[Product Monograph Template – Schedule D – Biosimilar Biologic Drug]

[Title Page]

PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

<Scheduling Symbol> <**BRAND NAME**>

<Proper name>

<Dosage Form(s), Strength(s) and Route(s) of Administration>

<Pharmaceutical Standard (if applicable)>

<Therapeutic Classification>

<Sponsor Name>
<Sponsor Address>

Date of Initial Approval:
<MON DD,YYYY>

Date of Revision:
<MON DD,YYYY>

Submission Control No: <control number>

RECENT MAJOR LABEL CHANGES

<Section Heading>, <Subsection heading> <(Section or Subsection number)> <MON, YYYY>

TABLE OF CONTENTS

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

<Biosimilar brand name (proper name)> is a biosimilar biologic drug (biosimilar) to <Reference biologic drug brand name>.

PART I: HEALTH PROFESSIONAL INFORMATION

[Part I should be completed by importing information from the reference biologic drug's product monograph pertaining to indications to be authorized for the biosimilar. Specific differences between the biosimilar and the reference biologic drug (for example, formulation or presentation differences) should be noted in the appropriate sections.]

1 INDICATIONS

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

<Biosimilar brand name (proper name)> is indicated for:

- <text>
- <text>

<text>

[The wording of each indication authorized for the biosimilar should be identical to the reference biologic drug product monograph.]

1.1 Pediatrics

<text>

1.2 Geriatrics

<text>

2 CONTRAINDICATIONS

<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 Dosage Forms, Strengths, Composition and Packaging.

- <text>
- <text>

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

<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

[Briefly list all situations that may affect dosing of the drug:]
- <text>
- <text>

4.2 Recommended Dose and Dosage Adjustment

[Include dosages for each indication, route of administration and/or dosage form.]
<text>

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

Health Canada has not authorized an indication for pediatric use. <(cross-reference to relevant sections, if applicable)>

4.3 Administration

<text and/or table>

4.4 Reconstitution

Oral Solutions: <text and/or table>
Parenteral Products: <table and text>

Table - Reconstitution

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

[Include any specific precautions, storage periods and incompatibilities.]

4.5 Missed Dose

<text>

5 OVERDOSAGE

<text>

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.

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>

7 DESCRIPTION

[Insert 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].
<text>

8 WARNINGS AND PRECAUTIONS

[If applicable, include the following statement:]

Please see the Serious Warnings and Precautions Box at the beginning of Part I: Health Professional Information.

[Subheadings to be included as applicable, in alphabetical order:]
General
<text>

Carcinogenesis and Mutagenesis
<text>

Cardiovascular
<text>

Dependence/Tolerance
<text>

Driving and Operating Machinery
[This subheading should include the following or similar statement:]

Due caution should be exercised when driving or operating a vehicle or potentially dangerous machinery.

Ear/Nose/Throat
<text>

Endocrine and Metabolism
<text>

Gastrointestinal
<text>

Genitourinary
<text>

Hematologic
<text>

Hepatic/Biliary/Pancreatic
<text>

Immune
<text>

Monitoring and Laboratory Tests
<text>

Neurologic
<text>

Ophthalmologic
<text>

Peri-Operative Considerations
<text>

Psychiatric
<text>

Renal
<text>

Respiratory
<text>

Sensitivity/Resistance
<text>

Sexual Health
Reproduction
<text>

Function
<text>

Fertility
<text>

8.1 Special Populations

8.1.1 Pregnant Women

<text>

8.1.2 Breast-feeding

<text>

8.1.3 Pediatrics

<text>

8.1.4 Geriatrics

<text>

9 ADVERSE REACTIONS

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.

[Adverse drug reaction information in sections 9.1 to 9.6 should be identical to that in the reference biologic drug product monograph (including narratives and tables) except that only adverse reaction information that is relevant to indications authorized for the biosimilar should be included.]

9.1 Adverse Reaction Overview

<text>

9.2 Clinical Trial Adverse Reactions

Because clinical trials are conducted under very specific conditions, the adverse reaction rates observed in the clinical trials 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 is useful for identifying drug-related adverse events and for approximating rates.

