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Our ref: RA12-616 / TGA
24 August 2012

Dear TGA Labelling and Packaging Review

Re: Janssen submission to the TGA Labelling and Packaging Review

Janssen is a research-based pharmaceutical company that currently sponsors many prescription medicines in Australia. As a subsidiary of Johnson & Johnson, Janssen strongly supports appropriate regulatory measures that enhance quality use of medicines and medicine safety, consistent with J&J's Credo.

However, Janssen is concerned that the proposals in the review do not reflect global best practice, have not been developed in a manner that will support the principles of the National Medicines Policy objectives for Quality Use of Medicines, and will be an undue burden on the Australian medicines industry.

Janssen believes that the proposals in this review demonstrate limited understanding or examination of the impact of these proposals on either the causes of, or the prevalence of, medication errors related to packaging and labelling. The proposals also do not consider the regulatory burden of creating unique Australian requirements on either the cost or viability of maintaining access to products in the Australian environment. The specific proposals made are, in most instances, overly prescriptive; some specific proposals would not be possible to implement.

While the TGA's proposals provide recommendations on regulatory changes to packaging and labelling requirements for medicines, evidence is not provided that these proposals will result in reductions in medication errors.

Therefore, Janssen does not support implementation of the proposals in this consultation. We recommend that additional work is conducted in partnership with the TGA, industry and other stakeholders to further clarify. Detailed comments on the specific proposals are provided as an attachment to this document. In particular, Janssen has analysed the medication errors identified by TGA in the consultation (see information under "Look-alike and sound-alike medicine brand names and look-alike packaging and branding"), and believe the conclusions of Janssen's analysis will be useful in refining TGA's proposals.

Please feel free to contact Duncan Purvis at Janssen if further information is required on any matters addressed in this consultation. Janssen would be pleased to be involved in further consultations on medicine labels and packaging.

Yours faithfully

Duncan Purvis

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enc. Janssen Detailed response to TGA Medicine Labelling and Packaging Review

Janssen — Detailed Response to TGA medicine labelling and packaging review

General comments on labels and packaging changes

1. Janssen believes the strict implementation of all these proposals would mean changes to 100% of medicine labels in Australia, with several packaging components in each medicine. Any implementation of these changes should involve a grace period of around 5 years, so as not to unduly burden industry and to allow industry to spread transition costs over a long period and minimize write-offs of existing medicine stocks, where no safety issue is identified.
2. Conversely, high priority must be given to any issues where medicine labels or packaging cause actual negative health impacts on patients. In these situations a rapid response by all stakeholders is essential, including prioritization by TGA of any label or packaging changes proposed to resolve safety issues.

Prominence of active ingredients on medicine labels

1. It would be helpful for TGA to provide guidance on whether Tall-Man lettering is allowed or preferred (or required) for active ingredient names on medicine labels. The TGA consultation recommendations may be conflict with the outcomes of the Tall-Man project. Ref: http://www.safetyandquality.gov.au/wp-content/uploads/2012/02/National-Tall-Man-Lettering-Report-and-final-list.pdf.
2. It would also be helpful for TGA could state a position on whether Tall Man lettering is allowed or preferred for tradenames. Requiring Tall man lettering for tradenames is likely to conflict with intellectual property rights of trademark holders, so Tall Man lettering cannot be a TGA requirement.
3. TGA should clarify how tradenames that include active ingredient names as a component of the tradename meet the labelling requirements. Is it required to repeat atorvastatin immediately under the tradename Atorvastatin Pfizer, for example. Can use of the active ingredient name in the tradename mean that the active ingredient name does not need to appear again on the label?
4. TGA's example of labels also includes additional information next to the active ingredient name, the active ingredient quantity. As this is not being required in the consultation, the inclusion of the active ingredient quantity is confusing.
5. TGA's requirement for the capitalization of the first letter of the active ingredient with the remainder to be in lower case (recommendation 1.2.4) should definitely not be adopted. It is inconsistent with the capitalization of active ingredients used on the ARTG (all lower case), use by TGA of active ingredient names in this review document (all lower case), previous recommendation of the TGA's Best Practice Guideline (all lower case), and the recommendation for the tradename to be capitalized (lack of differentiation). This major change would require rework of many new labels for no identified benefit and should not be adopted.
6. TGA's requirement for the active ingredient to be equally prominent and in a consistent location immediately below the tradename is acceptable. The requirement for left justification of active ingredient name is overly prescriptive, the active ingredient name should be allowed to be centred or right justified under the tradename.

