[Title Page]

PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

[Scheduling Symbol] [**BRAND NAME**]

[Proper name in final dosage form]

[Dosage Form(s), Strength(s) and Route(s) of Administration]

[Pharmaceutical Standard (if applicable)]

[Therapeutic Classification]

[For products that have been authorized under the Notice of Compliance with Conditions (NOC/c) policy, include the following boxed statement:]

"[Brand name], indicated for:

- [ ]

has been issued market authorization with conditions, pending the results of trials to verify its clinical benefit. Patients should be advised of the nature of the authorization. For further information for <Brand name> please refer to Health Canada's Notice of Compliance with conditions - drug products web site: https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/notice-compliance/conditions.html"

[For market authorizations without conditions]

"[Brand name], indicated for:

- [ ]

has been issued market authorization without conditions."

[Sponsor Name]

[Sponsor Address]

Date of Initial Authorization:
[MON DD,YYYY]

Date of Revision:
[MON DD,YYYY]

Submission Control Number: [control number]

For all products authorized under the Notice of Compliance with Conditions policy, include the following information:

What is a Notice of Compliance with Conditions (NOC/c)?

An NOC/c is a form of market approval granted to a product on the basis of promising evidence of clinical effectiveness following review of the submission by Health Canada.

Products authorized under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.

RECENT MAJOR LABEL CHANGES

[Section number and heading], [Subsection number and heading]	[MM/YYYY]
[Section number and heading], [Subsection number and heading]	[MM/YYYY]

TABLE OF CONTENTS

Sections or subsections that are not applicable at the time of authorization are not listed.

[To update, right-click anywhere in the Table of Contents and select "Update Field", "Update entire table", click OK.]

For biosimilar biologic drugs (hereafter referred to as biosimilars), include the following statement:

> *[Biosimilar brand name (proper name)] is a biosimilar biologic drug (biosimilar) to [Reference biologic drug brand name].*

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

[BRAND NAME] (proper name in final dosage form) is indicated for:

- [text]
- [text]

[text]

For biosimilars, the wording of each indication authorized for the biosimilar should be identical to the reference biologic drug product monograph, and the following statement should be made:

> *Indications have been granted on the basis of similarity between [Biosimilar brand name] and the reference biologic drug [Reference biologic drug brand name].*

For NOC/c indications: include a brief statement regarding the uncertainties and/or limitations of the indications.

1.1 Pediatrics

One of the following or similar statements should be used:

> *Pediatrics (age range): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of [Brand name] in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use. [Include cross-reference to relevant sections.]*
>
> or
>
> *Pediatrics (age range): No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.*
>
> or
>
> *Pediatrics (age range): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of [Brand name] in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use. [Include cross-reference to relevant sections.]*

1.2 Geriatrics

One of the following or similar statements may be used:

Geriatrics: No data are available to Health Canada; therefore, Health Canada has not authorized an indication for geriatric use.

or

Geriatrics: Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness.

2 CONTRAINDICATIONS

- [text]

Describe absolute contraindications, meaning those situations in which the drug should not be used because the risk outweighs any potential therapeutic benefit. For example:

[Proper name] is contraindicated with co-administration of [Drug X] as it may result in increased concentrations of [Drug X] due to inhibition of CYP3A, which may lead to QT interval prolongation and torsades de pointes. See 7 WARNINGS AND PRECAUTIONS and 9 DRUG INTERACTIONS.

For hypersensitivity reactions, the following or similar statement should be used:

[Proper name] is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions

- [text]
- [text]

Clinically significant or serious (e.g., life-threatening) safety hazards should be placed in this box, with a cross reference to the relevant section(s) for more detailed information. Generally, this text should not exceed 20 lines.

For all radiopharmaceuticals the Serious Warnings and Precautions Box should contain the following or similar statement:

Radiopharmaceuticals should be used only by those health professionals who are appropriately qualified in the use of radioactive prescribed substances in or on humans.

In the absence of a serious warning or precaution identified at the time of authorization, this box is

omitted, along with the heading 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

4 DOSAGE AND ADMINISTRATION

Biosimilar specific properties should be considered, such as potentially allergenic product container materials or differences in product presentation that require biosimilar-specific storage and administration directions.

