Response to TGA Medicine Labelling and Packaging Consultation Paper

August 23, 2012

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ALLERGAN

Level 4, 810 Pacific Highway, Gordon NSW 2072, Locked Bag 1514, Pymble NSW 2073, Australia, Phone (612) 9498 0100, Fax (612) 9498 0290

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Note to Therapeutic Goods Administration

Thank you for the invitation to respond to your Consultation paper entitled "TGA Medicine Labelling and Packaging Review", issued in May 2012. Enclosed is a discussion of those proposed regulatory changes which may demonstrate the most implementation difficulties. As requested, a short commentary and alternative solutions have been provided where possible.

While general feedback has been provided by category, additional feedback is provided to select questions posed by the TGA. Thank you again for your consideration.

Sincerely,

Allergan Australia Pty Ltd

Prominence of Active Ingredients on Medicine Labels

Due Prominence of Active Ingredient

Active Pharmaceutical Ingredient (API) prominence on a drug label strongly contributes to patient/prescriber comprehension of drug identity. Numerous factors may help contribute to the distinction of the API name on the label (e.g. size, format, colour, and spacing). Ultimately, the most effective method of distinguishing the API name may utilise a combination of factors and it is uncertain whether any individual variable will provide any substantial benefit to consumer safety *per se*.

While promoting adequate prominence of the Active Ingredient, the TGA should consider that the proposed requirements will comprise more space on the label and may distract from other important requirements of the label (e.g. brand names, precautions/warnings, country of manufacture, trademarks, barcodes, statements such as "Keep out of reach of children"). In the interest of patient safety, the label should be clear, legible, and easily comprehended. As more components/formats are added to the TGA requirements, labels may become less intelligible and more confusing to the patient. This issue will become increasingly apparent as the container size decreases.

Thus, a degree of flexibility should be given with respect to exercising the individual proposed TGA recommendations and due focus should be given to the artwork as a whole.

API Font Size

The proposed recommendations for API font size in relation to the brand name ("The font size of the active ingredient must be at least 100% of the font size of the medicine brand name on the main/front label.") should give due consideration to the regulatory guidelines in other world regions. For example, the US FDA states that the API name should be written in a font size that is at least 50% of the brand name. It is understood that the patient and/or prescriber should be able to clearly read the name of the API on the front/main label. However, an API font size equivalent to 100% of the size of the brand name may be unnecessarily large and may render it difficult to include other critical components on the label. In the context of medicines with small containers or with more than one API, an API font that is 100% of the brand name may be

impractical and difficult to format. Therefore, it is suggested that due prominence of the API name can be achieved at 50% of the font size of the brand name.

API Prominence on 3 Non-Opposing Faces of a Carton

The TGA suggests that the active ingredient be included with, and of equal prominence as, the brand name on at least 3 non-opposing faces of a carton. This proposal would result in redundant information on the carton when instead space should be reserved to allow for additional state and TGA mandated text. Further, one must consider the feasibility of this request for small cartons.

Select TGA Question(s)

What is the smallest size font that you consider readable?

1.0 mm

Look-Alike Sound-Alike Names and Look-Alike Packaging

Risk Assessment Proposal

While it is understandable that LASA naming and packaging can be problematic, further discussion is necessary to determine what kind of "risk assessment" is necessary for proposed new medicine packaging and labelling. The final guidelines should be clear, objective and transparent.

As mentioned by the TGA, other health authorities (e.g. FDA, EMA) have instituted programs that are used during drug development to guide the naming process. Any new TGA guidance should consider a framework that is harmonised with other countries. A mutual recognition agreement between key countries (e.g. FDA, EMA) may lessen the TGA's workload and allow for brand names that are consistent internationally (thereby lessening confusion to patients travelling overseas).

The TGA should further consider how the proposed risk assessment will be incorporated into the current Australian Regulatory Review Process. A prolonged review phase will increase the time and financial burden on Industry and the TGA, and potentially inhibit patient access to valuable drugs that will mitigate, prevent, or even cure disease.

New/Existing Medicine Names Varying by Three Letters or Fewer

The TGA has stated that there is a potential safety risk associated with patients and pharmacists that accidentally confuse the name of one drug with that of a similarly-named drug. Look-alike packaging indeed may lead to the risk of patient/pharmacist confusion. However, the extent to which packaging with similar brand names differs should not be solely determined by the number of letters shared between drug names. In cases where drug names are similar, further consideration should be given to numerous factors including, but not limited to: mode of administration; dosage regimen; safety risk; shelf position (if non-prescription); or indication. In relation to new and existing medicines in the ARTG where confusion may pose a significant safety risk, the design of the label and package should contrast that of the existing product.