7. The requirement that the font size of the active ingredient must be at least 100% of the font size of the tradename is overly prescriptive.
8. The labeling requirements for active ingredients will be very onerous for medicines containing three or more active ingredients, particularly for multi-vitamins, and may not be helpful in distinguishing products due to the arbitrary choice of the three ingredients with the highest quantities. The proposed requirement is operationally simple but seems unlikely to be the best rule to enhance quality use of medicines. Is there any evidence regarding use of two versus three ingredients that forms the basis for this recommendation?
9. For products that have more than two active ingredients, TGA should consider allowing use of an informative product category descriptor under the tradename (e.g. multivitamin, vitamin and mineral preparation, cold and flu symptom relief) as an alternative to listing three active ingredients. This alternative proposal should be tested in comparison with the current TGA proposals.

Day and night preparations

1. The Day and Night preparations labelling requirements (recommendation 1.4) are overly restrictive, confusing and in conflict with the active ingredient requirements for other products. The term "composition" is used but not defined. If you define composition as the name and quantity of active ingredient, then these do not appear immediately below the tradename, they are separated by a dose form description and an "each tablet contains" statement.

Paracetamol and ibuprofen warning statements

1. It is not clear why paracetamol and particularly ibuprofen have been singled out for warning statements, as their toxicity in overdose are not similar. As of July 2012, paracetamol appears in 665 ARTG entries, ibuprofen appears in 191 entries, aspirin in 91 entries and codeine in 248 entries. Acute oral paracetamol overdose can be extremely serious because of the narrow margin between therapeutic and toxic doses, with the development of severe hepatocellular necrosis and less often renal tubular necrosis (Martindale, 37th edition, p112). Active treatment with an antidote is effective, highlighting the importance of early recognition of paracetamol overdose. In contrast, in general, symptoms of non-steroidal anti-inflammatory drugs (NSAIDs such as ibuprofen) overdose are generally mild, and treatment is entirely supportive (Martindale 37th edition, p 102). In my mind, this information supports the use of a warning statement or recognition device for products containing paracetamol, but does not provide any support for a warning for ibuprofen containing products, or all NSAIDs.
2. Janssen broadly supports use of an identifying statement or device on paracetamol containing medicines. Application of an identifying statement only to paracetamol-containing products is consistent with the approach take in Ireland, the USA and UK, as stated in the review.
3. The TGA's placement of the warning statement for paracetamol containing medicines in TGA's example http://www.tga.gov.au/newsroom/consult-labelling-packaging-review-120524-figure-04.htm, breaches the current requirements of the SUSMP, where no other text can appear on the same line as the signal heading. This highlights the complexity of the current requirements and the onerous labeling restrictions currently included in the SUSMP. The SUSMP requirement that no other text can appear on the same line as a medicine signal heading also means that controlled drug packaging

cannot be shared across Australia and New Zealand due to different legislation. These restrictive SUSMP requirements should be reviewed through referral to the National Coordinating Committee on Therapeutic Goods, to see if they would allow amendment of these requirements, in order to allow placement of a paracetamol warning statement and the inclusion of a New Zealand controlled drug identifier into the signal heading area.

4. As currently proposed in this consultation, the paracetamol and ibuprofen warnings are too similar in appearance and are likely to be confused by consumers. Use on only paracetamol would remove potential for confusion.
5. If warnings are to be introduced for products other than paracetamol, or it is expected that this may occur in the future, then the paracetamol statement should be differentiated from other text on the box, e.g. perhaps a large P in a distinctive shape could be used next to the statement or elsewhere on the box. Requirement for a particular colour may be too onerous, but might be considered as a option. A distinctive mark should only be introduced after a trademark search of relevant images, and TGA should register the distinctive mark with IP Australia and complete the registration process prior to implementing this change.