4.1 Dosing Considerations

- [text]

Briefly list all safety issues to consider that may affect dosing of the drug (e.g., renal or hepatic disease, concomitant therapy, changing from intravenous to oral therapy, lab values prior to infusion, rule out pregnancy prior to administration, pre-medication is required, duration of effect, imaging time post-injection).

4.2 Recommended Dose and Dosage Adjustment

- [text]

Include detailed dosage information for each indication, route of administration and/or dosage form, dosage schedules, booster doses, initial dose, titration of dose, dosage range, maximum daily dose, maintenance dosage, duration of treatment and drug discontinuance, considerations for special populations.

In the absence of a Health Canada authorized pediatric indication, the following or similar statement should be used, with a cross-reference to relevant sections, if applicable:

Health Canada has not authorized an indication for pediatric use.

4.3 Reconstitution

Oral Solutions:

- [text and/or table]

List all recommended diluents for reconstitution. Directions should include the volume and type of diluents to be added and the approximate volume and concentration of the resulting product.

Recommended storage period and conditions should be stated and include cross-reference to 11 STORAGE, STABILITY AND DISPOSAL.

Parenteral Products:

- [table and text]

For intravenous use, information should be separately described for direct intravenous injection, intermittent infusion, and continuous infusion; use of in-line filters etc.

Include any specific precautions, storage periods and incompatibilities, and include cross-reference to 11 STORAGE, STABILITY AND DISPOSAL.

Table - Reconstitution

Vial Size	Volume of Diluent to be Added to Vial	Approximate Available Volume	Concentration per mL

4.4 Administration

[text and/or table]

Include details concerning methods of administration. Specify any special considerations (e.g., do not crush, do not split if not scored, capsule contents can be sprinkled).

For radiopharmaceuticals, if applicable, include the following or similar statement:

> *The patient dose should be measured by a suitable radioactivity calibration system prior to administration.*

4.5 Missed Dose

[text]

Include actions to be taken in the event that a patient misses a dose.

4.6 Image Acquisition and Interpretation

[text]

For radiopharmaceuticals only, otherwise delete this subheading. Include specific requirements for image acquisition and interpretation such as type of equipment and calibration scanning or imaging time post injection, location of views, and frequency of images.

4.7 Instructions for Preparation and Use

[text]

For radiopharmaceuticals only, otherwise delete this subheading. The following or similar statement should be included:

The components of the reagent vial are sterile and nonpyrogenic. It is essential that the user follows the directions carefully and adheres to strict aseptic technique.

or

Use aseptic technique and wear waterproof gloves throughout the entire preparation procedure.

or

Make all transfers of radioactive solutions with an adequately shielded syringe and maintain adequate shielding around the vial during the useful life of the radioactive product.

4.8 Radiation Dosimetry

[For radiopharmaceuticals only, otherwise delete this subheading. This is an example of acceptable presentation of Dose Estimate Data:]

Final Dose Estimates: [The model and method of calculation should be specified.]

ORGAN	mGy/MBq	rad/mCi
Adrenals		
Brain		
Breasts		
Gallbladder Wall		
LLI Wall		
Small Intestine		
Stomach		
ULI Wall		
Heart Wall		
Kidneys		
Liver		
Lungs		
Muscle		
Ovaries		
Pancreas		
Red Marrow		
Bone Surfaces		
Skin		
Spleen		
Testes		
Thymus		
Thyroid		
Urinary Bladder		
Uterus		

Effective Dose Equivalent (mSv/MBq) (rem/mCi)

Effective Dose (mSv/MBq) (rem/mCi)

5 OVERDOSAGE

[text]

Include the following information:

- a description of the acute and/or long-term signs and symptoms of overdose,
- potential sequelae/complications which may occur with the drug e.g. organ toxicity,
- current recommended management of overdosage (e.g., monitoring, use of agonist/antagonist/antidotes, method to increase elimination and/or other clinical interventions), and
- procedures that, by experience with this or similar type drugs, are known or reasonably expected to be unnecessary or unsuitable (e.g., those that may be hazardous to the patient).

