Example Set A – Branded vs. Unbranded

What is acceptable in a branded vs. an unbranded context?

Contents

Background information on the promoted product

Drug: FERNANDAX
Class: CM8i
Indicated for the treatment of irritable bowel syndrome (IBS)

- Demonstrated effect in:
  - Abdominal Pain
  - Frequency of stool
- No demonstrated effect in:
  - Mental health
  - Fatigue

Discussing burdens of disease for which the product has not demonstrated an effect

In the following 3 examples, the goal of the APS is to discuss the mental health and fatigue burdens of IBS (burdens for which FERNANDAX, nor any other CM8i, have not demonstrated an effect).

NOTE: The sponsor may not run both branded and unbranded APSs that resemble each other.

Example A.1: Branded HCP Context

The following is an excerpt from an introductory "disease burden" page in a FERNANDAX-branded Detail Aid.

[Headline]
The IBS Impact

[Copy]
13–20% of Canadians struggle with IBS at any given time—how does it affect them?

[Subhead]
IBS Symptoms

[Infographic]

[Icon] 	[Copy] **Abdominal pain** A wide range of pain levels can occur due to IBS. In a survey of 2961 patients with IBS: • **39%** reported **mild** abdominal pain • **53%** reported **moderate** abdominal pain • **31%** reported **severe** abdominal pain during the past 3 months **Only 4%** of survey respondents did not experience abdominal pain in the past three months.
[Icon] 	[Copy] **Frequency of stool** **20%** of patients with IBS struggle with untimely passage of stool.

[Subhead]
Additional impacts

[Icon] 	[Copy] **Mental health** Patients with IBS may experience a wide range of emotions, such as anxiety, depression, fear, anger, guilt, or loss of self esteem. In a CSIR survey of 2961 patients with IBS: • **32%** of respondents had some form of mood disorder • **27%** an anxiety disorder

The disease information is **separate from the Product Information**. Distinction/separation can also be achieved through the use of headings or other visual elements. [Guidance 4.1]

Without a demonstrated effect from FERNANDAX, mental health and fatigue cannot be the only burdens of disease presented. However, they may be included as part of a **broader presentation** on disease information that includes burdens upon which the product has demonstrated an effect. The net presentation does not emphasize mental health or fatigue. [Guidance 4.2]

[Icon]	[Copy]
	**Fatigue** **Over 60%** of patients with IBS reported fatigue (compared to 5–20% of the general population), a per a 2013 study of 175 patients with moderate to severe IBS.

[Disclaimer copy] [75% size of body copy]
Data for FERNANDAX on abdominal pain and stool frequency are presented elsewhere in this detail aid. The effects of FERNANDAX on mental health and fatigue have not been evaluated as predefined endpoints in prospectively designed, well-controlled, randomized trials.

[Qualifiers]
CSIR=Canadian Society of Intestinal Research; IBS=irritable bowel syndrome.

[Footer Logo]
FERNANDAX

A **clear and prominent disclosure** about which described burdens the product has and has not demonstrated an effect on is required as part of the burden presentation. [Guidance 5.1]

Results for burdens against which FERNANDAX does have a demonstrated effect must be included elsewhere in the APS. [Guidance 5.1; consistent with previous practice]

Colours and logos may be used in the burdens of disease presentation in a manner that is cohesive with the remainder of the APS (e.g., logo as part of the standard footer in a slide deck). [Guidance 4.1]

Example A.2: Unbranded HCP Context – APS that Emphasizes or Distinguishes a Class

*The following is an excerpt from an introductory page in an unbranded piece that emphasizes the CM8i class (i.e., FERNANDAX's class) throughout the rest of the APS.**

[Headline]
The IBS Impact

[Copy]
13–20% of Canadians struggle with IBS at any given time—how does it affect them?

