MEDSAFE
New Zealand Medicines and Medical Devices Safety Authority

Proposed warning and advisory statements relating to the harm of long-term use and overuse of stimulant laxatives

07 June 2022

Consultation outcome

Contents

Executive Summary

Stimulant laxatives are either general sale or pharmacy-only medicines. General sale medicines can be purchased without advice from a healthcare professional, and there is no requirement for these medicines to have a data sheet or consumer medicine information leaflet. Consumers may receive inconsistent information relating to the potential harms of long term or excessive use.

From 29 September to 11 November 2021, Medsafe sought feedback on proposed warning statements to be included in the Label Statements Database for stimulant laxatives. Warning statements would ensure consumers have enough information on the package labelling to take stimulant laxatives safely and appropriately.

This report is a summary of the submissions received.

Medsafe received 21 valid submissions to the consultation. We would like to thank everyone for their contribution to this consultation.

In general, most respondents agreed with the proposed statements and the timeframe for implementation. However, some respondents, particularly healthcare professionals, had reservations about using the word ‘prolonged’ in relation to duration of use. Our response to issues raised are detailed below in the main part of this document.

In addition, there were other comments related to the Label Statements Database not belonging to other parts of this report. This has been addressed in the last section, ‘Other Comments’.

About the consultation

Medsafe's review of misuse of stimulant laxatives was prompted by the recent review and regulatory action by the United Kingdom's Medicines and Healthcare products Regulatory Agency which introduced new safety warnings for over-the-counter (OTC) stimulant laxatives.

This review was presented to the Medicines Adverse Reactions Committee (MARC) at their 186th meeting held on 10 June 2021. The MARC noted that although there was no literature documenting the misuse of stimulant laxatives in New Zealand, members of the Committee have anecdotally seen the misuse of laxatives through their various practice settings. The extent of the misuse is difficult to quantify.

The MARC considered several regulatory actions to minimise misuse of stimulant laxatives. The actions were reclassifying the medicine, introducing pack size restrictions, and updating the Label Statements Database (LSD).

The MARC recommended Medsafe to undertake a LSD consultation to include warning and advisory statements to the manufacturer's original pack for all stimulant laxatives to minimise its misuse (eg, 'does not help with weight loss' and 'prolonged or excessive use can be harmful').

See the Medsafe website for the minutes of the 186th MARC meeting and the report.

The Label Statements Database lists the warning and advisory statements that are required on medicine and related product labels under the Medicines Regulations 1984. Currently, there are no label statements required for stimulant laxatives. Therefore, the information contained on the package labelling of these products is variable.

Table 1 outlines the three warning and advisory statements for stimulant laxatives proposed by Medsafe. The proposed conditions and the date for implementation are also outlined below.

Table 1: Proposed warnings and advisory statements for stimulant laxatives

Medicine/Group/Class	Conditions	Statement	Required by
Stimulant laxatives Examples include: • Bisacodyl • Glycerol • Sennosides/senna • Sodium picosulfate	When for oral or rectal use (except glycerol for rectal use only)	• Does not help with weight loss • Prolonged or excessive use can be harmful • Consult a healthcare professional if symptoms persist	12 months from when the Label Statements Database is updated

As part of the consultation, Medsafe sought comments on:

- whether the package labelling for stimulant laxatives should include warning and advisory statements relating to the harm of long-term use and overuse
- the proposed wording of the statements (see Table 1)
- whether there are any other statements relating to the harm of long-term use and overuse of stimulant laxatives that should be included on the package labelling
- The proposed conditions and date of implementation.

Consultation results

Thank you to everyone who responded to the survey.

We have analysed and summarised the survey results.

The results are divided into nine parts as follows:

1. Overview of respondents
2. Summary of responses: Should there be Label Statements for stimulant laxatives?
3. Summary of responses for Statement 1: 'Does not help with weight loss'
4. Summary of responses for Statement 2: 'Prolonged or excessive use can be harmful'
5. Summary of responses for Statement 3: 'Consult a healthcare professional if symptoms persist'
6. Summary of responses: Other Label Statements to be considered
7. Proposed conditions
8. Proposed timeframe for implementation
9. Other comments related to Label Statements
10. Outcome

Part 1 summarises the respondent demographics by individual or organisation, location, respondent category, and by health profession.

Parts 2 to 8 contain a tabulated summary of respondents' agreement or disagreement with the proposed statements. This table is broken down by respondent category. Comments from respondents are grouped into themes, and a response from Medsafe and the final outcome for each part is included at the end.

Part 9 contains other comments raised by respondents on the Label Statements.