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

To help ensure the traceability of biologic products, including biosimilars, health professionals should recognise the importance of recording both the brand name and the non-proprietary (active ingredient) name as well as other product-specific identifiers such as the Drug Identification Number (DIN) and the batch/lot number of the product supplied.

To help ensure the traceability of vaccines for patient immunization record-keeping as well as safety monitoring, health professionals should record the time and date of administration, quantity of administered dose (if applicable), anatomical site and route of administration, brand name and generic name of the vaccine, the product lot number and expiry date.

Table – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
[oral]	[tablet 5 mg, 10 mg]	[List all non-medicinal ingredients in alphabetical order]

[text]

Description

[text]

For biosimilars only, otherwise delete this subheading. Include a narrative description of the biosimilar biologic drug that is similar to the narrative in the reference biologic drug monograph. Incorporate changes as necessary where there are descriptive differences between the biosimilar and the reference biologic drug due to, for example, differences in formulation.

6.1 Physical Characteristics

[table]

For radiopharmaceuticals only, otherwise delete this subheading. Include physical half-life, principle radiation emission data, physical decay chart (tabular format), parent and daughter radionuclides data.

6.2 External Radiation

[table]

For radiopharmaceuticals only, otherwise delete this subheading. Include specific gamma ray constant for the radioisotope, radiation attenuation by lead shielding (tabular format), parent and daughter radionuclides data.

7 WARNINGS AND PRECAUTIONS

If applicable, include one of the following statements:

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

For blood products:

This product is prepared from large pools of human plasma. Thus, there is a possibility it may contain causative agents of viral or other undetermined diseases.

For all radiopharmaceuticals:

The product should be administered under the supervision of a health professional who is experienced in the use of radiopharmaceuticals. Appropriate management of therapy and complications is only possible when adequate diagnostic and treatment facilities are readily available.

The radiopharmaceutical product may be received, used and administered only by authorized persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licenses of local competent official organizations.

As in the use of any other radioactive material, care should be taken to minimize radiation exposure to patients consistent with proper patient management, and to minimize radiation exposure to occupational workers.

[Subheadings to be included as applicable, in alphabetical order:]

General

Include information that does not fall under the subheadings listed below.

For products derived from plasma, explain the inherent risks when products have been derived from plasma.

[text]

Carcinogenesis and Mutagenesis

Include only human data where there is evidence that the drug is carcinogenic or mutagenic. Where there is only animal data, a cross-reference to the animal data in 16 NON-CLINICAL TOXICOLOGY should be provided.

[text]

Cardiovascular

Includes QTc prolongation (cross reference to 10.2 Pharmacodynamics as required.

[text]

Contamination

For radiopharmaceuticals, include practical information for the patient to minimize the contamination potential after receiving the drug. This information must also appear in the Patient Medication Information.

[text]

Dependence/Tolerance

Include effects for both physical and psychological dependence. Treatment of the effects of the dependence should be provided.

[text]

Driving and Operating Machinery

If applicable, this subheading should include the following or similar statement:

Exercise caution when driving or operating a vehicle or potentially dangerous machinery.

[text]

Ear/Nose/Throat

[text]

Endocrine and Metabolism

This subheading should specify genetic polymorphism where applicable.

[text]

Gastrointestinal

[text]

Genitourinary

[text]

Hematologic

[text]

Hepatic/Biliary/Pancreatic

When possible, idiopathic versus metabolic liver failure should be described.

[text]

Immune

[text]

Monitoring and Laboratory Tests

[text]

Musculoskeletal

[text]

Neurologic

[text]

Ophthalmologic

[text]

Peri-Operative Considerations

Include information on management before, during and after surgery.

[text]

Psychiatric

Behavioural changes, or potential (e.g., suicidal ideation) should be stated.

[text]

Renal

[text]

Reproductive Health: Female and Male Potential

Cross-reference to other relevant sections (e.g. 2 CONTRAINDICATIONS, 7.1.1 Pregnant Women);

consider contraception for both females and males.

- **Fertility**

  Include a summary of relevant information of effects of the drug on fertility from animal or human exposure. In the absence of information, clearly state that no data exist.

  [text]

- **Function**

  Include effects on sexual desire, erection, orgasm and ejaculation.

