Medicines Australia

Better health through research & innovation

Guidance: Developing and Communicating Compliant Promotional Claims

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1. Key Code Principles

Section 1 describes a number of principles that are relevant to making **promotional claims*** about prescription products to healthcare professionals, and should be read in conjunction with the Overarching Principles (Part A), and in particular with Principles 1, 3 and 8:

- **Principle 1.** All activities undertaken by Companies have the purpose of supporting the quality use of medicines.
- **Principle 3.** As the primary repository of information relating to their products, Companies are responsible for providing current, accurate, balanced, and scientifically valid information on products to support their appropriate use. The same standards apply to all other Company communications.
- **Principle 8.** All promotional claims are consistent with the Australian Product Information document, including claims about competitor products, irrespective of the source on which the claim is based.

(*Defined in the Code Glossary)

When promoting prescription products, all information, claims and graphical representations are:

- current
- accurate
- balanced
- consistent with the approved Product Information and the body of evidence, and
- not misleading – i.e. do not mislead directly, by implication, or by omission.

Section 1 of the Code describes how companies can make promotional claims consistent with these principles. You will see them reiterated in this guidance.

Companies should behave responsibly and ethically when making promotional claims so that a healthcare professional can appropriately interpret and evaluate the information, claims and graphical representations and make decisions that are in the best interest of patients and consumers.

This Guidance should be read in conjunction with Medicines Australia's Guidance on Balance in Product-related Materials, available in the Code Resource Toolkit, which supports Section 1.1 of the Code. The magnitude of each claim should always be considered before determining the complexity and risk of the piece. This guidance will assist companies to apply the principles of the Code when making promotional claims and use of different types of substantiating data to support them.

2. Section 1 – Interpreting "*Consistent with the Approved Product Information*"

"Consistent with the Product Information" relates to consistency with the PI as a whole, not only the approved indications. All claims and other information provided in promotional material should be consistent with the relevant information in the PI.

Consider the following to help decide whether a claim or other information is consistent with the PI:

- **Indication**: do the claims or representations about the product relate to a different or broader indication than that stated in the approved PI?
- **Patient population**: is the patient population presented or proposed in the material outside the approved patient population stated in the approved PI?
- **Limitations and directions for use**: do the information or claims in the material conflict with the limitations or directions for using the product stated in the approved PI?
- **Dose or use regimen and administration**: does the information about the product conflict with the recommended dose or use regimen, route of administration or strengths stated in the approved PI?
- **Endpoints/Outcomes/Safety**: is the claim about treatment outcomes, endpoints or safety consistent with those described in the approved PI? Consistent is not necessarily 'the same as'; all data relating to endpoints, outcomes and safety may not be specifically presented in the PI.

The Code and Appeals Committees, in their adjudication of complaints such as #1174, have considered the meaning of 'consistent' in relation to consistency of a claim with the Product Information.

Note that a company's responsibility relates not only to information or claims about the company's product being promoted but also to any claims made about other products, disease states or conditions.

Issues can arise where the approved PI for different products that are used in combination to treat a condition are inconsistent; for example, when a new product is registered and its indications differ in some way from the indications for another product with which it is used in combination therapy. Sometimes, this is a result of new clinical data that has become available since the other product was registered. **The primary focus should be on ensuring consistency with the approved PI for the product being promoted**, irrespective of whether this is also consistent with another product's PI.

A related issue can occur when the PBS reimbursement criteria for a product are different to its approved indications or other aspects of the approved PI following the evaluation of new information submitted to the PBAC.

In both these cases, a company may only make promotional claims for its product that are consistent with its product's approved PI. Medicines Australia has been advised by the TGA that a company **may** risk breaching the Therapeutic Goods legislation if it includes PBS listing details in promotional material where the PBS indications are broader than the approved indications. Carefully consider how much PBS listing detail should be included in promotional material other than a statement that the product is listed on the PBS. Refer to Code Section 2.1 e).

3. Section 1 – Avoiding Misleading Claims

The first paragraph of Section 1 of the Code requires that "all information, claims and graphical representations are current, accurate, balanced consistent with the approved product information, and **not mislead either, by implication, or by omission.**" This relates to promotional and medical claims, including taglines, made to healthcare professionals and all information and graphical representations provided to them.

Companies are responsible for ensuring that all promotional claims are referenced (Section 1 a)). Consistent with its "systems neutral" approach, Code Edition 20 does not specify a type size, font or colour for the reference citation or its location within the material. Overarching Principle 7 requires that "information relevant to prescribing, in particular product and safety information, are clearly communicated in all promotional materials". Reference citations should be communicated in a style and manner that will allow a reader to identify and readily locate all cited references.