Part 10 contains the overall outcome and the final statements, as they will appear in the Label Statements Database.

1. Overview of respondents

You can view the submissions that we have permission to publish.

A total of 22 submissions were received via the consultation tool. One submission was not valid, therefore only 21 submissions will be discussed in this report.

As shown in Table 2, most responses were submitted by individuals (67%). Seven respondents (33%) submitted on behalf of an organisation, group, or the industry.

Table 2: Respondent type – individual or organisation

Respondent	Number	Percentage (%)
As an individual	14	66.7
On behalf of an organisation or group	7	33.3
Total	**21**	**100.0**

Most respondents were based in New Zealand (81%), as shown in Table 3.

Table 3: Respondent location

Location	Number	Percentage (%)
New Zealand	17	81.0
Australia	3	14.3
Not Answered	1	4.7
Total	**21**	**100.0**

For the analysis, respondents have been categorised into one of four categories (see Table 4):

- Healthcare professional (HCP), n=12
- Public, n=3
- Industry, n=3
- Other, n=3.

Table 4: Respondent category

Respondent	Categorised as	Number	Percentage (%)
Healthcare professional	HCP	10	47.6
Professional body	HCP	2	9.5
Member of the public	Public	3	14.3
Sponsor	Industry	2	9.5
Industry organisation	Industry	1	4.8
Researcher	Other	1	4.8
Institution (eg, university, hospital)	Other	1	4.8
Other	Other	1	4.8
Total		**21**	**100.0**

Most healthcare professional respondents were in the nursing profession (see Table 5).

Table 5: Health care professional respondents

Profession	Number	Percentage (%)
General Practice	1	8.3
Clinical Pharmacology and Gastroenterology	1	8.3
Nurse Practitioner	1	8.3
Public Health Nurse	1	8.3
Registered Nurse/Nursing/Practice Nurse	5	41.7
Pharmacy	1	8.3
Professional body	2	16.7
Total	**12**	**100.0**

2. Summary of responses – Should there be Label Statements for stimulant laxatives?

Question

Should the package labelling for stimulant laxatives include warning and advisory statements relating to the harm of long-term use and overuse?

Include warning statements – Agree Y/N

- Yes, n=18
- No, n=3

Table 6: Include warning statements for stimulant laxatives – Summary of responses

		Respondent category									
		All (n=21)		HCP (n=12)		Public (n=3)		Industry (n=3)		Other (n=3)	
Question	**Response**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Include warning statements	Yes	18	85.7	11	91.7	3	100	1	33.3	3	100
	No	3	14.3	1	8.3	0	-	2	66.7	0	-

Question

Please add your comments

There were ten responses to this part of the question. Comments have been summarised by respondent category below:

Comments from Healthcare Professionals

The label statements should not be a substitute for managing a potentially undiagnosed health issue that needs to be medically reviewed and managed accordingly. Lifestyle factors such as a balanced diet and physical activities are much more important than stimulant laxatives.

There is a lack of awareness by the public on the potential harms. Knowledge of the potential harm is important as part of informed consent.

Medsafe's response

The label statements are not intended to replace advice given by a healthcare professional but rather allow consumers to have information they need to take stimulant laxatives safely and appropriately when purchasing OTC. The proposed warning statement 'Consult a healthcare professional if symptoms persist' aims to encourage consumers to seek healthcare professional advice early to determine underlying factors for their unresolved constipation and therefore prompt further discussion on their lifestyle and diet or consider undiagnosed conditions.

Comments from Public

The use of packaging labels to warn of the harm of long-term use and overuse was supported, with respondents citing that every avenue should be used to provide accurate information to the general consumer.

Comments from Industry

There were concerns that some products have New Zealand specific labels. The Industry asked Medsafe to consider the impact should sponsors of these products later wish to have a shared Australian-New Zealand label.

The Industry would like to see harmonisation and alignment of warning statements with Australia where possible. In Australia, all laxatives (except for bulk-forming laxatives) are required to have the statement 'Prolonged use is undesirable and may lead to dependence'. In addition, hydroxyanthracene derivatives must also include some additional warning statements. The sponsor requested that Medsafe considers allowing using these warning statements as 'words of a similar meaning'.

Medsafe's response

Medsafe endeavours to harmonise wording between the New Zealand and Australian labelling. However, this may not be possible for the proposed stimulant laxative statements as the New Zealand concepts do not overlap with what is required in Australia.

There are currently two products registered in Australia that are also supplied in New Zealand. Therefore, lack of harmonisation of warning statements is not considered a material issue to New Zealand consumers being able to access these products.