  [text]

- **Teratogenic Risk**

  Teratogenic and nonteratogenic effects on the fetus should be included. If contraindicated in pregnancy, this should be stated in 2 CONTRAINDICATIONS.

  [text]

Respiratory

[text]

Sensitivity/Resistance

[text]

Skin

Include information on local reactions to vaccination, human photosensitivity where applicable, etc.

[text]

7.1 Special Populations

7.1.1 Pregnant Women

Include information related to Pregnancy Registries. The availability of a pregnancy exposure registry should also be included in the Patient Medication Information. If information on birth defects and miscarriage is available for the patient population for whom the drug is labelled, it must also be included, along with the following, when available:

- Disease-associated maternal and/or fetal risk
- Maternal adverse reactions
- Embryo/Fetal/Neonatal adverse reactions
- Labour and/or delivery

The extent of exposure in pregnancy during clinical trials should be included:

Wide: > 1,000 pregnancies

Limited: < 1,000 pregnancies
Very Limited: individual cases only
No experience.

For radiopharmaceuticals the following or similar statement may be included:

Ideally, examinations using radiopharmaceuticals, especially those elective in nature of women of childbearing capability, should be performed during the first ten days following the onset of menses, or after ensuring the woman is not pregnant. The benefit of using a diagnostic radiopharmaceutical should be weighed against the possible risk to an embryo or a fetus.

[text]

7.1.2 Breast-feeding

If studies have shown that the drug is not excreted in human breast milk, it should be stated. In the absence of human data, pertinent animal data should be included along with the following or similar statement:

It is unknown if [Brand name] [product] is excreted in human milk. Precaution should be exercised because many drugs can be excreted in human milk.

For radiopharmaceuticals, the following or similar statement should be included:

Where an assessment of the risk to benefit ratio suggests the use of this product in nursing mothers, formula feeding should be substituted for breast feeding.

[text]

7.1.3 Pediatrics

In the absence of a Health Canada authorized pediatric indication, the following statement should be used:

Pediatrics (age range): *No data are available to Health Canada; therefore, Health Canada has not authorized an indication for pediatric use.*

or

Pediatrics (age range): *Based on the data submitted and reviewed by Health Canada, the safety and efficacy of [Brand name] in pediatric patients has not been established; therefore, Health Canada has not authorized an indication for pediatric use. [Include cross-reference to relevant sections.]*

[text]

7.1.4 Geriatrics

[text]

8 ADVERSE REACTIONS

For biosimilars, include the following or similar statement:

The adverse drug reaction profiles reported in clinical studies that compared [Biosimilar brand name] to the reference biologic drug were comparable. The description of adverse reactions in this section is based on clinical experience with the reference biologic drug.

8.1 Adverse Reaction Overview

[text]

Provide information on the most serious and/or most frequently occurring adverse reactions, or those where there have been reports of particularly severe cases. Frequencies to be stated as accurately as possible. It should not be a summary of the safety database.

8.2 Clinical Trial Adverse Reactions

Clinical trials are conducted under very specific conditions. The adverse reaction rates observed in the clinical trials; therefore, may not reflect the rates observed in practice and should not be compared to the rates in the clinical trials of another drug. Adverse reaction information from clinical trials may be useful in identifying and approximating rates of adverse drug reactions in real-world use.

[Include a brief description of data sources.]

[text]

Table [#] [Title of Table]

	[drug name] n = [#] (%)	**[placebo] n = [#] (%)**
[use MedDRA terms for headings, as applicable] **Cardiovascular** [text]		
Gastrointestinal [text]		

[text]

A brief narrative should follow the table to explain or supplement the information provided in the table where applicable. Separate tables may be required for different indications (e.g., oncology and a non-oncology indication) or different formulations (e.g., oral, intravenous) or different drug combinations.

Adverse reactions may also be related to genetically determined product metabolism. Subjects or patients deficient in the specific enzyme may experience a different rate or severity of adverse

reactions. This should be mentioned where relevant, and correlated with data from clinical trials.

8.2.1 Clinical Trial Adverse Reactions – Pediatrics

[text]

From pediatric studies include: age characteristics, any clinically relevant differences (i.e., seriousness or reversibility of adverse reaction) between safety profiles in adult and pediatric populations, or any relevant age groups, uncertainties due to limited experience. If the observed safety profile is consistent in children and adults this could be stated.