Look-alike and sound-alike medicine brand names and look-alike packaging and branding

1. TGA's example set of look-alike sound-alike medicine names are instructive in that all of the examples provided feature
    a. Prescription medicines most likely to be supplied by community pharmacies
    b. same or similar dosage forms
    c. same or similar active ingredient quantities, as well as
    d. medicine brand names close to each other alphabetically.

Intended Medicine	Medicine Received
Aldactone 25mg (spironolactone) tablet bottle	**Aldomet 250mg** (methyldopa) tablet bottle
Azopt (brinzolamide ophthalmic suspension) 1% 10 mg/mL eye drops	**Atropt** (atropine sulphate) 1% 10 mg/ml eye drops
Celapram (note correction) (citalopram hydrobromide) 10 mg, 20 mg, 40 mg tablet	**Celebrex** (celecoxib) 100 mg, 200 mg, 400 mg capsule
Deralin 10mg 1 bd (propranolol hydrochloride) tablet	**Deptran 10mg 1 bd** (doxepin) capsule
Losec (omeprazole magnesium) 10 mg 20 mg 40 mg tablet	**Lasix** (furosemide) 10 mg, 20 mg, 40 mg tablet.

Janssen also notes the confusion between the similarly packaged products **COVERSYL®** perindopril 5 mg tablets and **COUMADIN®** warfarin 5 mg tablets, reference http://jppr.shpa.org.au/lib/pdf/2011_03/MedSafety0311.pdf, p52. Also in this reference on p55 is a description of a nicotine patch and nitroglycerin patch mix-up, when these medicines were stored alphabetically by active ingredient name and were in similar-looking packages.

The Australian Commission on Safety and Quality in Health Care risk assessment process† for assessing likelihood of confusion of two drug products considered the relevant factors for confusing two drug products to be:

- Appearance of the drug name (orthography) ≈ look-alike
- Sound of the drug names (phonology) ≈ sound-alike
- Strengths of the product available
- Routes of administration or dose forms of the products available
- Indications for use

Janssen suggests the additional factor to capture the error occurring in the TGA examples:

- Physically close in the system that is used to store medicines, e.g. since the most common method of arranging medicines in community pharmacy is by tradename, the errors that currently occur are alphabetically close by tradename. If products were arranged by e.g. active ingredient, a different error set would be generated, with the source of confusion being similar non-proprietary names.

CONCLUSIONS:

1. Differentiation relies on a number of factors not just the product tradename, and any system for differentiating products should take into account the relevant factors identified above.
2. It appears that dispensing errors identified in the TGA's consultation are occurring in community pharmacy and are primarily driven by alphabetically close tradenames due to physical proximity, same or similar strengths of the product available, same or similar dose forms of the products, and similar packaging.
3. Dispensing errors in the TGA's set are NOT driven by similar active ingredient name or similar indications for use, indicating that these factors did not effectively distinguish the products at the time of dispensing. Increasing the size and prominence of the active ingredient as proposed elsewhere in this consultation would potentially help to differentiate these products at the time of dispensing, for this product type (prescription medicines dispensed in community pharmacy).
4. Successful differentiation of medicines should take into account active ingredient quantity and dose form in addition to tradename and active ingredient name, with particular attention paid to lookalike packaging for medicines to be stored in a similar location (e.g. alphabetically close tradenames if medicines are arranged by tradename, alphabetically close active ingredient names if medicines are arranged by active ingredient).
5. OTC medicines that are self-selected by consumers are usually arranged in pharmacy by product category so different errors will apply.

