Guidance on the Presentation of Burdens of Disease in Advertising

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Disease information can enhance the utility of an APS. However, to ensure the credibility of evidence-based drug advertising, it is important that benefits that have not been demonstrated by a drug product are not implicitly imputed to it. In our shift to expand the range of acceptable disease information in advertising, we are aiming for an approach that balances utility and credibility.

The focus of this guidance is burdens of disease for which the promoted product has not demonstrated an effect in an acceptable prospectively designed, well-controlled, randomized trial. Going forward, PAAB will accept information relating to burdens of disease in advertising even when the promoted product has not demonstrated an effect on the described burdens. However, to mitigate against any implied and unsubstantiated benefits for the promoted drug product, the following considerations apply:

1. Definitions/abbreviations

For the purpose of this guidance:

- "burdens upon which the product **has not** demonstrated an effect" denotes burdens of disease upon which the product has not demonstrated an effect in an acceptable prospectively designed, well-controlled, randomized trial
- "burdens upon which the product **has** demonstrated an effect" denotes burdens of disease upon which the product has demonstrated an effect in an acceptable prospectively designed, well-controlled, randomized trial
- "sequelae" denotes complications that may occur downstream in a disease; these can include progression of a disease to a later stage or a greater severity, or a new condition that may or may not be one for which other products are indicated (please see Appendix to Section 1 for more details)

2. Scope of the indication

Burdens of a disease should reflect widely accepted medical knowledge (please also see section 3). In the context of branded advertising, burdens need not be included in the TMA but must relate to the condition for which the product is indicated.

Burdens specific to the health of the patient fall within the scope of this guidance. Other types of burdens (e.g., caregiver effects, pharmacoeconomic impact, healthcare resource utilization, etc.) do not fall within the scope of this guidance. Our review approach to these latter types of burdens remains unchanged (i.e., the presentation of these burdens within APS will require high quality evidence quantifying the extent to which the product addresses these issues).

Subgroups: Although subgroups are not a burden of disease, we received many queries about them. To clarify our current and continuing review approach:

- A patient with a comorbidity or a risk factor who falls within the scope of the indication and is not contraindicated may be presented as a candidate for a product.

- This patient subtype should not be emphasized unless the advertised product has demonstrated an effect in this subtype in an acceptable prospectively designed, well-controlled, randomized trial.

Unmet needs from other therapies and burdens caused by other therapies (e.g., toxicity) are also not part of the scope of this guidance.

3. References

The establishment of a burden as related to a disease should be based on references representing widely accepted medical knowledge, such as medical textbooks, authoritative consensus guidelines or publications from authoritative health organizations (e.g., World Health Organization, Public Health Agency of Canada, etc.). These sources may be Canadian or international.

Alternatively, if another product indicated for the same disease has demonstrated an effect on a burden according to a validated measurement in an acceptable prospectively designed, well-controlled, randomized trial and can claim an effect on said burden, that is also sufficient to establish a burden as related to a disease.

In the case of diseases for which the sources listed above are not available (e.g., rare diseases), we may consider the preponderance of currently available medical and scientific literature on a case-by-case basis.

Once a burden has been established as related to a disease based on the types of references cited above, additional published and peer-reviewed references may be used to build a more detailed picture of the burden. These can include systematic reviews, meta-analyses, randomized controlled trials, Canadian or North American epidemiological studies, cohort studies and case-controlled studies. Sources that have not been published or that have not been peer-reviewed are not acceptable references (e.g., abstracts, posters, supplement-published papers that have not been peer reviewed).

With specific reference to patient directed APS, once a burden has been established as related to a disease based on the types of references cited above, resources from standard setting organizations for consumers and patients (e.g., disease associations, patient advocacy groups, etc.) may be used as a reference for patient-friendly language.

4. Presentation

4.1. Separation of disease information and product information

Burdens of disease upon which the product has not demonstrated an effect should be presented separately from product information. Burdens of disease should be clearly portrayed as disease information and not as outcomes that can be improved by the product. They should look like visually distinct presentations; this can be achieved by presenting on separate pages or

through the use of headings and other visual elements (similar to how clinical and non-clinical presentations are separated). 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).

4.2. Emphasis

There should be no emphasis on burdens upon which the product has not demonstrated an effect. They should not set the context for presentations, and they should not be the only information on burdens in an APS. Repetition in multiple patient cases is also considered a form of emphasis.