We note New Zealand stimulant laxative products have Australian required statements. In general, additional statements can be added to labels over and above the required statements if they do not conflict with our proposed label statements.

Outcome

The majority of submissions agreed that there should be label statements for stimulant laxatives.

3. Summary of responses for Statement 1: Does not help with weight loss

Question

Do you agree with the proposed statement 'Does not help with weight loss'?

Agree Y/N

- Yes, n=19
- No, n= 1
- Not Answered, n= 1

Table 7: Statement 1: Does not help with weight loss – Summary of responses

		Respondent category									
		All (n=21)		HCP (n=12)		Public (n=3)		Industry (n=3)		Other (n=3)	
Question	Response	No.	%	No.	%	No.	%	No.	%	No.	%
Agree with proposed statement	Yes	19	90.5	10	100	2	66.6	2	66.6	5	100
	No	1	4.8	0	-	0	-	1	33.3	0	-
	Not Answered	1	4.8	0	-	1	33.3	0	0	0	-

Question

If no, please suggest an alternative statement, or why it should not be included

There were four responses received to this part of the question. Comments have been summarised by respondent category below:

Comments from Industry

Alternative wording was suggested: 'laxatives do not help in weight loss' or 'laxatives do not help in long-term weight loss'.

Medsafe's proposed statement is not present in the labelling for products required by the Australian Therapeutics Goods Administration (TGA). Medsafe should consider the implications the additional statement could have on products that are harmonised with Australia.

Medsafe's response

Words of a similar meaning to the statement may be used and individual statements may be combined provided the intent is not changed. The second statement, 'laxatives do not help in long-term weight loss' should not be used as it could be interpreted that laxatives could be used for shorter term weight loss.

We note that the TGA's Australian Regulatory Guidelines for over-the-counter medicines (ARGOM) state that the TGA will not approve weight loss claims for laxatives. There are, therefore, no marketed laxative products registered in Australia that make weight loss claims. The proposed statement does not impact or contradict the Australian labelling requirements.

Comments from Public

If the proposed stimulants are holistic herb stimulants, they should have the statements 'Used to temporarily enhance elimination,' or 'should not be relied upon as part of a weight loss programme. Over stimulation is damaging to the gastrointestinal tract.'

Medsafe's response

This statement is intended to apply to stimulant laxatives. Any product that is a stimulant laxative, whether herbal or otherwise, is a medicine and requires consent for distribution before it can be supplied in New Zealand. Some products that are bulking agents and have a laxative effect by increasing the fibre content of the diet may be marketed as medicines or supplemented foods depending on the claims and the intended market. The above statements do not apply to these products.

The wording 'enhance elimination' could cause confusion to some consumers as laxatives may be used to maintain a regular bowel motion. The wording also could be interpreted that stimulant laxatives can be used as a body cleansing agent.

The statement 'should not be relied upon as part of a weight loss programme' can give the impression that these laxatives are conventionally used in weight loss programmes.

In response to the statement 'Over stimulation is damaging to the gastrointestinal tract', the proposed statement on prolonged or excessive use can be harmful is discussed in Part 4.

Outcome

Medsafe will adopt the statement 'Does not help with weight loss' statement as the majority of respondents agreed with the proposed wording.

4. Summary of responses for Statement 2: Prolonged or excessive use can be harmful

Question

Do you agree with the proposed statement 'Prolonged or excessive use can be harmful'?

Agree Y/N

- Yes, n=17
- No, n= 4

Table 8: Statement 2: Prolonged or excessive use can be harmful – Summary of responses

		Respondent category									
		All (n=21)		HCP (n=12)		Public (n=3)		Industry (n=3)		Other (n=3)	
Question	**Response**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Agree with the proposed statement	Yes	17	81.0	9	75	3	100	2	66.7	3	100
	No	4	19.0	3	25	0	-	1	33.3	0	-

Question

If no, please suggest an alternative statement, or why it should not be included.

There were seven responses received to this part of the question. Comments have been summarised by respondent category below:

Comments from Healthcare professionals

The word 'prolonged' may not be appropriate as there are patients who take stimulant laxatives regularly for a specific clinical condition under the care of a health professional. These patients have been advised by their healthcare professional that long-term use is safe.

Medsafe's response

Medsafe considers the proposed statement is unlikely to cause confusion in patients who have been counselled by their healthcare professional to take laxatives long-term. The label statements are to inform the group of consumers who may be purchasing these products long term without medical oversight.

Comments from both Industry and Healthcare professionals

There is insufficient evidence showing stimulant laxatives are directly harmful long term.

