Health Canada Santé Canada

Your health and safety… our priority. *Votre santé et votre sécurité… notre priorité.*

Product Monograph Project
Part I: Health Professional Information, Part II: Scientific Information

Michelle Remillard

Bureau of Policy, Science and International Programs
Therapeutic Products Directorate
Health Products and Food Branch
Health Canada

June 9, 2015

Canada

Outline

1. Objective
2. Key Messages
3. What is the Canadian Product Monograph?
4. Product Monograph Evolution
5. Plain Language Labelling
6. Pre-consultation
7. The Consultation
8. Current Guidance outline:
   - Part I: Health Professional Information,
   - Part II: Scientific Information
9. Areas Under Examination
10. What We Heard
11. Next Steps

Objective

- To provide an update of current work underway respecting the Product Monograph Guidance: Part I – Health Professional Information, and Part II – Scientific Information
    - Areas under examination
    - Consultation feedback

Key Messages

1. Significant collaborative effort with excellent participation and engagement with affected stakeholders

2. Proposed revisions on several different topics and areas, some scientific

3. Revisions will better communicate Health Canada's expectations and make health professional information easier to read and critical safety information easier to find

What is the Canadian Product Monograph?

- Food and Drugs Act defines ‘label’
- Food and Drug Regulations, Division 8 (New Drugs)
  - Adequate Directions for Use interpreted under C.08.002(2)(k):
    - Indications for use
    - Single and Daily Dosage or Dosage Range
    - Duration of Treatment
    - Route of Administration
    - Contra-indications, Warnings, Precautions
- Product Monograph Guidance definition:

  “A factual, scientific document that describes the properties, claims, indications and conditions of use of a drug and contains any other information that may be required for optimal, safe and effective use of the drug.”

Product Monograph Evolution

- 1968: First use of Product Monographs
- 1976: First Guidance Document on Format and Content
- 1989: First Major Revision of Guidance
- 2003: Second Major revision of Guidance
  - Part I: Health Professional Information
  - Part II: Scientific Information
  - Part III: Consumer Information (based on Parts I & II and used to produce the package leaflet)
- 2008: Product Monographs available on website
- 2010: Part III Revision: Patient Medication Information
- 2014: Phase I rollout of Patient Medication Information
- 2014 – present: Parts I, II Revision

Plain Language Labelling

- The Department is continuing its work to improve drug product labels as part of the Plain Language Labelling Initiative
  - Announced in June 2013, the Plain Language Labelling Initiative aims to improve drug labels, making them easier to read and understand
  - Plain language labels assist Canadians in making better informed decisions about their health and can reduce preventable medication errors
- The Product Monograph was identified as a label in need of plain language improvements, for two distinct audiences

Plain Language Labelling, cont'd

- June 1, 2014, Health Canada began implementing the revised Product Monograph Guidance Part III: Patient Medication Information
  - Plain language revisions made to Part III create an easier to read and understand patient/consumer document
- Now, the Department is in the process of doing the same for Parts I and II
  - Improvements to Parts I and II aim to make health professional information easier to read and critical safety information easier to find
- Plain language is designed for the target audience

Parts I and II Pre-consultation Work

- Web survey for external stakeholders – April, 2013
- Face-to-face meetings with external stakeholders – May, 2013
- Paediatric Expert Advisory Committee (PEAC) – November, 2013
- Informal communications with Pharmaceutical Advertising Advisory Board (PAAB)

The Consultation

- 75 day external consultation December 19, 2014 to March 4, 2015
- 27 different stakeholder groups participated: health professionals, industry, consumer/patient groups, and academia
- Approximately 500 comments were received
- Considerable support generally, stakeholders anticipating for some time
- Comments were valuable in pointing out where more clarity was needed, where the level of detail was too constraining

Current Part I: Health Professional Information

- **Part I: Health Professional Information**
  - Summary Product Information
  - Indications and Clinical Use
  - Contraindications
  - Warnings and Precautions
  - Adverse Reactions
  - Drug Interactions
  - Dosage and Administration
  - Overdosage
  - Action and Clinical Pharmacology
  - Storage and Stability
  - Special Handling Instructions
  - Dosage Forms, Composition and Packaging

Current Part II: Scientific Information

- **Part II: Scientific Information**
  - Pharmaceutical Information
  - Clinical Trials
  - Detailed Pharmacology
  - Microbiology
  - Toxicology
  - References

2003 Product Monograph

1 INTRODUCTION
2 PREPARING A STANDARD PRODUCT MONOGRAPH
2.1 General Instructions
2.2 Style Guide
2.3 Title Page
2.4 Table of Contents
3 **PART I: HEALTH PROFESSIONAL INFORMATION**
3.1 Summary Product Information
3.2 Indications and Clinical Use
3.3 Contraindications
3.4 Warnings and Precautions
***SWP Box is to be placed here*
- Serious Warnings and Precautions Box
- Specific Subheadings