† Reference: http://www.safetyandquality.gov.au/wp-content/uploads/2012/02/National-Tall-Man-Lettering-Appendix-B-Part-A-Risk-Assessment-Processes.pdf, page 5

Standardised information format: the Medicine Information Box

1. A medicine information box would be helpful for over-the-counter and complementary medicines. Often, storage instructions (in particular) are difficult to locate. The ARTG entry number is an additional piece of information that should be put in this area as it does not effectively differentiate medicines, but needs to go on the product. Having the option to locate this information in the medicine information box may be helpful in reducing the amount of information required on the front panel of the medicine.

Dispensing label space

1. Janssen supports in principle a designated space on product labelling for a dispensing label, where space and/or pack size permits. The space must be consistent with international best practice (70 mm x 30mm) to ensure global labelling templates for label generation can be utilised. While we support a designated space for the dispensing label, we believe that the standard size of the dispensing label used in pharmacies in Australia should be selected to fit within this space.

Blister strip labelling

1. The requirement that the batch number and expiry date must be repeated every two units cannot be achieved by many pharmaceutical manufacturing operations. This is variable data which cannot be pre-printed and must be added during manufacture, commonly through printing or embossing each blister platform. Many packaging machines can only apply this information once on a blister strip. There are likely to be significant shortages of medicines if this restrictive requirement is introduced. Manufacturers should be able to provide variable data once on a blister strip that is not intended to be segmented and does not facilitate segmentation.

2. The requirement for this information to be included on each segment of a strip that can be segmented is reasonable.

3. The requirement for 3 active ingredients is too onerous for multivitamins as recognized by the consultation, where the alternative proposal not to include all active ingredients is the only feasible solution.

4. TGA has proposed pragmatic solutions for multivitamins and blister strips with a race track format. TGA should also accept pragmatic solutions for other situations that may arise through ongoing consultation and implementation.

Small containers

1. The TGA should future proof these requirements to allow future electronic delivery of information to also meet the requirements for small containers, in addition to the use of package inserts.

2. Guidance on the dimensions of the clear space required to affix a folded sticker should be provided, in consultation with dispensing stakeholders.

Pack inserts

1. The package insert requirements are overly prescriptive and allowance should be made for electronic delivery of label information through smartphones and internet.

2. Package inserts should not be mandatory for injectable medicines. In particular, the Product Information document should not be required as a pack insert for an injectable medicine, as it contains a lot of information that is not directly relevant at the point of dispensing, and there is a risk of relying on an old pack insert if the Product Information is updated. The electronic form of the PI should be the preferred reference for the PI. Only the administration instructions should be required labeling for injectable medicines; either on the carton label (optionally on the container label), or as a pack insert, with only the administration information forming the mandatory pack insert text. This will allow the critical administration information to be presented in a large font with clear diagrams if required.

3. Package inserts can provide educational material for consumers and patients on their medicines and what to expect when using the product to improve QUM outcomes. Patient support program contact or enrolment information should be allowed to be included on pack inserts. Consumer medicine information should always be acceptable as a pack insert.

Labels and packaging advisory committee

1. Any process for decision making by TGA around tradenames, labels and packaging will need to be robust and have a sound administrative basis, as changes to tradenames, labels and packaging are costly and likely to be contentious. The process should quantify the impact of any hazard that is identified.

2. TGA should consider the expertise and processes of the Australian Commission on Safety and Quality in Health Care when devising their process.

3. The TGA process should also take into account the intellectual property process around registration of trademarks and the duration of this process.

4. The TGA process should be predictable, timely and transparent. The process should balance timely access to medicines with the goal of optimizing consumer safety, considering the identified hazards.

Minor comments

1. As labelling is sometimes used (particularly in overseas jurisdictions) as an alternative name for Product Information, calling this review the TGA medicine labels and packaging review would be less confusing – we do want to reduce confusion from look-alike, sound-alike terms like labels and labelling!
2. Many of the statements in the review are referenced but the references are not provided, is this the standard of transparency expected for a public review? Janssen believes references should be publically available or if not publically available, should be included in the review where they support a controversial assertion in the text. In particular, the references around paracetamol safety do not appear to clearly support the review's proposals.