Health Canada / Santé Canada

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

INTERIM ORDER– TERMS AND CONDITIONS
Company: Verity Pharmaceuticals Inc.
Product: Covishield Vaccine (ChAdOx1-S)
Dossier ID: HC6-024-E248651

Background:

The Interim Order allows the Minister to impose or amend terms and conditions, and request additional information, in relation to a COVID-19 drug submission, authorization, 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 22, 2021:

Total Number: *20*

Ongoing/pending: *14*

Closed: *6*

Table: Terms and Conditions

	Terms and Conditions	Issued	Status
1	Provide updated safety and efficacy data, when available, for clinical studies underway with the COVISHIELD vaccine.	Feb 26, 2021	Pending availability of data
2	Provide data and information regarding protection against emerging variants, when available (e.g.UK, Brazil, South Africa).	Feb 26, 2021	Pending availability of data
3	All lots to be sold in Canada should comply with the approved specifications for drug substance (DS) and drug product (DP). A Lot Release Protocol should be submitted to the Biologic and Radiopharmaceutical Drugs Directorate (BRDD) for each lot to be distributed in Canada, the Sponsor requires a lot release letter from BRDD prior to distribution in the Canadian market. A summary of batch	Feb 26, 2021	Ongoing

	Terms and Conditions	Issued	Status
	disposition should be submitted on a biannual basis from the facilities approved to supply Canada. The summary should include all DS and DP lots produced, failed, or aborted and a brief description of the issue(s) where this is relevant. Health Canada may revisit this requirement at any time based on the risk profile of the product. The email address where this information should be sent will be provided to the Sponsor in an additional correspondence.		
4	Post-authorization the following information should be submitted as soon as it is available: • Updates on process validations at full commercial scale including all additional PPQ batches, comparability data for all facilities included in authorization and in subsequent amendments. • Updates on all assay validation studies completed post-authorization, including assay performance and comparability of all laboratory testing sites. Please note all analytical assays must be validated prior to New Drug Submission. • Any critical changes to the manufacturing process, the specifications for critical quality attributes or to the key analytical assays should be submitted promptly as amendments to the authorization. • All information available to any new facilities relevant to the Canadian supply chain when available.	Feb 26, 2021	Ongoing
5	Harmonize batch release testing and specifications with those approved for AstraZeneca COVID-19 Vaccine. • Including Polysorbate 80 and subvisible particles count. • Specifications should be aligned as per the clarification request issued February 9th.	Feb 26, 2021	Ongoing
6	Provide stability information in a timely manner to support extension of the expiry date or implementation of new manufacturing processes. Once approved, relevant databases should be updated with the new expiry date.	Feb 26, 2021	Ongoing
7	Provide notification of changes in GMP status for any of the facilities included in the authorization as well as any new facilities relevant to the Canadian supply chain when available.	Feb 26, 2021	Ongoing
8	Verity Pharmaceuticals Inc. is required to provide, prior to distribution: • The roles and responsibilities of Verity Pharmaceuticals Inc. and AstraZeneca as described in the Safety Data Exchange Agreement related to pharmacovigilance (PV) activities and adverse reaction reporting for COVISHIELD to meet regulatory requirements and support brand-specific signal detection and assessment. • The revised educational materials (i.e., health professional guide and patient guide) related to COVISHIELD based on Health Canada's review. • Vaccination reminder cards to vaccination sites to support traceability, where required, which will include elements such as name of vaccinee, vaccine brand name, manufacturer name, space for recording dates of first and second doses and associated batch/lot numbers, and information on how to report any adverse events.	Feb 26, 2021	Closed
9	As per the Interim Order authorized drugs, Verity Pharmaceuticals Inc. will:	Feb 26, 2021	Ongoing

	Terms and Conditions	Issued	Status
	• Treat adverse reactions associated with COVISHIELD as priority and submit the corresponding reports to Health Canada without delay; and • Identify in the report that COVISHIELD is a Verity Pharmaceuticals Inc. product authorized under the Interim Order.		
10	Verity Pharmaceuticals Inc. is required to submit monthly safety reports for the period of the Interim Order authorization, unless otherwise determined by Health Canada. The monthly safety reports should be submitted within 15 days after the last day of a month, beginning after the first full calendar month after authorization. These reports should contain the following: • Interval and cumulative number of reports (serious and non-serious), overall and by age groups and in special populations (e.g. pregnant women); • Interval and cumulative number of reports; • Total number of adverse event reports in Canada and Globally; • Exposure data stratified by country, including any available data on age groups, race, ethnicity, on frail elderly, patients with chronic illness, immunocompromised and on indigenous populations and remote communities; • Changes to reference safety information in the interval; • Ongoing and closed signals in the interval; • List of adverse events of special interest including the Safety Platform for Emergency vACcines (SPEAC) list and RMP safety concerns (including the additional missing information): reports–numbers and relevant cases, including time-to-onset and observed/expected analyses; • Fatal reports–numbers and relevant cases, including observed/expected analyses; • Vaccination failure / lack of efficacy (including confirmed and suspected cases) reports and vaccination errors (categories according to preferred terms); • Potential interaction with other vaccines/concomitant treatments-number and relevant cases; • Summary outcomes of some of the routine pharmacovigilance activities (as presented in the Canadian Addendum) should be included for the purpose of rapid signal detection and communication activities. Summary of all ongoing registries and studies should be included in the six-month scheduled PBRERs, unless a safety signal is identified that requires immediate regulatory action; and • Overall risk/benefit assessment.	Feb 26, 2021	Ongoing
11	Verity Pharmaceuticals Inc. is required to provide an updated Core Risk Management Plan (RMP) in conjunction with the Canadian Addendum to the RMP within 2 weeks following authorization. This Canadian addendum should follow Health Canada guidance (1. Guidance Document Submission of Risk Management Plans and Follow-Up Commitments; 2. Guidance for market authorization requirements for COVID-19 vaccines; 3. Notice of clarification to drug manufacturers and sponsors: Canadian specific considerations in risk management plans) and include the following:	Feb 26, 2021	Received and under review