The practicality of the design should also be considered. Any change in design that may affect readability or interpretation of the package or label should be discouraged.

Look-Alike Medicine Branding: Marketing the Same API for a Subset of Uses

While the packaging and labelling of one drug product should not differentiate one indication over another, the TGA has proposed that the same API should not be selectively "marketed" for a subset of symptoms or uses, unless the medicine has specific characteristics that make it more suitable for a particular symptom. In this capacity, the TGA should further clarify the term "marketing."

Outside the scope of information presented on medicine containers, "marketing" can be understood as a broad set of communications to consumers (e.g. patients/ healthcare

professionals). Communications with healthcare professionals regarding drugs with multiple indications commonly occur in the context of specific indications. This is important because communications regarding specific indications allow communication of specific modes of administration, dosing information and safety information for specific indications of a given drug. Simultaneous presentation of all indications would be burdensome to the healthcare professional and may result in critical safety information being lost in the process.

Look-Alike Medicine Branding: Applying One Brand Name to Multiple Products

The TGA has proposed that the same brand name cannot be applied to products that have different active ingredients or combinations of active ingredients unless the active ingredients are closely related. The TGA should define the term "closely related."

A common brand name used in the correct circumstance is an important part of product identification and supports patient safety. For example, one brand of drug may contain a single API but the API may be supplied at different doses to support the drug metabolism of individual patients. In this case, one brand name would cover multiple formulations, each with distinct API concentrations. One brand name with multiple concentrations of API would reinforce the API identity.

In cases of differing APIs within the same brand, the risk of umbrella branding should be determined based on a hierarchical strategy which places importance primarily on those drugs that reflect an increased safety profile (e.g. medicines with notable drug-drug interactions, toxicities, overdosage, adverse events). Heightened attention should be placed on prescription drugs which pose a higher level of risk to patients, rather than non-prescription drugs for which the assessed level of risk is low. A shared brand name for low risk products may not pose a safety risk if adequate distinction between products is provided and, in this case, a differentiating prefix/suffix may be sufficient for product identification.

A further threat to patient safety is posed if this proposal is to be retrospectively enforced for existing registered and listed medicines on the ARTG. After years of approved marketing and

usage in Australia, unpredictable brand name changes will certainly add to consumer/prescriber confusion and may potentiate medication errors. Given that this proposal will require significant industry and government investment (time and money) if enacted retrospectively, a thorough assessment of the current versus potential harm to patient safety should be conducted before any name changes are initiated.

Select TGA Question(s)

Do you think the proposed changes to address LASA names, LA packaging and LA branding will improve medicine safety? Why/why not?

As mentioned in the Consultation paper, there are certain key risks to consumers if the name or identity of a medicine is confused by consumers and/or healthcare practitioners. The potential for the aforementioned proposed regulatory changes to significantly improve patient safety varies depending on the drug. Heightened attention should be placed on prescription drugs which pose a higher level of risk to patients, rather than non-prescription drugs for which the determined level of risk is low. A shared brand name for a low risk product may not pose a safety risk if adequate distinction between products is provided.

Standardised Information Format: the Medicine Information Box

A substantial change in non-prescription and complimentary medicines labelling format is proposed by the TGA by suggesting that non-prescription labels include a Medicine Information Box. The inclusion of the Box allows for cross-comparability between drugs by the consumer. However, it minimises the ability of the sponsor to effectively differentiate brands by packaging designs (*n.b.* this is particularly important in consideration of the TGA proposals previously discussed in this response). Ultimately, similar information could be presented in an array of manners and remain equally effective. Many agencies choose to regulate the content of packaging information without necessitating strict format requirements.

The impact of this proposal on the package design of small bottles and containers is substantial. A minimum font size of 1.5mm (with heading height at least 2 mm) is difficult to achieve on small container labels (e.g. eye drop containers holding less than 3 millilitres). Thus, the inherent nuance of this regulation is that almost all non-prescription small bottles and containers will require larger packaging and/or pack inserts, thereby causing sponsors to incur additional production costs.

Furthermore, the imposition of a Medicine Information Box on non-traditional containers (e.g. tubes without outer containers) may be difficult. If the Medicine Information Box does not fit on such a container, addition of an outer carton would be required, increasing the cost of goods.