[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>		

[A brief narrative should follow the table to explain or supplement the information provided in the table:]

<text>

9.3 Less Common Clinical Trial Adverse Reactions

[Present as a list, categorized by System Organ Class, alphabetically:]
Cardiovascular: <text>
Gastrointestinal: <text>

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

<table>

9.5 Clinical Trial Adverse Reactions (Pediatrics)

<text>

9.6 Post-Market Adverse Reactions

<text and/or table>

10 DRUG INTERACTIONS

10.1 Serious Drug Interactions Box

<box>

10.2 Overview

<text>

10.3 Drug-Drug Interactions

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).

[or]

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 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

10.4 Drug-Food Interactions

<text>

10.5 Drug-Herb Interactions

<text>

10.6 Drug-Laboratory Test Interactions

<text>

10.7 Drug-Lifestyle Interactions

<text>

11 ACTION AND CLINICAL PHARMACOLOGY

[Comparative pharmacokinetic/pharmacodynamic (PK/PD) data from the biosimilar program should not be presented in this section. Biosimilar data should be presented in Part II: Scientific Information, Clinical Trials.]

11.1 Mechanism of Action

<text>

11.2 Pharmacodynamics

<text>

11.3 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: <text>

Special Populations and Conditions

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>

12 STORAGE, STABILITY AND DISPOSAL

[Directions may differ from those in the reference biologic drug product monograph.]

<text>

13 SPECIAL HANDLING INSTRUCTIONS

[Directions may differ from those in the reference biologic drug product monograph.]

<text>

PART II: SCIENTIFIC INFORMATION

14 PHARMACEUTICAL INFORMATION

[Pharmaceutical information should be based entirely on information pertaining to the biosimilar.]

Drug Substance

Proper name: <text>

Chemical name: <text>

Molecular formula and molecular mass: <text>

Structural formula: <image>

Physicochemical properties: <text>

Product Characteristics

<text>

15 COMPARATIVE CLINICAL TRIALS

15.1 Comparative Trial Design and Study Demographics

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.]

An overview of the study design(s) and demographic characteristics of patients enrolled in each clinical study are presented in Table <#>.

Table <#> - Summary of trial design and patient demographics

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

[Provide a narrative describing additional trial design as necessary (see *Guidance Document - Product Monograph*, sections 4.2.1 – Efficacy and Safety Studies and 4.2.2 – Pivotal

Comparative Bioavailability Studies).]
<text>

15.2 Comparative Study Results

[There should be no claims of bioequivalence or clinical equivalence between the biosimilar and the reference biologic drug.]

15.2.1 Comparative Bioavailability Studies

15.2.1.1 Pharmacokinetics

[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 (units)				
AUC_I (units)				
C_{MAX} (units)				
T_{MAX}[4] (h)				
$T_{½}$[5] (h)				

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

[Table for multiple dose studies:]

Analyte Name **(__ x __ mg)** **From measured data** **Geometric Mean** **Arithmetic Mean (CV %)**

Parameter	**Test**[6]	**Reference**[7]	**% Ratio of Geometric Means**	**Confidence Interval**[8]
AUC_{tau} (units)				
C_{MAX} (units)				
C_{MIN} (units)				
T_{MAX}[9] (h)				

15.2.1.2 Pharmacodynamics [if applicable]

[In some cases a pharmacodynamic (PD) marker may be used in lieu of clinical endpoints or as additional support for similarity. If this is the case, insert a comparative PD section with a brief narrative describing the study and a tabulation of the PD results including the appropriate statistical analyses].
<text>
<table>

15.2.2 Comparative Safety and Efficacy

15.2.2.1 Efficacy

Table <#> - Results of study <#> in <specific indication>
[Results of the primary endpoint(s) comparing the biosimilar biologic drug to the reference biologic drug should be captured in a table including the estimated treatment effect(s) and the corresponding measures of uncertainty (p-values, confidence intervals). The table should include footnotes describing any statistical method used and any applied acceptance criteria (i.e., the "equivalence margin"). (See *Guidance Document - Product Monograph*, section 4.2.1 – Efficacy and Safety Studies, Study Results).]
<table>

6 Identity of the test product.
7 Identity of the reference product, including the manufacturer, and origin (country of purchase),where applicable.
8 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).
9 Expressed as either the arithmetic mean (CV%) or the median (range) only.