Overarching Principle 8 relates to promotional claims about a company's product as well as claims about competitor products, irrespective of the source on which the claim is based. Comparative promotional claims and materials should meet all the requirements of Code Section 1, including Sections 1.1 Balance and 1.2 Substantiating Data.

When comparative claims are made, care should be taken to ensure that they are supported by appropriate substantiating evidence, reflective of the body of evidence and are communicated accurately and without distortion or undue emphasis. "Hanging" comparative claims should not be used (Code Section 1 h).

The Code and Appeals Committee, in their adjudication of complaints such as #1169, have commented on the importance of taking extra care when using comparative claims.

The Appendix of this Guidance contains examples of situations where material may be considered to be misleading and therefore likely to be in breach of the Code. This list is not exhaustive.

Note: Many complaints adjudicated by the Code Committee, in which material was found to be misleading, have also frequently been determined to breach Overarching Principle 1.

4. Using Substantiating Data to Support Claims

The approved PI is not the only reference source for supporting promotional claims. Companies can use additional data not included in a product's PI provided that the data is consistent with, and does not contradict the approved PI. If there is new data about a product that is not consistent with its PI, companies should carefully consider whether the data should be used to support promotional claims.

4.1 What type or level of substantiating data is required to support a promotional claim?

Section 1 a) states that the cited reference/s to support a promotional claim should "provide the appropriate level of evidence for the claim being made". The Code does not specify that certain types or levels of substantiating data are required to support different types of claims. Section 1.2 covers the issues companies should consider when deciding whether the evidence is appropriate to substantiate a claim and, importantly, how to ensure that a healthcare professional has sufficient information to enable them to properly evaluate the validity of the claim.

The level of evidence that is appropriate to support a claim will vary according to both the claim being made and the body of evidence. The nature of the study or type of data should be made clear to a reader.

Claims should be substantiated with evidence commensurate with the significance of the claim. Claims that may significantly influence prescribing should be substantiated with evidence appropriate to support the claim and be consistent with the body of evidence and the PI. For example, a comparative claim that one product is more effective or better tolerated than another should be substantiated by unequivocal evidence regarding the claimed superiority of the product.

5. Types and Levels of Substantiating Data

5.1. Hierarchy of evidence

The concept of a hierarchy of evidence has been discussed in the medical literature for several decades. There are a number of variations on the hierarchy or levels of evidence available from reputable sources via the internet. The evidence hierarchy is often visually represented as a pyramid with the highest quality evidence at the top.

The appropriate use of some levels of evidence, such as posters, abstracts and personal communication and observational data, appear in several subsections of Section 1.2 Substantiating Data.

Companies should use the highest level of evidence available to support a claim and the type of evidence that is referenced should be clear to a reader to enable them to evaluate the validity of the claim. For example, observational studies (Section 1.2 h) are lower in the

evidence hierarchy, but they might be the highest level of evidence available. When there is no data available from a higher evidence hierarchy source, the most relevant and highest available level of evidence could be from observational data. These data may be used to substantiate a claim. The nature of the study used to substantiate the claim should be made clear to the reader. The decision to reference an observational study should be considered on a case-by-case basis with consideration given to the quality of the observational study and the type of claim it is being used to substantiate.

5.2. Meta-analyses

In the hierarchy of evidence, a systematic review is usually the highest level of evidence. Meta-analysis can be used to statistically combine and analyse the results of several studies within a systematic review, but a meta-analysis is not equivalent to a systematic review.

Meta-analyses have limitations, including study selection bias, heterogeneity between studies, the quality of included studies, publication bias, and accounting for important differences between studies when combining data. For example, the individual studies might not have been statistically powered to enable the comparison of treatment effects.These limitations can lead to misleading conclusions if not carefully understood and interpreted.

If a meta-analysis is used to substantiate a claim, any limitations of the analysis should be[1] clear to a healthcare professional so they can appropriately interpret the claim and to ensure that it is not misleading. Consistent with Code Section 1.2, any claim based on a meta-analysis should be consistent with the approved PI for the promoted product and the PI for any comparator product and the body of evidence.

5.3. Network Meta-Analyses (NMAs) & other forms of indirect evidence

While NMAs and indirect evidence may contribute to the overall evidence base of a product, they are generally insufficient on their own to substantiate strong comparative claims, particularly in the absence of direct, randomised, placebo-controlled, head-to-head trial data. NMAs are subject to inherent limitations, including reliance on assumptions of similarity, consistency and transitivity across studies; potential heterogeneity in patient populations, study designs and outcome measures; variations in comparator choice and quality of included trials; and an increased risk of bias through selective reporting or publication bias. These factors can reduce the reliability and clinical interpretability of comparative conclusions.

