Health Canada | Santé Canada

Health Products and Food Branch | Direction générale des produits de santé et des aliments

TERMS AND CONDITIONS

Company: AstraZeneca Canada Inc.

Product: Vaxzevria (ChAdOx1-S [recombinant])

Dossier ID: HC6-024-E252737

Background:

The Food and Drug Regulations allows the Minister to impose or amend terms and conditions, and request additional information, in relation to a COVID-19 drug submission, Drug Identification Number (DIN), or establishment licence, at any time while it is in effect. In light of the severity of the COVID-19 pandemic, this allows the Minister to act quickly to gather important safety information or mitigate risk in a timely manner.

Depending on the requirement, terms and conditions can be ongoing (e.g., require a monthly report), have a defined time (e.g., a report is due to Health Canada on a specific day) or are to be completed once the data is available (e.g., a clinical trial is completed).

The status of the Terms and Conditions will be updated on a regular basis.

Status as of April 4, 2023:

Total Number: 10

Ongoing/pending: 7

Closed: 3

Table: Terms and Conditions

	Terms and Conditions	Issued	Status
1	Provide full study reports, including safety, efficacy and immunogenicity data when available, for study D8110C00001 and the four University of Oxford studies (COV001, COV002, COV003, and COV005).	November 19, 2021	Pending availability of data
2	Provide a safety update of the Phase 3 study (D8110C00001) 6 months after the second dose, when available, for at least 3,000 vaccinated subjects as well as for available and relevant data from placebo subjects.	November 19, 2021	Pending availability of data
3	Provide the following information: a. Results from ongoing hold time validation studies for drug substance (DS)/drug product (DP). If intermediate holding times are adjusted based on	November 19, 2021	Closed

	Terms and Conditions	Issued	Status
	these studies, corresponding eCTD sections should be updated. This information should be provided as soon as the results are available. b. Results of product specific qualification for the adventitious agent test. This information should be provided as soon as the results are available. c. Outstanding results for the validation of the scale up formulation process as soon as the information is available. d. Results of the DP photostability study. e. Information regarding the implementation of the corrective and preventive actions (CAPAs) associated with the out of specification (OOS) results and any additional changes made to the manufacturing process following method validation. f. A Notifiable Change (NC) to support the implementation of additional assays for release of DS and DP. g. Update DS and DP comparability criteria information sections in Module 3 to reflect changes to the comparability assessment criteria. h. Update the Canadian Lot Release Protocol to include: i. The manufacturing suite for each DS lot ii. Whether the DS lot underwent reprocessing iii. If an alternative is performed, this information should be included in the bulk virus harvest results.		
4	AstraZeneca Canada Inc. is required to treat adverse reactions associated with Vaxzevria as priority and submit the corresponding reports to Health Canada without delay.	November 19, 2021	Ongoing
5	AstraZeneca Canada Inc. is required to submit bi-monthly safety reports, unless otherwise determined by Health Canada. The bi-monthly safety reports should be submitted within 15 days after the last day of every second month, beginning the first full calendar month after authorization. These reports should contain the following: a. Interval and cumulative number of reports (serious and non-serious), overall and by age groups and in special populations (e.g. pregnant women); b. Interval and cumulative number of reports per High Level Term (HLT) and System Organ Class (SOC); c. Number of reports in Canada and Global;	November 19, 2021	Closed