15.2.2.2 Safety

The types, frequency and severity of adverse events were comparable between the biosimilar and the reference biologic drug.

15.2.2.3 Immunogenicity

[Include 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]
<text>

16 COMPARATIVE NON-CLINICAL PHARMACOLOGY AND TOXICOLOGY

16.1 Comparative Non-Clinical Pharmacodynamics

***In vitro* Studies**

[Provide a narrative and/or table]
<text>
<table>

16.2 Comparative Toxicology

[Provide a narrative and/or table]
<text>
<table>

17 CLINICAL TRIALS – REFERENCE BIOLOGIC DRUG

[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.]
<text>

18 NON-CLINICAL TOXICOLOGY – REFERENCE BIOLOGIC DRUG

[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.]

<text>

19 SUPPORTING PRODUCT MONOGRAPHS

[Where there are no supporting product monographs, this section should be omitted.]

[numbered list:]
<Brand name> <(dosage form, strength)>, submission control <number>, Product Monograph, <sponsor>. <(MON, DD, YYYY)>

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[This section should be based on the Canadian Patient Medication Information for the reference biologic drug. Only information that is relevant to indications authorized for the biosimilar should be included. Incorporate changes as necessary where there are differences between the biosimilar and reference biologic drug in, for example, presentation, administration instructions, or allergens in packaging.]

PATIENT MEDICATION INFORMATION

<BRAND NAME> (pronounced) <basic phonetic spelling>
<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>**.

<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**>**

What is <Brand name> used for?

- **<**text**>**
- **<**text**>**

How does <Brand name> work?

[At the grade 6-8 reading level, explain the mechanism of action, in one or two sentences. Indicate how long it takes to work and how to know if it is working.]
<text>

What are the ingredients in <Brand name>?

Medicinal ingredients: [List all medicinal ingredients from Part I.]
Non-medicinal ingredients: [List all non-medicinal ingredients in alphabetical order from Part I.]

<Brand name> comes in the following dosage forms:

[To maintain brevity, this is the only information required in this section.]
<dosage form(s) and strength(s**)>**

Do not use <Brand name> if:

[Enter one point for each contraindication from Part I.]

- **<**text**>**
- **<**text**>**

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:

[Enter one point for each warning and precaution from Part I.]

- **<**text**>**
- **<**text**>**

Other warnings you should know about:

[Enter general information that would not appear in the serious warnings and precautions box or other existing headings. Otherwise this heading is not required.]

<text**>**

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**>**

How to take <Brand name>:

<text**>**

Usual dose:

<text**>**

Overdose:

<text**>**

If you think you have taken too much <Brand name>, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

[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 feel when taking <Brand name>. If you experience any side effects not listed here, contact your healthcare professional.

<text**>**

[Self-limiting side effects should be described in the text section only. Serious side effects must be listed in the serious side effects table. Each side effect should appear only once, in text or in the table, as duplication generally is not wanted in Part III.]

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	Stop taking drug

	Only if severe	In all cases	and get immediate medical help
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, talk to 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 (http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/index-eng.php) 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 the general public: Should you experience a side effect following immunization, please report it to your doctor, nurse, or pharmacist.

Should you require information related to the management of the side effect, please contact your healthcare provider. 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 (http://www.phac-aspc.gc.ca/im/aefi-essi-form-eng.php) appropriate for your province/territory and send it to your local Health Unit.

[Include the text box that is appropriate, according to the biologic drug 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 (http://hc-sc.gc.ca/index-eng.php); the manufacturer's website <website>, or by calling 1-800-<phone number>.

This leaflet was prepared by <Sponsor Name>

Last Revised <MON-DD-YYYY>