[Subhead]
IBS Symptoms

[Infographic]

[Icon]	[Copy]
	**Abdominal pain** A wide range of pain levels can occur due to IBS. In a survey of 2961 patients with IBS: • **39%** reported **mild** abdominal pain • **53%** reported **moderate** abdominal pain • **31%** reported **severe** abdominal pain during the past 3 months **Only 4%** of survey respondents did not experience abdominal pain in the past three months.
[Icon]	[Copy]
	**Frequency of stool** **20%** of patients with IBS struggle with untimely passage of stool.

[Subhead]
Additional impacts

[Icon]	[Copy]
	**Mental health** Patients with IBS may experience a wide range of emotions, such as anxiety, depression, fear, anger, guilt, or loss of self esteem. In a CSIR survey of 2961 patients with IBS: • **32%** of respondents had some form of mood disorder • **27%** an anxiety disorder

This hypothetical APS emphasizes the CM8i class on other pages that are not shown. Some of the key requirements discussed in the branded example will still apply, as shown below.

Without a demonstrated effect from a member of the CM8i class, mental health and fatigue cannot be the only burdens of disease presented. However, they may be included as part of a **broader presentation** on disease information that includes burdens for which a member of the class has demonstrated an effect (i.e., abdominal pain and stool frequency). The net presentation does not emphasize mental health or fatigue. [Guidance 4.2, 5.3] **This is the same principle discussed in the branded example above.**

[Icon] 	[Copy] **Fatigue** **Over 60%** of patients with IBS reported fatigue (compared to 5–20% of the general population), a per a 2013 study of 175 patients with moderate to severe IBS.

[Disclaimer copy] [75% size of body copy]
The effects of CM8is on mental health and fatigue have not been evaluated as predefined endpoints in prospectively designed, well-controlled, randomized trials.

[Qualifiers]
CSIR=Canadian Society of Intestinal Research; IBS=irritable bowel syndrome.

A **clear and prominent disclosure** about the described burdens for which there is no demonstrated effect from a member of the CM8i class is required as part of the burden presentation. [Guidance 5.3]
This is similar to the burden discussed in the branded example above.

* An unbranded piece that specifically focuses on a class of drugs (e.g., CM8is in our example) cannot imply that the class is the only option in the management of the disease).

Example A.3: Unbranded HCP Context – APS Without Emphasis on a Drug Class (Speaks to Treatment Generally)

The following is an excerpt from an unbranded newsletter, which speaks to treatment generally with no emphasis on a particular class.

[Headline]
The IBS Impact — Going beyond the Gut

[Copy]
13–20% of Canadians struggle with IBS at any given time—how does it affect them?

[Icon] 	[Copy] **Mental health** Patients with IBS may experience a wide range of emotions, such as anxiety, depression, fear, anger, guilt, or loss of self esteem. In a CSIR survey of 2961 patients with IBS: • **32%** of respondents had some form of mood disorder • **27%** an anxiety disorder
[Icon] 	[Copy] **Fatigue** **Over 60%** of patients with IBS reported fatigue (compared to 5–20% of the general population), a per a 2013 study of 175 patients with moderate to severe IBS.

[Subhead]
Consider various management strategies for IBS:

[Copy]
- Medications
- Probiotics
- Dietary and lifestyle modifications
- Physiotherapy/pelvic floor rehabilitation

[Qualifiers]
CSIR=Canadian Society of Intestinal Research; IBS=irritable bowel syndrome.

By placing no emphasis on a drug class/group, **we can emphasize burdens for which no effect has been demonstrated. There is no requirement to include burdens where an effect has been demonstrated**. The entire disease burden presentation can focus on the mental health and fatigue burdens of IBS.

As discussed above, the APS **speaks to treatment generally (no emphasis on a class)**. As a reminder, if the newsletter did not allude to drug therapy whatsoever, it may qualify for PAAB exemption.