	Terms and Conditions	Issued	Status
	• Confirmation of linkage between the AstraZeneca EU RMP and the Canadian Addendum to the RMP for COVISHIELD. • A detailed description of the routine pharmacovigilance activities, including collection, processing, follow-up, and analysis of individual adverse event reports and aggregate data. • A description of the additional pharmacovigilance activities for monitoring of safety and effectiveness in Canada and globally. • A description of the planned pharmacovigilance activities for recording and accessibility of brand and batch/lot numbers for healthcare professionals and patients in Canada (i.e., traceability) and specifically under the Safety Data Exchange Agreement between AstraZeneca and Verity Pharmaceuticals Inc.		
12	Verity Pharmaceuticals 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 in the context of the COVID-19 drugs submitted for authorization under the Interim Order: • A safety specification that details the identified risks, potential risks, and missing information for the AstraZeneca COVID-19 Vaccine; • 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 • A risk minimization plan, if applicable, to manage risks that may require additional measures beyond those considered routine (for instance, labelling).	Feb 26, 2021	Ongoing
13	Verity Pharmaceuticals Inc. to submit final snapshots of all components of the electronic platform, containing Canadian-specific labelling information for COVISHIELD in French and English for Health Canada's review and records, prior to launch of the electronic platform.	Feb 26, 2021	Ongoing
14	Verity Pharmaceuticals Inc. to develop and distribute a Healthcare Product Risk Communication (HPRC), in French and English, with Health Canada approval and endorsement, to inform healthcare professionals about the authorization of COVISHIELD under the Interim Order Respecting the Importation, Sale and Advertising of Drugs for Use in Relation to COVID-19 with foreign English-only vial and carton labels with the brand name COVISHIELD, to expedite global access of the drug in the context of the pandemic. • The letter should direct healthcare professionals to the electronic platform where they can find information about Canadian-specific labelling in both official languages and should be issued prior to and alongside the distribution of the vaccine. • The letter should specify when the Canadian-specific labels will be implemented. • The letter should state that the use of the brand name COVISHIELD is temporarily being accepted in Canada due to the urgent public health need.	Feb 26, 2021	Closed

	Terms and Conditions	Issued	Status
15	Verity Pharmaceuticals Inc. to commit to developing Canadian-specific bilingual labelling for COVISHIELD and implementing such labelling at a point when the global supply and pandemic situation will allow. Health Canada should be kept informed of estimated timelines and proposed strategies concerning the development and implementation of Canadian-specific bilingual labels. • During the period prior to implementation of the Canadian-specific bilingual labeling, interim Canadian reference labels should be made available to healthcare professionals as reference.	Feb 26, 2021	Ongoing
16	Verity Pharmaceuticals Inc. to commit to changing the brand name COVISHIELD on all Canadian-specific labels at a point when the global supply and pandemic situation will allow.	Feb 26, 2021	Ongoing
17	Verity Pharmaceuticals Inc. will provide by April 5, 2021, an assessment of the benefits and the risks, stratified by sex and age, for the use of the COVID-19 vaccine in the current Canadian context, taking into consideration disease projections and the epidemiology of circulating variants, and post-market reports of rare thrombotic events, including those associated with thrombocytopenia.	March 29, 2021	Extension granted to April 7 Closed
18	Verity Pharmaceuticals Inc. will provide an analysis, by March 31, 2021, of the proposed or alternate mechanisms of development of thrombotic events with thrombocytopenia considering available case reports and data.	March 29, 2021	Closed
19	Verity Pharmaceuticals Inc. will propose additional pharmacovigilance activities, including in the Canadian context, for those individuals who receive(d) the vaccine, to be submitted by March 31, 2021.	March 29, 2021	Closed
20	Verity Pharmaceuticals Inc. will provide an assessment of the need for and propose any additional risk minimization measures that could be applied in the Canadian context, to be submitted by March 31, 2021.	March 29, 2021	Closed