- Previous hypotheses suggested that chronic stimulant laxative use might result in disordered gut function with tolerance and cathartic colon in the most severe form. This was never proven, and it is now believed that the natural history of the underlying constipation condition led to gradual worsening of constipation, despite being on stimulant laxatives, rather than as a result of laxative use.

- Guidelines exist that consider stimulant laxatives to be a safe option for long term treatment.
- Unintended use of higher than approved doses of stimulant laxatives over prolonged periods can lead to adverse events such as hypokalaemia. There was support for an alternative statement (eg, 'Excessive use can be harmful' and 'Prolonged excessive use can be harmful'). If this statement is to be added for stimulant laxatives, it would also need to be added to any other laxatives that cause frequent loose stools as the risk is the same, in the form of electrolyte disturbance and dehydration.
- *'Prolonged'* seems suitable to produce Type 4 stools (Bristol Classification), and the word '*excessive'* refers to treatment other than chronic constipation and therefore carries the risk of electrolyte disturbances with it.

Medsafe's response

Medsafe acknowledges the limited evidence around the harms of stimulant laxatives. However, there is evidence that excessive use can be harmful as it carries the risk of dehydration and electrolyte imbalances, such as hypokalaemia. This warning is not currently on the package labelling for stimulant laxatives.

Comments from Public

'Prolonged or excessive use can be harmful' is likely to be ignored and instead a brief statement on the potential harm would be more useful instead. For example, '*body building up a tolerance.*'

Comments from Industry

The TGA's ARGOM requires all Australian registered laxatives to contain the statement '*Prolonged use of laxatives is undesirable and may lead to dependence'* and hydroxyanthracene derivatives also require the additional statement '*Prolonged use may cause serious bowel problems'*. Medsafe should consider the statements required by Australian packaging to be acceptable to allow for harmonised packaging.

Medsafe's response

The current statements required by the TGA does not warn patients of harm caused by excessive use. We consider that 'dependence' does not adequately cover the harms. Harmonisation of statements are not possible in this case as our proposed statement differs in concept with the TGA's requirement.

Outcome

Medsafe will adopt the statement 'Excessive use can be harmful'. It would be informative to specify the harms such as diarrhoea, dehydration, and changes in electrolytes. However, we understand the space constraints on the packaging. Medsafe supports sponsors to specify the harm if space is permitted.

Please note the required statement '*Prolonged use of laxatives is undesirable and may lead to dependence'* set out by the TGA for laxatives (excluding bulk-forming laxatives) will not be considered words of a similar meaning to our proposed statement 'Excessive use can be harmful'.

5. Summary of responses for Statement 3: Consult a healthcare professional if symptoms persist

Question

Do you agree with the proposed statement 'Consult a healthcare professional if symptoms persist'?

Agree Y/N

- Yes, n=20
- No, n= 1

Table 9: Statement 3: Consult a healthcare professional if symptoms persist – Summary of responses

		Respondent category									
		All (n=21)		HCP (n=12)		Public (n=3)		Industry (n=3)		Other (n=3)	
Question	**Response**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Agree with proposed statement	Yes	20	95.2	9	90	3	100	3	100	5	100
	No	1	4.8	1	10	0	-	0	-	0	-
	Not Answered	0	-	0	-	0	-	0	-	0	-

Question

If no, please suggest an alternative statement, or why it should not be included.

There were three responses received to this part of the question. Comments have been summarised by respondent category below:

Comments from Healthcare Professionals

HCPs commented that there is a need for labelling guidance around the timeframes for when consumers should seek advice from a healthcare professional if their symptoms persist. HCPs also commented that older populations are less likely to 'Google' this information.

Medsafe's response

Medsafe acknowledges that it would be informative for consumers to have printed advice on the medicine label on when to seek advice from a healthcare professional. However, Medsafe notes the impracticalities of giving standard advice or timeframe that would be appropriate for all consumers. Each timeframe would vary from person to person. When sold in a pharmacy, more emphasis should be placed on effective patient counselling at the point of purchase so that tailored advice is given to the individual consumer based on their medical history.

Comments from Industry

Some product labels already contain a similar statement to that effect.

Medsafe's response

Words of a similar meaning to the statements may be used and individual statements may be combined, provided the intent is not changed. A required statement for laxatives in the TGA's ARGOM is 'If symptoms persist seek medical advice'. Medsafe will adopt this statement to harmonise with the TGA requirements.

Outcome

Medsafe will change the wording to be the same as the TGA's ARGOM statement: 'If symptoms persist seek medical advice'.