3.5 Adverse Drug Reactions
- Adverse Drug Reaction Overview
- Clinical Trial Adverse Drug Reactions
- Less Common Clinical Trial Adverse Drug Reactions
- Abnormal Hematologic and Clinical Chemistry Findings
- Post-Market Adverse Drug Reactions

3.6 Drug Interactions
3.7 Dosage and Administration
3.8 Overdosage
3.9 Action and Clinical Pharmacology
3.10 Storage and Stability
3.11 Special Handling Instructions
3.12 Dosage Forms, Strengths, Composition and Packaging
4 **PART II: SCIENTIFIC INFORMATION**
4.1 Pharmaceutical Information
4.2 Clinical Trials
4.3 Detailed Pharmacology
4.4 Microbiology
4.5 Toxicology
4.6 References
5 **PART III: PATIENT MEDICATION INFORMATION**
6 GLOSSARY
APPENDICES

1 INTRODUCTION
2 PREPARING A STANDARD PRODUCT MONOGRAPH
2.1 General Instructions
2.2 Style Guide
2.3 Title Page
2.4 Recent Major Label Changes
2.5 Table of Contents
3 **PART I: HEALTH PROFESSIONAL INFORMATION**
3.1 Approved Indications
3.2 Contraindications
***SWP Box is to be placed here*
3.3 Dosage and Administration
3.4 Overdosage
3.5 Dosage Forms, Strengths, Composition and Packaging
3.6 Warnings and Precautions
- Serious Warnings and Precautions Box
- Specific Subheadings

3.7 Adverse Reactions
- Definitions and Terminology
- General Information
- Adverse Reaction Overview
- Clinical Trial Adverse Reactions
- Less Common Clinical Trial Adverse Reactions
- Abnormal Laboratory Findings…
- Clinical Trial Adverse Reactions (Pediatrics)
- Post-Market Adverse Reactions

3.8 Drug Interactions
3.9 Action and Clinical Pharmacology
3.10 Storage and Stability
3.11 Special Handling Instructions
4 **PART II: SCIENTIFIC INFORMATION**
4.1 Pharmaceutical Information
4.2 Clinical Trials
4.3 Microbiology
4.4 Non-clinical Toxicology
4.5 Supporting Product Monographs
5 **PART III: PATIENT MEDICATION INFORMATION**
6 GLOSSARY
APPENDICES

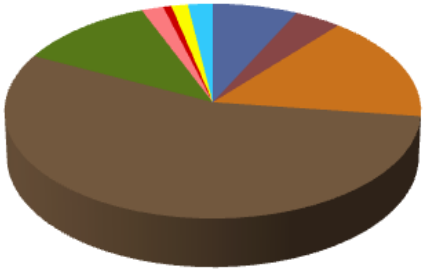
Proposed in the 2014 consultation

Areas Under Examination

- Inclusion of pediatric data
- Pharmacology
- Toxicology
- Adverse reactions
- Inclusion of comparative efficacy data
- Plain language improvements
  - Making critical information easier to find and read
  - Development of a highlight or comprehensive summary section
- References section

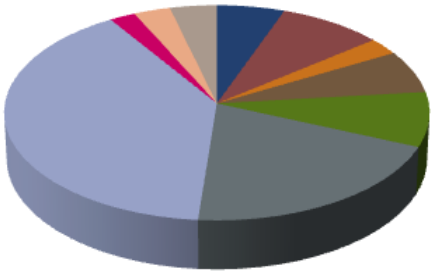
What We Heard

PM Guidance Sections



- General
- 1-Introduction
- 2- Preparing a Standard Product Monograph
- 3- Part I: Health Professional Information
- 4- Part II: Scientific Information
- 5- Part III: Patient Medication Information
- 6- Glossary
- Apendices
- Sample Template

Part I: Health Professional Information



- Approved Indications
- Patient Subsets
- Contraindications
- Dosage and Administration
- Dosage Forms, Strengths, Comp & Pkging
- Warnings and Precautions
- Adverse Reactions
- Drug Interactions
- Action and Clinical Pharmacology
- Storage and Stability

Topic: Pediatrics

- Why did we look at this?
  - In the absence of pediatric labelling claims, clear guidance is needed for stakeholders on the data to be included and its placement, so that prescribers are properly informed of safety information that they need to consider when making the decision to prescribe off-label to a child
- What were the proposed changes?
  - Clearer language, new statements on approved vs. unapproved indications
  - emphasize differences in risk profile between children and adults
  - Add a reference to the ICH E11 categorization for pediatric populations and recognize the importance of identifying other criteria (e.g. weight) in the absence of a specified age range
  - Create a new Clinical Trial Adverse Events for Pediatrics section to include brief information on observed clinical trial ADRs in the absence of an HC approved pediatric indication
- What we heard
  - Proposed statements were difficult to understand and repetitive
  - New section well received
  - Happy to see pediatric data in the absence of claims