There is **no required disclosure** about a product/class having no demonstrated effect on these burdens. [Guidance 5.3]

Summary of Key Principles

<table>
<tr><th>Branded HCP</th><th>Unbranded HCP</th></tr>
<tr><td rowspan="2">

We can present content about the mental health and fatigue burdens of IBS. [Guidance Introduction]
However, we need to discuss burdens such as frequency of stool and abdominal pain as well (for which FERNANDAX has a demonstrated effect). [Guidance 4.2]

Without a demonstrated effect from FERNANDAX, mental health and fatigue information cannot be the only information on burdens. However, it may be included as part of a broader presentation on disease information that includes burdens upon which the product has demonstrated an effect. [Guidance 4.2]
The FERNANDAX results for frequency of stool and abdominal pain must be included within the APS. [Guidance 5.1]

Note that this would not be required if these burdens were specified as part of the FERNANDAX indication. [Guidance 5.1]

The information needs to be separate from product information. [Guidance 4.1]
A clear and prominent disclosure about which described burdens the product has and has not demonstrated an effect is required as part of the burden presentation. [Guidance 5.1]

</td><td>
In an APS that emphasizes the CM8i class:

To discuss burdens such as mental health and weight loss in IBS, we need to discuss some burdens where an effect has been demonstrated by a member of the CM8i class (e.g., frequency of stool and abdominal pain). [Guidance 4.2, 5.3]
Include a disclosure for burdens where no effect has been demonstrated by the CM8i class. [Guidance 5.3]

</td></tr>
<tr><td>
In a piece with no emphasis on a drug class (speaks to treatment generally):

Can emphasize burdens where no effect has been demonstrated—there is no need to include burdens where an effect has been demonstrated)—the entire presentation can focus on mental health and IBS. [Guidance 5.3]

</td></tr>
</table>

Discuss only burdens of disease for which the product has demonstrated an effect

If we want to discuss how IBS presents a burden to patients with regards to abdominal pain and frequency of stool only (burdens for which FERNANDAX has demonstrated an effect), the requirements and key principles have not changed with the implementation of this new Guidance:

Branded HCP	Unbranded HCP

• We can discuss frequency of stool and abdominal pain as a burdens of disease in IBS.
  ○ This presentation can be mixed with product messaging, such as “Act with FERNANDAX for the treatment of your IBS patients”
• The FERNANDAX results for frequency of stool and abdominal pain must be included within the APS. [Guidance 5.1]
  ○ Note that this would not be required if these burdens were specified as part of the FERNANDAX indication. [Guidance 5.1]
• No disclosure is required. [Guidance 5.1]
	• We can discuss frequency of stool and abdominal pain as a burdens of disease in IBS.
	• We can choose to emphasize the CM8i drug class in the piece OR speak to treatment generally.

Example Set B - Patient Profiles

Example B.1 – Acceptable APS

John, diagnosed with oHCM NYHA Class II

Meet John, recently diagnosed with oHCM

Age: 27 | **Height:** 1.65 m | **Weight:** 77 kg

Lifelong athlete and hockey player
Semi-professional league hockey coach

1

Family history

- John's younger brother, also a hockey player, died from sudden cardiac death 2 years ago at age 21

Medical history

- Concerned about daily fatigue and recurring dizziness
- Dyspnea worsens with effort
- Has experienced occasional palpitations and chest pain when playing that force him to stop

Diagnosis

- Based on family history and symptoms, John was assessed for obstructive HCM
- Diagnosed 1 month ago; NYHA Class II
- Echocardiography findings: LVOT gradient, Valsalva: 55 mmHg; LVEF 62%; septum thickness 23 mm

Day-to-day impacts

- John's major complaint is fear about limitations to physical activities
- Symptoms cause him concern about being an athlete in general, as well as his position as coach
- He feels that the major impact of symptoms is on his quality of life

Classic symptoms of oHCM

- Dyspnea is the most common complaint among symptomatic patients.
- Patients may also complain of presyncope, syncope, angina, palpitations (secondary to arrhythmia), or dizziness.

2

Data for PRODUCT X on dizziness, dyspnea and palpitations are presented elsewhere in this piece. Product X's effects on cardiovascular mortality, presyncope, syncope, angina, fatigue, chest pain, daily functioning and quality of life have not been evaluated.