8.3 Less Common Clinical Trial Adverse Reactions

[text]

Present as a list, categorized by System Organ Class, alphabetically: e.g.,
Cardiovascular: [text]
Gastrointestinal: [text]

8.3.1 Less Common Clinical Trial Adverse Reactions – Pediatrics

[text]

Present as a list, categorized by System Organ Class, alphabetically: e.g.,
Cardiovascular: [text]
Gastrointestinal: [text]

8.4 Abnormal Laboratory Findings: Hematologic, Clinical Chemistry and Other Quantitative Data

Clinical Trial Findings

[table]

Outline any differences between adults, geriatrics and pediatrics as necessary with regard to abnormal laboratory findings.

Post-Market Findings

[table]

Outline any differences between adults, geriatrics and pediatrics as necessary with regard to post-market abnormal laboratory findings.

8.5 Post-Market Adverse Reactions

[text and/or table]

Include Canadian and international post-market adverse reactions including serious and/or unexpected adverse reactions that are reported through post-market surveillance and/or identified in Phase IV clinical trials. Adverse reactions already listed in the Clinical Trial Adverse Reactions section should not be repeated in this section unless there are changes in severity, frequency or character.

9 DRUG INTERACTIONS

9.1 Serious Drug Interactions

Serious Drug Interactions

[Serious (e.g., life-threatening) drug interactions should be highlighted in this box, with a cross-reference to detailed information in 9.4 Drug-Drug Interactions. Not to exceed 20 lines.]

- [text]
- [text]

If there are no serious drug interactions at the time of authorization, this box is omitted, along with the heading 9.1 Serious Drug Interactions.

9.2 Drug Interactions Overview

[text]

9.3 Drug-Behavioural Interactions

[text]

Briefly present potential interactions in terms of individual behavioural risks including, but not limited to, alcohol consumption, sexual activity, and smoking, which may result in unfavourable adverse events or treatment outcomes.

9.4 Drug-Drug Interactions

The following or similar statement should precede the table:

The drugs listed in this table are based on either drug interaction case reports or studies, or potential interactions due to the expected magnitude and seriousness of the interaction (i.e., those identified as contraindicated).

Where no interaction data is known the following or similar statement should be included:

Interactions with other drugs have not been established.

Table [#] - Established or Potential Drug-Drug Interactions

[Proper/Common name]	Source of Evidence	Effect	Clinical comment
[drug A]	[level/source of evidence, see legend]	[drug A] conc	[Caution is warranted and therapeutic concentration monitoring is recommended]

Legend: C = Case Study; CT = Clinical Trial; T = Theoretical

9.5 Drug-Food Interactions

[text]

Briefly present known or potential interactions with food or beverages (e.g., grapefruit, caffeine). Cross-referencing to 4 DOSAGE AND ADMINISTRATION may be required when the timing of food consumption should be considered.

Where no interaction data is known, the following or similar statement should be included:

Interactions with food have not been established.

9.6 Drug-Herb Interactions

[text]

Briefly present known or potential interactions with herbal products and practical guidance for the health professional.

Where no interaction data is known, the following or similar statement should be included:

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

[text]

Briefly present laboratory tests affected by the presence of the drug, such as interfering with the accuracy of the test results or methods (e.g., antihistamines diminish the positive reactions to dermal reactivity indicators).

Where no interaction data is known, the following or similar statement should be included:

Interactions with laboratory tests have not been established.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

[text]

10.2 Pharmacodynamics

[text]

10.3 Pharmacokinetics

Table [#] - Summary of [proper name] Pharmacokinetic Parameters in [specific patient population]

	C_{max}	T_{max}	$t_{½}$ (h)	$AUC_{0-\infty}$	CL	Vd
Single dose mean						

Absorption

[text]

Distribution:

[text]

Metabolism:

[text]

Elimination

[text]

Duration of Effect

This subsection applies specifically to vaccines and should describe the duration of effect of the recommended dose (e.g., duration of detectable levels of antibodies and/or conferred immunity status).