Topic: Pharmacology

- Why did we look at this?
  - Stakeholders told us of difficulties with retrieval of information due to (1) separation of the pharmacology information into two different areas, and (2) length and level of detail in Part II
  - It is sometimes difficult for sponsors to determine where to put information
- What were the proposed changes?
  - Move all pharmacology information into one section under Part I, and limit the amount of animal data that is presented to most relevant (e.g. safety only), where human studies are lacking or deficient or the information helps the healthcare professional with interpretation of toxicity or mode of action
  - Improve organization of pharmacology information under Part I with additional headings or bullets where needed (e.g., additional subheadings for ECG intervals).
- What we heard
  - Feeling that Health Canada is asking for additional information and more detail
  - Requirements for subheadings not understood

Topic: Toxicology

- Why did we look at this?
  - Toxicology section has been criticized for its length, often with numerous tables
  - Question whether extensive data is useful or relevant for health care professionals
- What are the proposed changes?
  - Move any human tolerance studies to Part I
  - Limit animal data to important findings only
  - Provide additional instruction to explain what to include
  - Discourage use of tables
- What we heard
  - Feeling that Health Canada is asking for additional information and more detail

Topic: Adverse Reactions

- Why did we look at this?
  - Stakeholders identified lack of clarity around:
    - Definition of ‘adverse events’ vs. ‘adverse reactions’
    - Threshold requirements for adverse reaction data
    - Placement of information
- What are the proposed changes?
  - New sections and text to provide clearer instruction, including definitions, criteria for inclusion of data
  - Flexibility with regard to threshold requirements
  - Addition of Department position outlined in 2010 notice regarding practice of reassessing causality of previously reported adverse events
  - Clarification of HC expectations on both pre-market and post-market adverse reaction data
- What we heard
  - Need further clarification of‘adverse events’ vs. ‘adverse reactions’
  - Flexibility around threshold requirements isn’t well defined
  - Placement of data between pre-market and post-market sections not well understood

Topic: Comparator Data

- Why did we look at this?
  - Inconsistent approaches to the inclusion of comparator data and comparator claims in the Product Monograph, which can impact advertising and decisions by provincial and territorial formularies
- What are the proposed changes?
  - Describe conditions under which the inclusion of comparator data is acceptable as well as unacceptable
  - Provide direction to avoid the use of words or phrases that lack a commonly understood meaning, are not easily defined, are vague, misleading, or promotional in tone (e.g., unique, convenient)
  - Add instruction to indicate where comparator data should appear, and conditions under which it will be permitted
  - Add a definition of pivotal trials to Glossary
- What we heard
  - Exclusion of comparator data in general was questioned
  - Text should be modified to limit reporting of potentially biased active comparisons

Topic: General Plain Language Improvements

- Why did we look at this?
  - Parts I and II had not yet been assessed from a plain language perspective, stakeholder comments supported the need to do so especially with respect to organization of information and the ability (or lack thereof) to find critical information
- What are the proposed changes?
  - Better cross-referencing between sections rather than duplication of data
  - More standardized text
  - New Recent Major Label Changes section
  - Addition of sub-headings and weblinks to the table of contents
  - Streamlining of certain sections (limiting information or removing)
  - Change of location of some sections (e.g. Dosage and Administration)
- What we heard
  - Happy with new location of Dosage and Administration
  - Prefer not to separate the Serious Warnings and Precautions Box from the Warnings and Precautions section; although like the SWP Box moved upfront
  - Web links and section numbering well received
  - Like the Recent Major Label Changes section but some clarification needed

Topic: References Section

- Why did we look at this?
  - Identified as an issue by internal and external stakeholders with respect to usefulness, length
- What are the proposed changes?
  - Remove References section; only include references as a footnote in very select cases, and only when requested by Health Canada in the relevant section of the product monograph (e.g. those impacted by class labelling, safety data requested references)
  - Create new section, “Supporting Product Monographs”
  - New section “Supporting Product Monographs” should only list authorized Health Canada product monographs that were supportive in the development of the product monograph (e.g., for certain generic drug products, subsequent market entry drug products or combination products)
  - Where there are no supporting product monographs, this section should be removed
- What we heard
  - Some wanted Reference section to remain
  - Clarity needed on how to list supporting product monographs

Next Steps

- Consultation feedback analysis
- Final revisions, where applicable, made to Product Monograph Guidance
- Development of phased implementation strategy
- Posting of final Product Monograph Guidance 2016

Questions?

Michelle Remillard

Senior Policy Analyst

Bureau of Policy, Science and International Programs
Therapeutic Products Directorate

Health Products and Food Branch

michelle.remillard@hc-sc.gc.ca

Thank-you for your continued support and engagement on this project!