Would you consider PRODUCT X to manage John's oHCM?

Example B.2 – unacceptable APS

John, diagnosed with oHCM NYHA Class II

Meet John, recently diagnosed with oHCM

Age: 27 | **Height:** 1.65 m | **Weight:** 77 kg

Lifelong athlete and hockey player
Semi-professional league hockey coach

Family history

- John's younger brother, also a hockey player, died from sudden cardiac death 2 years ago at age 21

Medical history

- Daily fatigue and recurring dizziness
- Dyspnea worsens with effort
- Occasional palpitations and chest pain when playing that force him to stop

Day-to-day impacts

"I don't want to deal with limitations on my life – I have a job I love"

- He says he is managing with the dyspnea and fatigue now, but is anxious about them worsening
- Palpitations make him fearful about "my heart just stopping"
- He is still grieving the loss of his brother, and has talked to his doctor about depression

Diagnosis

- Based on family history and symptoms, John was assessed for obstructive HCM
- Diagnosed 1 month ago; NYHA Class II
- Echocardiography findings: LVOT gradient, Valsalva: 55 mmHg; LVEF 62%; septum thickness 23 mm

3

Classic symptoms of oHCM

- Dyspnea is the most common complaint among symptomatic patients.
- Patients may also complain of presyncope, syncope, angina, palpitations, or dizziness.

Possible complications

- Ventricular arrhythmias
- Congestive heart failure
- Infective endocarditis of the mitral valve
- Atrial fibrillation
- Sudden death

Playing and staying active is everything to John.

Would you consider PRODUCT X to manage his oHCM?