The concept of the Medicine Information Box could be further improved by understanding Australian-specific consumer needs (i.e. which information is most important for patient safety and how does the patient access that information?) and by implementing further Industry discussions to determine the final crucial elements/layouts of the Box. Exemptions should also be put in place to allow for small containers.

Dispensing Label Space

The TGA has suggested that prescription drug dispensing labels may occlude information provided on the primary containers of prescription medicines. In general, provision of a CMI alleviates this problem. Larger cartons may easily comply with the 70 mm x 30 mm dispensing space requirement, however, dispensing label space designation can be difficult and impractical on small bottles or cartons. The TGA has suggested that “a clear space should be provided [on small containers] to affix the edges of a folded dispensing label,” but the interpretation of “a clear space” is subjective. The minimum space dimensions for small containers should be delineated, or exemptions provided.

Small Containers

Inclusion of a Pack Insert

Due to the small labelling/packaging capacity of small containers, the TGA has proposed that small containers be enclosed in a primary pack with a pack insert. Currently, a CMI is enclosed in the cartons of some prescription medicines, but there is no existing pack insert requirement for non-prescription medicines. As mentioned previously, inclusion of a pack insert will add to the current costs of production.

Container Label Requirements

The proposed container requirements expand upon the current state and country regulations for small container labelling. The ability to apply these requirements strongly depends on the size of the small container: Compliance of a container with a nominal capacity of 20 millilitres will be significantly less problematic than that of 3 millilitres.

With regard to prescription ophthalmic preparations, the new requirements impose the addition of antimicrobial preservative names and a statement to the effect that the medicine should not be used longer than four weeks after the container is first opened (if multidose) on the immediate container. These additional requirements not only result in a redesign of all small container labels, but also add further text to already condensed labelling. Given that the minimum font is suggested to be 1.5 mm, it is doubtful that all proposed text can be added easily to labels of small containers. As a result, it is suggested that the minimum text size be decreased to 1 mm, or exemptions allowed. If the latter were not introduced, the proposed changes would necessitate changes to pack sizes and/or bottle sizes. Any changes to container and pack sizes would have a deleterious impact on manufacturing, procurement, shipping, and storage costs and need to be considered in conjunction with the current NSW regulations regarding misleading packaging.

With regard to non-prescription medicines, the new requirements also propose the addition of warnings and directions to the container label (through use of a Medicine Information Box). Inclusion of this information adds to the existing requirements from the state, TGA and Medsafe (if the drugs share a stock-keeping unit between Australia and New Zealand). Placement of all new information on the label in the required format will result in a crowded label where relevant information is difficult for a consumer to find and is logistically problematic.

Labels and Packaging Advisory Committee

A transparent labelling and packaging committee with well-defined rules of operation may benefit Industry, the TGA and the consumer. However, the mechanism by which this advisory committee is integrated into product-specific reviews should be further delineated.

A labelling and packaging advisory committee could serve to improve the process by which initial labels/packages are evaluated, provided that the time and point of advisory committee product evaluation is well-defined and that the advisory committee review does not substantially impede the application review time. Therefore, the committee framework (e.g. composition of members, rules and processes) should be composed such that decisions will be made in an organised, informed and consistent manner.

Implementation of Changes

Labelling/Packaging Updates

The TGA provides a definitive three year time period in which industry is expected to comply with the new requirements once they come into force. However, it should be noted that these labelling propositions likely will necessitate updates to most (if not all) registered and listed medicines in the ARTG. Labelling changes will have to be submitted to, and reviewed by, all countries in which a given drug shares a stock-keeping unit (e.g. Medsafe). Such a conversion will require substantial time and financial support by Industry, the TGA and other Health Authorities. Therefore, a more flexible period of transition is suggested, whereby the Sponsor brings their existing registered and listed medicines into compliance with the new requirements as labelling/packaging updates are otherwise required.

LASA Naming Changes

As mentioned previously, brand name changes to existing medicines will likely potentiate consumer/prescriber confusion and medication errors. Given that this proposal will require significant Industry and government investment (time and money) if enacted retrospectively, a thorough assessment of the current versus potential harm to patient safety should be evaluated before any name changes are initiated. Further discussion regarding the implications of this

proposal (Item 3.6 of the TGA Consolidated List of Recommendations) and the possibility of "grandfathering" certain existing brand names would be beneficial.

Prescription versus Non-Prescription Medicines

Due to the differential natures of Prescription and Non-prescription medicine labelling, packaging, branding and human factors, the TGA should consider discussing the aforementioned labelling issues in separate forums.