Where NMAs or other analytical approaches based on indirect evidence are used to substantiate promotional claims, it is recommended to include a clear explanation of the methodology and its limitations. As a lesser-known form of statistical analysis, NMAs require a higher degree of qualifying and explanatory information to support appropriate interpretation by healthcare professionals.

The Code and Appeals Committees' adjudication of complaints such as #1179, have commented on circumstances such as these.

Transparency regarding study funding and sponsorship is considered best practice, particularly where NMAs are industry funded, as this facilitates critical appraisal and informed decision-making.

5.4. Real World Evidence (RWE)

RWE provides evidence of the usage and potential benefits or risks of a medical product [1] Common sources include electronic health records, hospital episode data, claims data (e.g. PBS and MBS) and patient registry data (product and disease), chart reviews, clinical audits, and observational cohorts. RWE can provide a more complete picture of treatment effectiveness and safety within a real-world patient population.

RWE may be used to substantiate a promotional claim as long as it is of sufficient quality, is consistent with the body of evidence and is appropriate for and relevant to the claim being made. RWE may be used as secondary evidence to substantiate a claim where the primary evidence is higher in the evidence hierarchy, or where the RWE is the only available evidence. For example, in some cases randomised controlled trials have not been undertaken to compare one treatment to another in a head-to-head study. Data comparing the treatments may only be available from RWE observational studies, which is the highest level of evidence of comparative efficacy available for the products. Such RWE may be used to support a promotional claim relating to the comparative efficacy of the two treatments as long as:

- it is clear to a reader that the evidence is from RWE observational studies and it is not evidence from a head-to-head study
- the RWE is consistent with the body of evidence on the efficacy and safety of the products individually [1]
- is consistent with the approved Product Information for each product
- the RWE is the highest level of evidence available.

In all cases, care should be taken and sufficient context provided to ensure a reader understands the strengths and limitations of the RWE in order to assess the validity of the claim.

5.5. Non-clinical (animal or laboratory) data

The Code recognises that animal or laboratory data may be used as one type of evidence to support a promotional claim. Care should be taken when using these data, to avoid misleading a reader that there is some clinical effect based on non-clinical data. If such data are used, the nature of the data needs to be clear to a healthcare professional reader through use of a qualifying statement as described in Code Sections 1 c) and 1.2 i).

These principles apply to all types of animal or laboratory data, such as when describing the molecular structure of an active ingredient and/or its mechanism of action if these are derived through animal models or laboratory analysis. This is especially important when non-clinical data is used in the same promotional material as clinical data to substantiate promotional claims about a product. It should be clear to a reader that a claim about clinical effects can be substantiated by appropriate clinical evidence and is not based on non-clinical animal or laboratory data.

A qualifying statement such as “Clinical efficacy not yet established” for non-clinical data may be found to be misleading because it infers that a clinical effect may be able to be established in future, which cannot be substantiated.

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[1] U.S. Food and Drug Administration, Real-World Evidence, United States Government, 2022

5.6. Abstracts and posters (Section 1.2 a) and conference presentations

In general, abstracts and poster presentations that have not undergone significant peer review and/or have not been accepted for publication in peer reviewed journals are insufficient to provide the sole supporting evidence for a promotional claim. This does not mean that these data sources cannot be used at all.

It may be acceptable to use an abstract or poster as the basis for a promotional claim if the relevant clinical study has undergone peer review through evaluation by the Therapeutic Goods Administration (TGA) and has been included in the PI but has not yet been published other than as an abstract or poster.In addition, if the data presented in an abstract or poster is consistent with other published peer reviewed papers, if it further expands or supplements other observations and identifies no contradictory evidence, this will further support the acceptability of the use of an abstract or poster as a secondary reference. Companies should reference the primary source and/or approved PI in addition to referencing the abstract or poster. Companies should make it clear (in the citation) that the secondary reference for the claim is a poster or abstract.

Can a conference presentation be used to substantiate a promotional claim? The Code does not refer to conference presentations as a form of substantiating data. Whilst a presentation might include more information and detail than an abstract or poster, a presentation is unlikely to have been subject to rigorous peer review. Therefore, it is recommended that a conference presentation be treated as equivalent evidence to an abstract or poster presentation and therefore not used as the sole evidence to support a claim. When used as a secondary reference, companies should make it clear (in the citation) that it is a conference presentation.