[text]

Special Populations and Conditions

[text]

- **Pediatrics** [text]
- **Geriatrics** [text]
- **Sex** [text]
- **Pregnancy and Breast-feeding** [text]
- **Genetic Polymorphism** [text]
- **Ethnic Origin** [text]
- **Hepatic Insufficiency** [text]
- **Renal Insufficiency** [text]
- **Obesity** [text]

11 STORAGE, STABILITY AND DISPOSAL

[text]

Include recommended storage conditions for each dosage form as supported by stability studies.

For reconstituted products, including parenterals, the recommended storage period and conditions should be stated.

Disposal instructions should be included for all drug products. Include a cross-reference to more detailed safe disposal instructions under 12 SPECIAL HANDLING INSTRUCTIONS where appropriate.

For radiopharmaceutical kits include the following or similar statement:

> *Do not use the kit beyond the expiration date stamped on the box. After preparation [product] should be stored at room temperature until administration, within [x] hours of radiolabelling.*

12 SPECIAL HANDLING INSTRUCTIONS

[text]

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: [text]

Chemical name: [text]

Molecular formula and molecular mass: [text]

Structural formula: [image]

Physicochemical properties: [text]

Pharmaceutical standard: [for biologics] [text]

Product Characteristics:

[text]

For radiopharmaceuticals, provide detailed information or a lengthier description of product characteristics that are in addition to those mentioned under 6.1 Physical Characteristics.

For biologics, this subsection should describe the method of manufacture. Sponsors are not expected to supply proprietary information, but they must provide enough detail to provide health professionals with an understanding of how the product is prepared.

Viral Inactivation

[text]

For products derived from plasma, detail the viral reduction steps. Include information on selection criteria for donors, if applicable.

14 CLINICAL TRIALS

14.1 Trial Design and Study Demographics

For biosimilars, include the following or similar statement for comparative trials:

Clinical studies conducted to support similarity between [Biosimilar brand name] and the reference biologic drug included:

- [text] [Provide a general description of study 1, for example, a randomized comparative bioavailability study performed in healthy volunteers.]
- [text] [Provide a general description of study 2, for example, a double-blind, randomized, comparative safety and efficacy study performed in patients with moderate to severe rheumatoid arthritis.]

Table [#] - Summary of patient demographics for clinical trials in [specific indication]

Study #	Study design	Dosage, route of administration and duration	Study subjects (n)	Mean age (Range)	Sex

[Provide a brief narrative describing the demographic characteristics of the study population:]

[text]

14.2 Study Results

For biosimilars, there should be no claims of bioequivalence or clinical equivalence between the biosimilar and the reference biologic drug. For biosimilar submissions that include only comparative bioavailability studies, leave this section blank and include the following statement:

See 14.3 Comparative Bioavailability Studies.

Table [#] - Results of study [#] in [specific indication]

Primary Endpoints	Associated value and statistical significance for Drug at specific dosages	Associated value and statistical significance for Placebo or active control

14.3 Comparative Bioavailability Studies

[text]

Provide a narrative outlining the design of the bioequivalence study. The values in the table should be based on the measured data from the study. No potency correction should be applied.

For biosimilars, comparative pharmacokinetic (PK) studies should be conducted to rule out differences in PK characteristics between the biosimilar and the reference biologic drug. For clinical studies conducted to support similarity between a biosimilar and the reference biologic drug, there may be cases where a pharmacodynamic (PD) marker may be used in lieu of clinical endpoints or as additional support for similarity. If this is the case, include a brief narrative describing the study and a tabulation of the PD results including the appropriate statistical analyses.

[Table for single dose studies:]

Analyte Name (__ x __ mg) From measured data Geometric Mean Arithmetic Mean (CV %)				
Parameter	**Test**[1]	**Reference**[2]	**% Ratio of Geometric Means**	**Confidence Interval**[3]
AUC_T[4] (units)				
AUC_I (units)				
C_{MAX} (units)				
T_{MAX}[5] (h)			Not applicable	Not applicable
$T_{½}$[6] (h)			Not applicable	Not applicable

[Table for multiple dose studies:]

1 Identity of the test product.

2 Identity of the reference product, including the manufacturer, and origin (country of purchase).

3 Indicate % Confidence Interval (i.e., 90% or 95%) in the column heading and list for the AUC_T, AUC_I and C_{MAX} (if required).