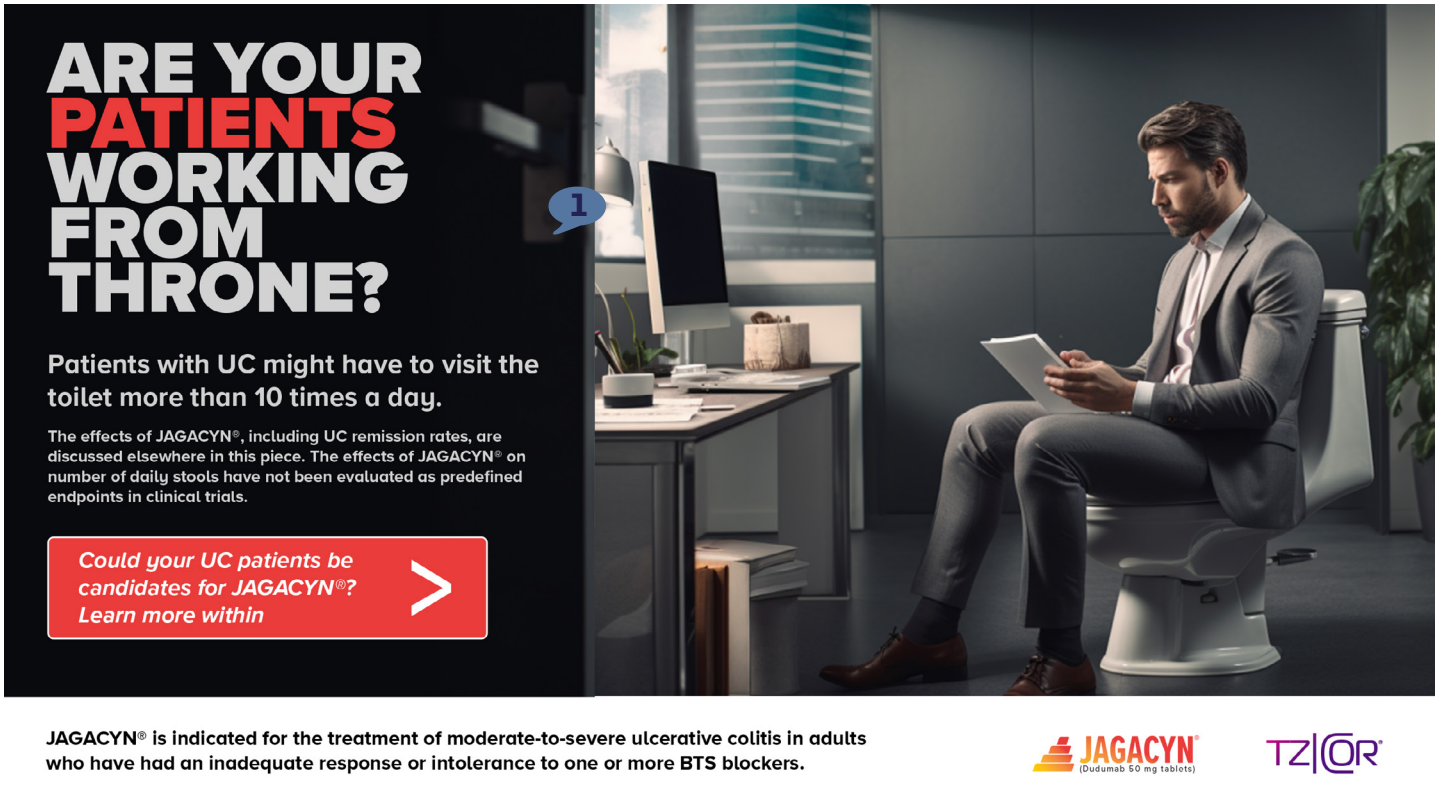
4

Product X's effects on daily functioning and quality of life have not been evaluated.