Substantiating data should be current at the time the promotional claims are made. For example, although a supporting study is subsequently published in a peer reviewed journal, this would not be an appropriate justification for using the study poster or abstract as the sole substantiating data to support a claim before that publication occurs.

5.7. Secondary Endpoints and post-hoc analyses (Sections 1.2 e) and g))

The Code allows for use of pre-specified secondary endpoints as they often provide valuable insight into a product's efficacy and safety. If the primary endpoint/s was met, qualification may not be required but companies should ensure that there is sufficient context provided to ensure that a healthcare professional understands the claim.

The Code states that if a claim is based on a pre-specified secondary endpoint where the primary endpoints in the study were **not** met, the claim can be used if it is:

- consistent with the body of evidence; and
- accurately reflects the conclusion of the study, and
- it is clear to a reader that the primary endpoint was not met.

Post-hoc analyses can be used if clearly identified as post-hoc, used in context of the primary endpoint/s and appropriately qualified.

The Code and Appeals Committee, in their adjudication of complaints such as #1173, have commented on expectations for communicating when claims are derived from exploratory analysis.

5.8. Statistical significance and statistical comparisons

Sections 1.2 j), k) and l) outline requirements for statistical comparisons and communicating statistical significance, or lack of significance to a reader. Section 1.2 m) addresses requirements for comparative claims about clinically important differences.

It is important that it is clear to a reader how they should understand the statistical significance of the data in the context of the claim. A statistically significant comparison of a particular parameter or outcome might not be relevant or important clinically in treating or managing a patient.

Also, it may be misleading if a p-value is given that appears to be statistically significant, but the p-value is of nominal significance in the overall context of the clinical study. For example, an outcome tested after formal hierarchical testing has ceased due to an earlier non-significant finding is considered nominal (even if it is statistically significant). In this case, providing the effect estimate and confidence interval might be considered.

The Code and Appeals Committees' adjudication of complaint #1174 is an example relevant to the statistical significance of data to support a claim.

The Code doesn't require inclusion of additional statistical measures for communicating effectiveness between treatments. However, careful consideration of including confidence intervals, absolute risk reduction (ARR), relative risk reduction (RRR), and number needed to treat (NNT) can clarify claims for HCPs. These additional details may help to avoid potentially misleading healthcare professionals.

5.9. Representation of data in tables and graphs

Where a table or graph has been adapted from other sources, companies are encouraged to ensure that the adaptation does not alter the conclusions of the original source and that the graph or table is clearly identified as being adapted from another source. The adapted table or graph should be an accurate reflection of the original findings and should be clear and not confusing to a reader or intended to disguise, play down or exaggerate the results, which would be misleading.

Situations may arise where studies include some aspects that may not be consistent with the PI. For example, if a referenced study included an arm using a dose that is higher than the approved dose in the PI. Companies should consider how to present the original study findings in a transparent manner without promoting an unapproved dose. Carefully consider whether or not to include an 'off-label' dose arm from data presented in tables or graphs. The same principles apply to other features of studies that include an off-label arm. The key is to be clear and not misleading to healthcare professionals whilst remaining consistent with the PI.

Where a table or graph represents data based on different kinds of analyses in a comparative manner, the different methods of analysis should be clear to a reader. For example, where results from an intention-to-treat analysis are compared with a retrospective sub-group analysis, it should be clear to a reader that the analyses are based on different methodologies and should be interpreted on that basis.

The presentation of data from different studies within one graph or table in promotional material in a manner that implies the data relates to head-to-head studies may be misleading and should not be used. When graphs or tables from different studies are placed side by side due to layout in

promotional material, the graphs/tables should be accompanied by qualifying text of sufficient detail to allow a reader to understand the differences between the respective data sets.

5.10. Using taglines

Promotional taglines, similarly to any other promotional claim, should comply with all provisions of Section 1.If a tagline makes an implicit or explicit claim, as with any other claim, there should be sufficient evidence to support such a claim and it is appropriately referenced and qualified.

5.11. Qualifying statements (Section 1 b))

A qualifying statement is a phrase or statement that is linked to a claim, tagline or information represented diagrammatically which modifies, limits, or restricts the claim or other information. A qualifying statement should assist a reader to correctly interpret the information presented. If a qualifying statement is used, it should be linked to the relevant claim with a readily identifiable symbol. This may be an asterisk or similar device. The qualifying statement should appear directly below or adjacent to the claim and should be prominent.

A citation of the reference publication from which a claim, statement or other information is sourced or substantiated is not a qualifying statement; it is a reference. Similarly, a summary of study details, such as study design, methodology, results etc, is not a qualifying statement.