4 For drugs with a half-life greater than 24 hours AUC_T should be replaced with AUC_{0-72}.

5 Expressed as either the arithmetic mean (CV%) or the median (range) only.

6 Expressed as the arithmetic mean (CV%) only.

Analyte Name (__ x __ mg) From measured data Geometric Mean Arithmetic Mean (CV %)				
Parameter	**Test[7]**	**Reference[8]**	**% Ratio of Geometric Means**	**Confidence Interval[9]**
AUC_{tau} (units)				
C_{MAX} (units)				
C_{MIN} (units)				
T_{MAX}[10] (h)			Not applicable	Not applicable

14.4 Immunogenicity

[text]

For vaccines, include information on efficacy by class of individuals, to recognize differences in immunogenicity.

For biosimilars, include comparative immunogenicity results, if applicable, with a brief narrative describing the testing strategy for anti-drug antibodies (ADA) and the overall incidence of treatment emergent or treatment enhanced confirmed binding antibodies.

The following or similar statements may be included:

Comparing the incidences of antibodies between studies or between products may be misleading due to differences in the types, sensitivities and/or specificities of the assays employed.

or

As with all therapeutic proteins, there is a potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

---

7 Identity of the test product.

8 Identity of the reference product, including the manufacturer, and origin (country of purchase),where applicable.

9 Indicate % Confidence Interval (i.e., 90% or 95%) in the column heading and list for the AUC_T, AUC_I and C_{MAX} (if required).

10 Expressed as either the arithmetic mean (CV%) or the median (range) only.

14.5 Clinical Trials - Reference Biologic Drug

[text]

For biosimilars only, otherwise delete this subheading. Import the clinical trial information that appears in the reference biologic drug's monograph with respect to indications to be authorized for the biosimilar. Clinical trial data for indications that will not be authorized for the biosimilar should not be included.

15 MICROBIOLOGY

[text]

[table]

For drugs with no antimicrobial properties, include the following statement:

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

Only use a table if presentation will be more concise. The following or similar statements should be included where applicable:

No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether [Brand name] affects fertility in males or females.

As with other radiopharmaceuticals which distribute intracellularly, there may be increased risk of chromosome damage from Auger electrons if nuclear uptake occurs.

For biologics, this section should confirm if long-term studies have been done to evaluate immunogenicity.

For biosimilars, include toxicology information that appears in the reference biologic drug product monograph. The reference biologic drug brand name should be changed to the proper name (INN). Data that relates only to indications that will not be authorized for the biosimilar should not be included.

General Toxicology: [text]

Carcinogenicity: [text]

Genotoxicity: [text]

Reproductive and Developmental Toxicology: [text]

Special Toxicology: [text]

Juvenile Toxicity: [text]

16.1 Comparative Non-Clinical Pharmacology and Toxicology

For biosimilars only, otherwise delete this subheading, as well as 16.1.1 Comparative Non-Clinical Pharmacodynamics and 16.1.2. Comparative Toxicology.

16.1.1 Comparative Non-Clinical Pharmacodynamics

In vitro Studies

[provide a narrative and/or table]

[text]

[table]

16.1.2 Comparative Toxicology

[provide a narrative and/or table]

[text]

[table]

17 SUPPORTING PRODUCT MONOGRAPHS

[numbered list:]

[Brand name] [dosage form, strength], submission control [number], Product Monograph, [Sponsor]. [(MON DD, YYYY)]

List only Health Canada authorized product monographs that were supportive in the development of the product monograph (e.g., Canadian Reference Product for a generic, or Reference Biologic Drug for a biosimilar biologic drug), combination product, or subsequent entry product.

Where there are no such supporting product monographs, this section, including heading, should be omitted.

PATIENT MEDICATION INFORMATION

The Patient Medication Information section should be written at the grade 6-8 reading literacy level.

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[BRAND NAME]

[Proper Name in final dosage form]

Read this carefully before you start taking **[Brand name]** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **[Brand name]**.

