Health Canada
Santé Canada

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

Biologic and Radiopharmaceutical Drugs Directorate
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TERMS AND CONDITIONS

Further to the Terms and Conditions Letter issued for Comirnaty Omicron XBB.1.5 (raxtozinameran) on September 28, 2023, the terms and conditions have been amended. In accordance with section C.01.014.21 (1.1) of the *Food and Drug Regulations*, the following terms and conditions are imposed on the Drug Identification Numbers (DINs) 02541823, 02541858, 02552035 and 02552078 assigned to Comirnaty (mRNA encoding SARS-CoV-2 spike protein, 5' [$m_2^{7,3'\text{-O}}$Gppp($m_1^{2'\text{-O}}$)ApG] cap, 110-nucleotide 3' poly(A) tail with a 10-nucleotide linker sequence):

Terms and Conditions		**Issued (YY/MM/DD)**	**Status**
CLINICAL:			
1	Provide interim analyses at 1 month of the immunogenicity and safety data from **Study C4591048 Substudy A, Phase 1** pertaining to the primary, secondary, and exploratory immunogenicity and safety objectives, estimands and endpoints (following the administration of the XBB formulation [Dose 4]) together with the 6 month interim clinical study report, and if an update to the Comirnaty Core Data Sheet is warranted based on this data, file an updated Product Monograph as a Supplement to a New Drug Submission (SNDS).	2024-09-24	Ongoing
2	Provide interim analyses at 6 months of the safety data from **Study C4591048 Substudy A**, **Phase 1** pertaining to the primary, secondary, and exploratory safety objectives, estimands and endpoints (following the administration of the XBB formulation)~~,~~ and if an update to the Comirnaty Core Data Sheet is warranted based on this data, file an updated Product Monograph as a Supplement to a New Drug Submission (SNDS)	2024-09-24	Ongoing
3	Provide interim analyses at 1 month of the immunogenicity and safety data from **Study C4591048 Substudy A, Phase 2/3** pertaining to the primary, secondary, and exploratory immunogenicity and safety objectives, estimands and endpoints (following the administration of the XBB formulation) together with ~~Provide~~ final analyses at 6 months of the safety data from **Study C4591048 Substudy A**, **Phase 2/3**	2024-09-24	Ongoing

	pertaining to the primary, secondary, and exploratory safety objectives, estimands and endpoints (following the administration of the XBB formulation) simultaneously in one final 6 month clinical study report as a Supplement to a New Drug Submission (SNDS)		
4	Provide interim analyses at 1 month of the immunogenicity and safety data from **Study C4591048 Substudy E** pertaining to the primary, secondary, and exploratory immunogenicity and safety objectives, estimands and endpoints (following the administration of the XBB formulation) together with ~~Provide~~ final analyses at 6 months of the safety data from **Study C4591048 Substudy E**, pertaining to the primary, secondary, and exploratory safety objectives, estimands and endpoints (following the administration of the XBB formulation) simultaneously in one final 6 month clinical study report as a Supplement to a New Drug Submission (SNDS)	2024-09-24	Ongoing
5	Provide interim analyses at 1 month of the immunogenicity and safety data from **Study C4591054 Substudy A**, pertaining to the primary, and exploratory immunogenicity and safety objectives, estimands and endpoints (following the administration of the XBB formulation) as soon as it becomes available as a Supplement to a New Drug Submission (SNDS).	2023-09-28	Ongoing
6	Provide final analyses at 6 months of the safety and immunogenicity data from **Study C4591054 Substudy A** pertaining to the primary, and exploratory immunogenicity and safety objectives, estimands and endpoints (following the administration of the XBB formulation) as soon as it becomes available as a Supplement to a New Drug Submission (SNDS).	2023-09-28	Ongoing
7	Provide interim analyses at 1 month of the immunogenicity and safety data from **Study C4591054 Substudy B**, pertaining to the primary, and exploratory immunogenicity and safety objectives, estimands and endpoints (following the administration of the XBB formulation) as soon as it becomes available as a Supplement to a New Drug Submission (SNDS).	2023-09-28	Ongoing
8	Provide final analyses at 6 months of the safety and immunogenicity data from **Study C4591054 Substudy B,** pertaining to the primary, and exploratory immunogenicity and safety objectives, estimands and endpoints (following the administration of the XBB formulation) as soon as it becomes available as a Supplement to a New Drug Submission (SNDS).	2023-09-28	Ongoing
PHARMACOVIGILANCE:			
1	BioNTech Manufacturing GmbH is required to submit Periodic Safety Update Reports (PSURs)/Periodic Benefit Risk Evaluation Reports (PBRERs) every 6 months for Comirnaty Omicron XBB.1.5 [COVID-19 mRNA vaccine, Monovalent (Omicron XBB.1.5)], unless otherwise determined by Health Canada.	2023-09-28	Closed

2	BioNTech Manufacturing GmbH is required to submit an updated core Risk Management Plan (RMP) with the Canadian Addendum in a timely manner as requested by Health Canada. 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 Comirnaty Omicron XBB.1.5 [COVID-19 mRNA vaccine, Monovalent (Omicron XBB.1.5)]; 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.	2023-09-28	Closed
LABELLING:			
1	BioNTech Manufacturing GmbH to provide a summary of the changes made to the website for Health Canada's review with each update. a. BioNTech Manufacturing GmbH to attest that the content of the website (CVDVaccine.ca) is consistent with the approved Canadian-specific labelling information for Comirnaty in French and English. The website content related to the appropriate storage & handling and preparation & administration of Comirnaty should be aligned with information in the Product Monograph.	2024-09-24	Ongoing
2	BioNTech Manufacturing GmbH 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 BioNTech Manufacturing GmbH and Pfizer Canada ULC will delay the implementation of Canadian-specific inner/outer labels following approval for Comirnaty, and that interim inner/outer labels will be used for the short term. Please note the following: a. BioNTech Manufacturing GmbH 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	2024-09-24	Ongoing

	find information about the approved Canadian-specific labelling in both official languages 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, BioNTech Manufacturing GmbH is welcome to seek courtesy feedback from BRDD. BioNTech Manufacturing GmbH 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.		
3	BioNTech Manufacturing GmbH to commit to developing Canadian specific bilingual labelling for Comirnaty presentations Drug Identification Numbers (DINs) currently marketed in Canada, to be submitted in Q1 of 2025, and implementing such labelling once supplies are transitioned to Canadian dedicated supplies. 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, Canadian reference labels should be made available to healthcare professionals.	2024-09-24	Ongoing