Burdens upon which the product has not demonstrated an effect may be included as part of a broader presentation on disease information that includes burdens upon which the product has demonstrated an effect.

This section does not apply to vaccines due to the nature of their indications and their historic TMAs.

4.2.1. Visuals in the creative concept

A visual of a patient that reflects burdens that may be present when a patient is diagnosed with or presents with a condition (e.g., signs and symptoms, quality of life issues, etc.) may be included as part of the creative. Such a visual should be framed as a patient who has a condition and is eligible for treatment with a product with an indication for that condition.

A visual of a patient that reflects sequelae may not be emphasized as part of the creative. Consistent with section 4.2, this does not apply to vaccines.

Please note that, should the visual reflect burdens for which a product has not demonstrated an effect, there should be no additional visuals that suggest efficacy for managing these burdens (e.g., before and after visuals of the same patient demonstrating improvement).

5. Disclosure

5.1. Branded HCP materials

In presentations that refer to both burdens against which the product has demonstrated an effect and burdens against which the product has not demonstrated an effect, 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. Disclosures should be presented with similar prominence to the burdens. In the scenario where the sponsor is aware that the promoted product has been studied for its effect on a described burden and failed to

demonstrate efficacy against that burden, that should also be disclosed. Footnotes are not sufficient for disclosures.

The disclosure may take the following form: “Data for Product X on outcomes A, B, and C are presented elsewhere in this piece. Product X's effects on D, E, and F have not been evaluated as predefined endpoints in prospectively designed, well-controlled, randomized trials”.

Consistent with existing practice, product results for burdens against which the product has demonstrated an effect must be included within the APS. An exception to this requirement is burdens for which the product is indicated.

NOTE: A disclosure statement is not required for presentations that refer only to burdens against which the product has demonstrated an effect.

Vaccines are exempt from the requirement of disclosing which burdens the product has demonstrated an effect on. Disclosure of which burdens the product has not demonstrated an effect on will continue to be required.

5.2. Branded patient materials

Clear and prominent disclosure is required when a presentation includes burdens against which the product has not demonstrated an effect. Unlike HCP materials, patient materials are non-promotional in nature so a general disclosure statement similar to “This presentation provides information on the condition and may not reflect benefits of the product” included as part of the burden presentation may be adequate. A footnote is not sufficient for disclosures.

5.3. Unbranded materials

If an unbranded APS emphasizes or distinguishes a particular class or group of drugs, there should be clear and prominent disclosure about the described burden(s) against which none of the class or group of drugs has not demonstrated an effect. Such APSs may not contain only burdens for which none of the class/group has demonstrated an effect.

If an unbranded APS speaks to treatment generally and there is no emphasis on a particular class or group of drugs, no disclosure is required.

Appendix to Section 1

Whether a disease burden is a sign/symptom or a sequalae is often self-evident. Signs and symptoms are manifestations of the indicated disease at a particular point in time while sequalae are complications or consequences of the indicated disease that may occur downstream in the disease continuum. Sequalae can include progression of a disease to a later stage or a greater severity, or a new condition that may or may not be one for which other products are indicated.

Product/Indication	Sequelae (for which the product has no data) should not be emphasized
Antihypertensive: treatment of mild to moderate hypertension	MI, stroke, death, renal function
Estrogen replacement therapy: relief of menopausal and postmenopausal symptoms occurring in naturally or surgically induced estrogen deficiency	Cardiovascular outcomes, dementia, cancer
Treatment for actinic keratosis	Squamous cell carcinoma

However, for some burdens, the distinction can be more challenging and context-dependent. In such cases, it is helpful to consider whether the burden presentation conveys passage of time or progression across the disease continuum. In these cases, burdens are generally not considered to be sequelae if BOTH of the following are true:

- The presentation does not feature or imply a relationship between the disease state and time.

  For example, the presentation of a single snapshot in time depicting how patients experience the indicated disease.

- The presentation does not feature or imply a disease continuum.

  For example, the presentation does not feature:

  - progression from a current or historic state within the indicated disease to an advanced state within that same indicated disease
  - progression from the indicated disease state that entails the layering of consequences/complications of that same disease OR a transition to a different disease