	Terms and Conditions	Issued	Status
	d. Exposure data, stratified by country , age groups and including, if available, race and ethnicity e. Changes to reference safety information in the interval; f. Ongoing and closed signals in the interval; g. Updated list of adverse events of special interest including the Safety Platform for Emergency Vaccines list and RMP safety concerns (including the additional missing information): reports – numbers and relevant cases, time-to-onset and observed/expected analyses including causality assessment; h. Fatal reports – numbers and relevant cases, including observed/expected analyses; i. Vaccination failure / lack of efficacy (including confirmed and suspected cases) and errors-number relevant cases; j. Potential interaction with other vaccines/concomitant treatments-number and relevant cases; k. Summary outcomes of some of the routine pharmacovigilance activities (as presented in the EU RMP Part III and applied in the Canadian context) should be included for the purpose of rapid signal detection and communication activities. Summary of all ongoing studies can be included in the first six-month scheduled PBRER, unless a safety signal is identified that requires immediate regulatory action.; and l. Overall risk/benefit consideration		
6	AstraZeneca Canada Inc. is required to provide an updated Core RMP and Canadian Addendum in a timely manner if a signal of safety issue is observed in post-authorization surveillance. The RMP format should follow the guidance (Guidance Document Submission of Risk Management Plans and Follow-Up Commitments) and should include the following: a. a safety specification that details the identified risks, potential risks, and missing information for the Vaxzevria; b. a pharmacovigilance plan that details specific measures to be taken to identify and report safety issues in COVID-19 patients, including adverse reaction reporting, periodic reporting, and ongoing/planned studies; and c. a risk minimization plan, if applicable, to manage risks that may require additional measures beyond those considered standard (for instance, labelling).	November 19, 2021	Ongoing
7	AstraZeneca Canada Inc. is requested to develop and distribute a Health Product Risk Communication (HPRC), in French and English, should a decision be made to	November 19, 2021	Closed

	Terms and Conditions	Issued	Status
	import, for Canadian sites, non-Canadian labelled supplies. In this case, the HPRC would need to be developed with Health Canada approval and endorsement, to inform healthcare professionals that AstraZeneca Canada Inc. will delay implementation of Canadian-specific inner/outer labels following NDS-CV approval for Vaxzevria, and that interim non Canadian inner/outer labels will be used for the short term. Please note the following: a. AstraZeneca Canada Inc. should include images and texts of these labels in the HPRC and clearly outline all deviations from Canadian requirements; b. The HPRC should direct healthcare professionals to the electronic platform where they can find information about the approved Canadian-specific labelling in both official languages; and c. The HPRC should include an alternative method for the health care professionals to obtain a paper copy of the HPRC and/or Product Monograph by mail or fax from AstraZeneca Canada Inc., if they cannot access the internet Finally, AstraZeneca Canada Inc. should devise an appropriate dissemination strategy to ensure the HPRC reaches the intended audience in a timely manner.		
8	AstraZeneca Canada Inc. to submit final snapshots of all components of the electronic platform (linked to on the any foreign or Canadian specific labels), containing the approved Canadian-specific labelling information for Vaxzevria in French and English for Health Canada's review and records, prior to launch of the electronic platform, and for each subsequent update.	November 19, 2021	Ongoing
9	AstraZeneca Canada Inc. is required to submit Periodic Safety Update Reports (PSURs) / Periodic Benefit Risk Evaluation Reports (PBRERs) every 6 months, unless otherwise determined by Health Canada. The core PSUR/PBRER format should follow international guidance for COVID-19 vaccines.	February 28, 2022	Ongoing
10	AstraZeneca Canada Inc. is requested to develop and distribute a company-led customer communication, in English and French, should a decision be made to import non-Canadian labelled supplies for Canadian sites. The customer communication should aim to inform healthcare professionals that AstraZeneca Canada Inc. will delay the implementation of Canadian-specific inner/outer labels following NDS-CV approval for Vaxzevria (ChAdOx1-S [recombinant]), and that interim inner/outer labels will be used for the short term. Please note the following: a. AstraZeneca Canada Inc. should consider including images and texts of these labels in the customer communication and clearly outline all deviations from Canadian requirements; b. The customer communication should direct healthcare professionals to the electronic platform where they can find information about the approved Canadian-specific labelling in both official languages;	April 4, 2023	Ongoing

	c. The customer communication should not resemble a Health Canada-endorsed Health Product Risk Communication and should not reflect a red banner at the top of the document. A company-led risk communication may take the form of a letter carrying the company letterhead, for example. The company-led customer communication does not require review by Health Canada; however, AstraZeneca Canada Inc. is welcome to seek courtesy feedback from BRDD. AstraZeneca Canada Inc. is expected to exercise due discretion to ensure prompt finalization and dissemination of the customer communication. Please provide a copy of the final, signed customer communication in English and French via eCTD once available.		