For biosimilars include the following statement:

> ***[Brand name]*** *is a biosimilar biologic drug (biosimilar) to the reference biologic drug [Reference biologic drug brand name]. A biosimilar is authorized based on its similarity to a reference biologic drug that was already authorized for sale.*

Serious Warnings and Precautions

- [text]
- [text]

The box should contain a plain language version of the information provided in 3 SERIOUS WARNINGS AND PRECAUTIONS BOX. Delete this box if there are no Serious Warnings and Precautions.

What is [Brand name] used for?

- [text]
- [text]

[For products that have been authorized under the Notice of Compliance with Conditions (NOC/c) policy, include the following boxed statement:]

"For the following indication(s) [Brand name] has been approved with conditions (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional."

[Provide a bullet listing of the indications from Part I.]

- [text]

[If the Indications section includes lifestyle recommendations as part of the therapy, they should be included here.]

"For the following indication(s) [Brand name] has been approved without conditions. This means it has passed Health Canada's review and can be bought and sold in Canada."

[Provide a bullet listing of the indications from Part I.]

- [text]

[If the Indications section includes lifestyle recommendations as part of the therapy, they should be included here.]

For products that have been authorized under the NOC/c policy, the following text must be included:

What is a Notice of Compliance with Conditions (NOC/c)?

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How does [Brand name] work?

[text]

What are the ingredients in [Brand name]?

Medicinal ingredients: [List all medicinal ingredients]

Non-medicinal ingredients: [List all non-medicinal ingredients in alphabetical order.]

[Brand name] comes in the following dosage forms:

[dosage form(s) and strength(s)]

To maintain brevity, this is the only information required in this section.

Do not use [Brand name] if:

- [text]
- [text]

Enter one point for each contraindication from 2 CONTRAINDICATIONS.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take [Brand name]. Talk about any health conditions or problems you may have, including if you:

- [text]
- [text]

Enter one point for each item listed in 7 WARNINGS AND PRECAUTIONS.

Other warnings you should know about:

[text]

Enter general information that would not appear in the Serious Warnings and Precautions Box or other existing headings. Otherwise this heading is not required.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with [Brand name]:

- [list]

Include information from 9 DRUG INTERACTIONS. If no relevant interactions are known, add a statement to reflect this.

How to take [Brand name]:

- [text]

Consider the following or similar statements as required:

Do not use this medication if it looks cloudy or is leaking.
or
[Brand name] will be given to you by a healthcare professional in a healthcare setting.
or
[for radiopharmaceuticals:] *[product] will be given to you by a healthcare professional who is experienced in the use of radiopharmaceuticals.*

Usual dose:

[text]

Overdose:

[text]

If you think you, or a person you are caring for, have taken too much [Brand name], contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

From 5 OVERDOSAGE, provide information on what to do if the individual has taken too much medication. The boxed message may be modified to provide the most appropriate advice according to current standards of care for this drug product.

Missed Dose:

[text]

What are possible side effects from using [Brand name]?

These are not all the possible side effects you may have when taking [Brand name]. If you experience any side effects not listed here, tell your healthcare professional.

[text]

Self-limiting side effects should be described in the text section only. Those listed in 3 SERIOUS WARNINGS AND PRECAUTIONS BOX must be listed in the serious side effects table. Each side effect should appear only once, in text or in the table to avoid duplication.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
[Condition: symptom / effect]			
[Condition: symptom / effect]			
COMMON			
[Condition: symptom / effect]			
[Condition: symptom / effect]			
RARE			
[Condition: symptom / effect]			
[Condition: symptom / effect]			

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to

interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Reporting Suspected Side Effects for Vaccines

For the general public: Should you experience a side effect following immunization, please report it to your healthcare professional.

Should you require information related to the management of the side effect, please contact your healthcare professional. The Public Health Agency of Canada, Health Canada and [Sponsor Name] cannot provide medical advice.

For healthcare professionals: If a patient experiences a side effect following immunization, please complete the Adverse Events Following Immunization (AEFI) Form appropriate for your province/territory (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) and send it to your local Health Unit.

Please choose the reporting box option that is most appropriate for this product.

Storage:

[text**]**

Keep out of reach and sight of children.

If you want more information about [Brand name]:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; the manufacturer's website [website], or by calling 1-800-[phone number].

This leaflet was prepared by [Sponsor Name].

Last Revised [MON DD, YYYY]