Example Set C - Creative Concepts

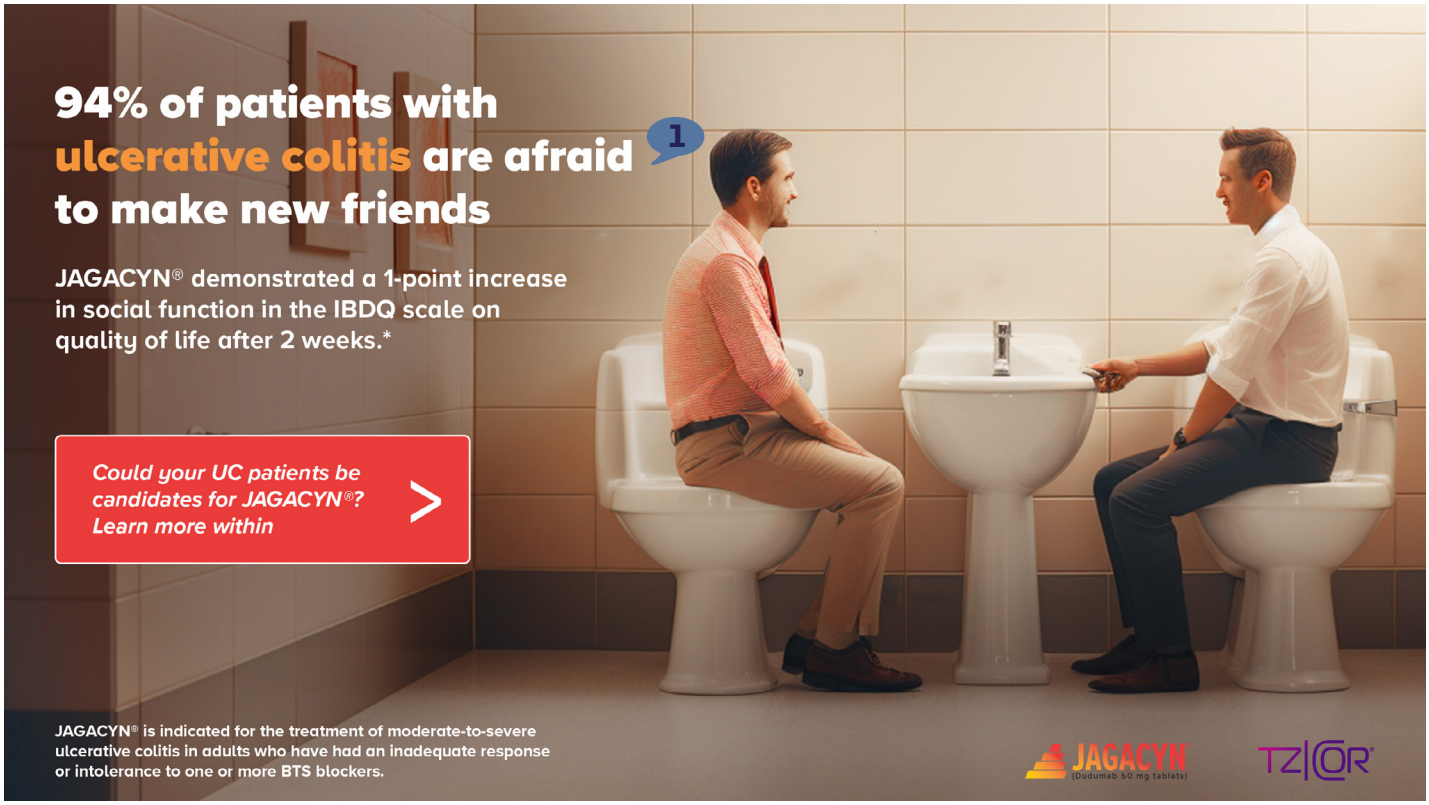
Example C.1 – Unacceptable APS

Background information: Jagacyn is a monoclonal antibody for the treatment of moderate-to-severe ulcerative colitis. The Terms of Market Authorization (TMA) includes data for statistically significant improvement of at least >2 MAYO score vs. placebo. The TMA also includes statistically significant data for an improvement in quality of life as measured by the IBDQ scale. Each measure of the social and emotional scale was seen to improve by at least one point but individual measures were not statistically analyzed.