It is for a company to determine whether a qualifying statement is required for any claim. There is no limit on the number of qualifying statements that may be used with a claim. The requirement for qualifying statements to be adjacent to or immediately below a claim naturally limits the number of qualifying statements. However, companies should give careful consideration to the validity of a claim if numerous qualifying statements are required.

Here are some examples to assist companies with the use and placement of qualifying statements:

- A qualifying statement for a single claim in promotional material should appear immediately below or adjacent to the claim, irrespective of where, or how many times the claim appears on the page or visual frame. It should not be placed at the bottom of the page or frame, or in a side panel, or following other text or claims that are placed below the claim that requires the qualification, or below a graph or figure that appears below the claim.
- One or more qualifying statements associated with a short list of dot point claims or statements may be placed together immediately below or adjacent to the dot point list. Companies should ensure that grouping several qualifying statements together, with different symbols linking each qualifier with the relevant statement, is not confusing due to the number of qualifying statements. Overuse of qualifying statements may be misleading because the claim cannot be properly understood and interpreted.
- A qualifying statement associated with a figure or graph should be placed immediately below or adjacent to the figure or graph. A qualifying statement may be included within the figure or graph if this does not obscure the figure or graph and assists a reader to easily find any qualifying information and correctly interpret the information presented.
- Care should be taken in the use of abbreviations in qualifying statements, in order to shorten them, if they are not well recognised.

Appendix 1 – Examples of Potentially Misleading Claims

a) Literature references or quotations derived from a study or studies and citations of individual opinions which are significantly more favourable or unfavourable than has been demonstrated either within the study, or by the body of clinical evidence or experience. It is unreasonable to cite the results of an excessively favourable (or excessively unfavourable to a comparator product) study in a manner that misleadingly suggests that those results are typical or reflect the body evidence.

b) Information or conclusions from a study that is clearly inadequate in design, scope or conduct to provide support for such information and conclusions.

c) Omission of qualifying statement that is necessary to modify, limit, or interpret the claim being made so that the claim could imply broader or different use.

d) Citation of data previously valid but made obsolete or false by the evaluation of new data.

d) Suggestions or representations of uses, dosages, indications or any other element of the Product Information which are not approved by the TGA.

e) Shortening an approved indication (for example, in a by-line) so as to remove a qualification or limitation to the indication.

f) Use of animal or laboratory data as the sole evidence to support a promotional claim. It should be noted that if animal or laboratory data are used a prominent statement identifying this type of data and acknowledging that such data do not necessarily predict clinical effects should appear directly below or adjacent to the claim/s. The original statement and the qualifying statement should be linked by use of a readily identifiable symbol. The qualifying statement should be prominent.

g) Presentation of information in such a manner, for example by type size and/or layout, that could produce an incorrect perspective to the casual reader. Any qualifying statement should appear directly below or adjacent to the relevant claim and should be prominent. The original statement and the qualifying statement should be linked by use of a readily identifiable symbol.

h) Statements made about a competitor product, particularly negative statements, not balanced with corresponding information about the product being promoted.

i) Shortening the title of graphical representations reproduced from literature in a manner that alters the original author's meaning.

j) Use of overseas Product Information to support a claim where that information is inconsistent with the Australian Product Information.

k) Literal or implied claims that a parameter, contraindication, cautionary statement, adverse reaction or limitation on a claim in the Product Information, is not cause for concern.

l) Lack of substantiation of claims that are not of a medical, clinical or scientific nature. This includes information or claims relating to marketing factors such as pricing and market share. Care should be taken when extrapolating prescribing practices from sales data to ensure this is not misleading.

Appendix 2 – Examples of Claims that May be Inconsistent with the PI

The following are examples where a claim or other information may be inconsistent with the PI:

a) efficacy claims are overstated beyond information included in the clinical trials section of the PI,

b) use in a patient population that is not included in the PI, such as use in children younger than the approved age range for use stated in the PI,

c) use at a dosage (higher or lower) or frequency of dose (shorter or longer dose interval) than is described in the PI,

d) claims that frequency or incidence of adverse effects is lower than stated in the PI,

e) claims about lowering the incidence of secondary complications (e.g. cardiovascular disease) whereas the PI only includes outcomes related to disease markers specific to the approved indication (e.g. diabetes),

f) use in an indication that is broader than or different to the approved indications, such as use in mild disease where the product is approved for use in severe disease, and/or

g) use for an indication in a manner not stated in the PI, such as use as monotherapy where the approved indication states the approved use is in combination with another medicine.