program (viability)?	**Yes.** It is affordable. The share of the cost to implement vaccination using *COVID-19 Vaccine AstraZeneca* will constitute 21.45% of the total allocated budget for vaccination and will cover 40% of the 70 million target vaccinees for 2021.	**Yes.** It is affordable. The share of the cost to implement vaccination using *COVID-19 Vaccine AstraZeneca* will constitute 6.19% of the total allocated budget for vaccination and will cover 12.14% of the 70 million target vaccinees for 2021.

	Yes, it is feasible as there are no significant barriers in vaccine implementation using *COVID-19 Vaccine AstraZeneca* in terms of storage, transport, and handling. However, there is still a need for training of vaccinators to ensure product integrity across the entire supply chain and close monitoring of adverse events.	**Yes**, it is feasible as there are no significant challenges in vaccine implementation using *COVID-19 Vaccine AstraZeneca* in terms of storage, transport, and handling. However, there is still a need for training of vaccinators to ensure product integrity across the entire supply chain and close monitoring of adverse events.
Does *COVID-19 Vaccine AstraZeneca* reduce out-of-pocket (OOP) expenses of households due to COVID-19?	**Yes.** Based on interim *results from the clinical trial, COVID-19 Vaccine AstraZeneca showed vaccine efficacy to reduce risk for hospitalization due to COVID-19 by 87.6%, based on low certainty of evidence. Thus, COVID-19 Vaccine AstraZeneca* has the potential to reduce out-of-pocket expenses of Filipino households due to reduction of hospitalizations.	**Yes.** Based on interim results from the clinical trial, *COVID-19 Vaccine AstraZeneca* showed vaccine efficacy to reduce risk for any symptomatic COVID-19 (including mild to moderate cases with stable comorbidities), hospitalization due to COVID-19. Thus, *COVID-19 Vaccine AstraZeneca* has the potential to reduce out-of-pocket expenses of Filipino households due to reduction of hospitalizations.
Does *COVID-19 Vaccine AstraZeneca* possess the characteristics desired by key stakeholders?	**Yes.** Based on short term outcomes, *COVID-19 Vaccine AstraZeneca* possesses most of the characteristics desired by key stakeholders.	No revision
Does *COVID-19 Vaccine AstraZeneca* reduce or not further add to existing inequities in the health system?	**Yes.** Because of non-stringent logistic requirements, *COVID-19 Vaccine AstraZeneca* **does not aggravate** health inequities related to inoculation of recipients residing in isolated and disadvantaged locations. We also note that the trial population did not include important groups such as individuals aged 18 and below, immunocompromised individuals, pregnant and lactating women.	No revision

The following sections describe the additional evidence considered in this updated HTAC recommendation.