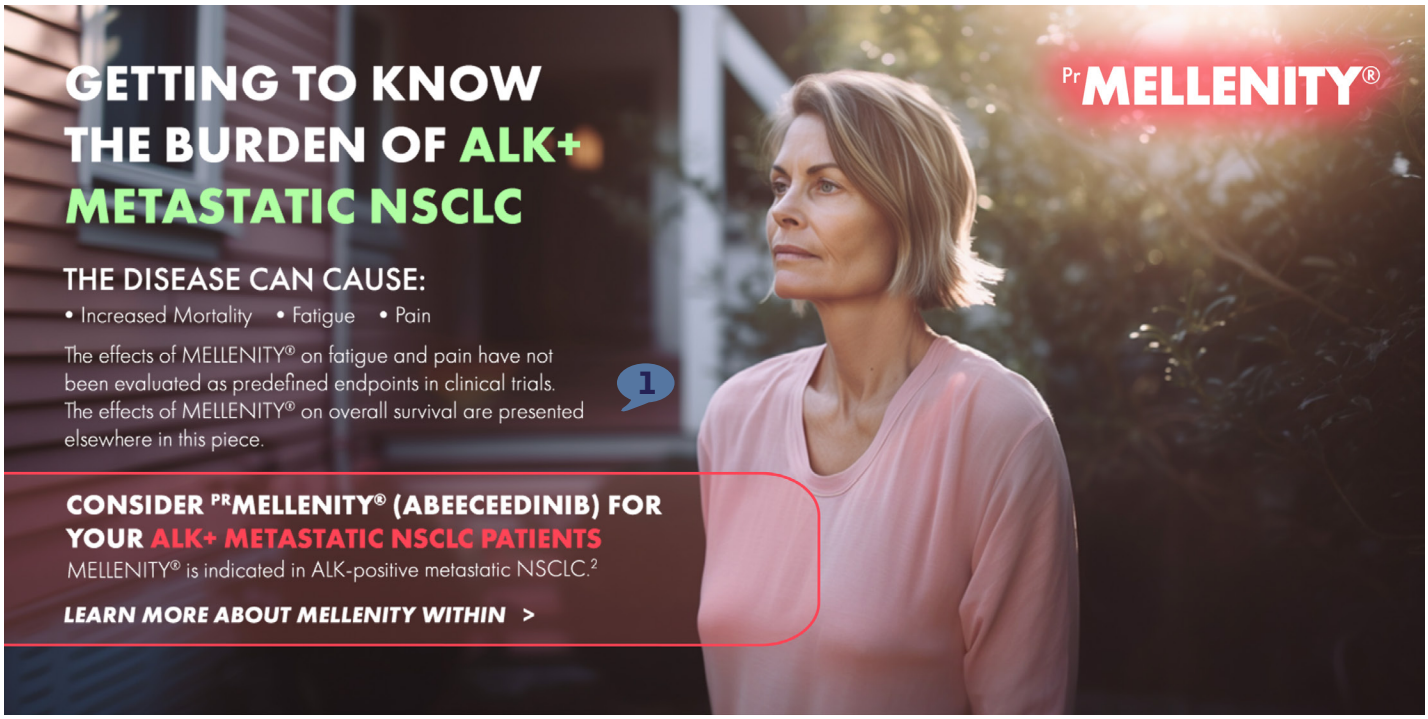
Example C.2 – Unacceptable APS

Background information: Jagacyn is a monoclonal antibody for the treatment of moderate-to-severe ulcerative colitis. The Terms of Market Authorization (TMA) includes data for statistically significant improvement of at least >2 MAYO score vs. placebo. The TMA also includes statistically significant data for an improvement in quality of life as measured by the IBDQ scale. Each measure of the social and emotional scale was seen to improve by at least one point but individual measures were not statistically analyzed.



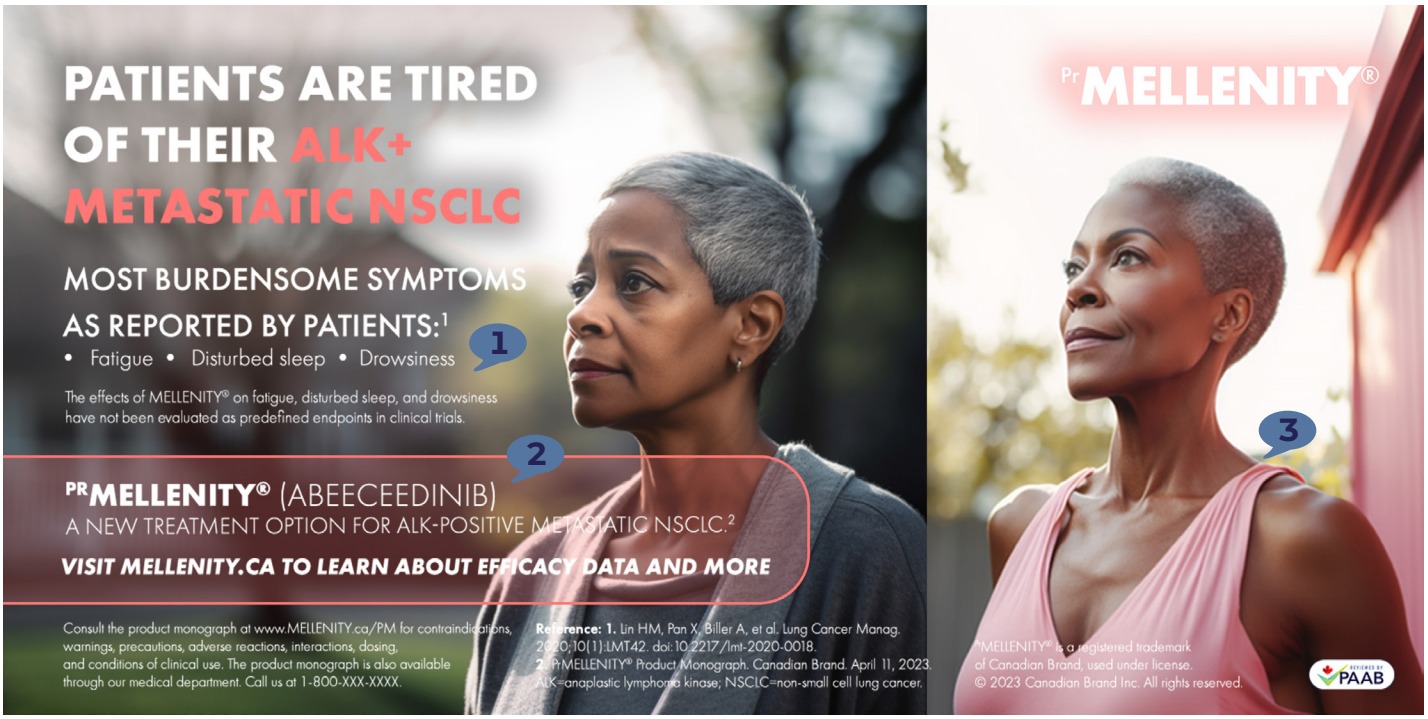
Example C.3 – Acceptable APS

Background information: Mellenity is an ALK inhibitor for the treatment of ALK+ metastatic non-small cell lung cancer (NSCLC). The Terms of Market Authorization includes a clinical trial demonstrated statistically significant improvement in overall survival and progression-free survival. The product has no data showing its effects on signs and symptoms (e.g., fatigue, pain).



Example C.4 – Unacceptable APS

Background information: Mellenity is an ALK inhibitor for the treatment of ALK+ metastatic non-small cell lung cancer (NSCLC). The Terms of Market Authorization includes a clinical trial demonstrated statistically significant improvement in overall survival and progression-free survival. The product has no data showing its effects on signs and symptoms (e.g., fatigue, pain).



Example C.5 – Unacceptable APS

Background information: Somnirta is a once-daily oral CGRP antagonist for the prevention of migraine. The Terms of Market Authorization includes data on a statistically significant reduction in monthly migraine days vs. placebo and statistically significant improvement in quality life as measured by the MSQ scale.

Example Set D

Example D.1 – Unacceptable APS

Background information: ADHDmed is product indicated for the treatment of ADHD in children. It has acceptable data for attention and behaviour at school but it does not have data for family relationships/life at home.

HEADLINE
ADHD can impact a child's attention and behaviour at school…

VISUAL
<image depicting frustrated parents and an upset child>

SUBHEAD
But did you know it can also impact family relationships? 1

COPY
Family conflict and disruption to family cohesion are recognized impacts of uncontrolled ADHD.1 [CADDRA, p37C, p34A]

CTA
When determining an ADHD treatment plan, consider the many ways ADHD can impact a child, including life at home.

DISCLAIMER – COPY SIZE
Data for Product X on classroom attention and behaviour (SKAMP-C) are presented elsewhere in this piece. Product X's effects on family relationships have not been evaluated as predefined endpoints in prospectively designed, well-controlled, randomized trials

Example D.2 – Acceptable APS

Background information: ADHDmed is product indicated for the treatment of ADHD in children. It has acceptable data for attention and behaviour at school but it does not have data for family relationships/life at home.

ADHD can impact a child in many ways.

When determining an ADHD treatment plan, consider the many ways ADHD can impact a child

ADHDMED

Example D.3 – Acceptable APS

Background information: ADHDmed is product indicated for the treatment of ADHD in children. It has acceptable data for attention and behaviour at school but it does not have data for family relationships/life at home.

ADHD can impact a child's attention and behaviour at school...

But did you know it can also impact family relationships?

1

When determining an ADHD treatment plan, consider the many ways ADHD can impact a child

Disclaimer: Data for Product X on classroom attention and behaviour (SKAMP-C) are presented elsewhere in this piece. Product X's effects on family relationships have not been evaluated as predefined endpoints in prospectively designed, well-controlled, randomized trials

2

ADHDMED

PAAB would like to thank bMod, CORE Health Communications, FCB Health Canada and GSW for their invaluable assistance in developing examples for this guidance.