6. Other Label Statements to be considered

Question

Are there any other statements relating to the harm of long-term use or overuse of stimulant laxatives that should be included on the package labelling?

Table 10: Other statements that should be included – Summary of responses

		Respondent category									
		All (n=21)		HCP (n=12)		Public (n=3)		Industry (n=3)		Other (n=3)	
Question	**Response**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Other statements	Yes	6	28.6	2	16.7	3	100	0	-	1	33.3
	No	14	66.7	9	75	0	-	0	-	2	66.7
	Not Answered	1	4.7	1	8.3	0	-	3	100	0	-

Suggestions of other Label Statements to be considered, with Medsafe responses

- 'Check with your Doctor to see if you are a suitable person to take this medicine'
- 'Use-by date or Discard date'

Medsafe response

The LSD lists specific warnings and advisory statements required for specific medicines. Medsafe acknowledges these suggestions, but believe it is out of the scope for this consultation as these apply to all OTC medicines.

The expiry date is already a requirement on the medicine labelling.

There were other suggestions made in this section of the consultation by the respondents and these have been responded to in the relevant section.

Outcome

No further statements were deemed to be required for the LSD for stimulant laxatives.

7. Proposed conditions

Question

Do you agree with the proposed conditions: 'When for oral or rectal use (except glycerol for rectal use only)'?

Agree Y/N

- Yes, n=18
- No, n= 3

Table 11: Agree with proposed conditions – Summary of responses

		Respondent category									
		All (n=21)		HCP (n=12)		Public (n=3)		Industry (n=3)		Other (n=3)	
Question	**Response**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Agree with proposed conditions	Yes	18	85.7	10	83.3	2	66.7	3	100	3	100
	No	3	14.3	2	16.7	1	33.3	0	0	0	-

Question

Do you agree with the proposed conditions? If no, please suggest alternative conditions.

There were two comments received in this section.

One was a general comment regarding the lack of clarity with the proposed condition.

The other response was not relevant to the scope of this consultation.

Please note the proposed statements do not apply to bowel cleansing preparations. This has been added to the conditions in Table 13.

8. Proposed timeframe for implementation

Question

Do you agree with the proposed implementation timeframe of 12 months following the update of the Label Statements Database on the Medsafe website?

Agree Y/N

- Yes, n=17
- No, n= 4

Table 12: Agree with proposed timeframe – Summary of responses

		Respondent category									
		All (n=21)		HCP (n=12)		Public (n=3)		Industry (n=3)		Other (n=3)	
Question	**Response**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Agree with proposed timeframe	Yes	17	81.0	11	91.7	3	100	2	66.7	1	33.3
	No	4	19.0	1	8.3	0	-	1	33.3	2	66.7

Question

If no, please suggest an alternative timeframe.

There were five responses received to this part of the question.

Comments

Most comments were supportive about the proposed implementation timeframe of 12 months. A six-month timeframe was suggested by two respondents, one respondent being a healthcare professional, the other being from 'Other'. A member of the public commented that implementation should happen at the earliest opportunity to maximise public awareness messaging.

There was one comment from Industry asking for an extension to the transition timeframe due to extended delays with supply chain and freight being experienced due to COVID-19. Many companies manufacture products overseas and import into both Australia and New Zealand. An extension to the timeframe was requested to enable a sell through of stocks and to avoid the need to recall stock in market and decrease possibility of consequential shortages.

Outcome

The usual timeframe for implementation of LSD changes is one year after the outcome is published on the Medsafe website. However, Medsafe also notes the pressures faced by the Industry in the context of a global pandemic with regards to supply chain issues, therefore Medsafe considers a timeframe of 18 months to be appropriate. The LSD will be updated on 1 September 2022. Affected products are required to have these statements by 1 March 2024.

9. Other comments related to Label Statements

Comment

There was concern about the safety of other classes of laxatives, stating that any laxative that can cause loose stools has the potential to cause electrolyte disturbances (eg, osmotic laxatives).

Medsafe's response

The aim of this consultation was to consider only stimulant laxatives. Stimulant laxatives are believed to be the most frequently abused class of laxatives which may be related to the quick action of stimulants [1]. In addition, osmotic laxatives generally have instructions to take with plenty of water.

Comment

There was concern regarding the vast number of complementary and alternative products being sold as laxative treatments which are used heavily by consumers. As these products contain sennosides and other active ingredients, thought should be given to managing this risk as well.

Medsafe's response

This comment addressed complementary and alternative products which is outside the remit of this consultation. Medsafe does not regulate the labelling for complementary and alternative products.

Comment

According to the New Zealand Medsafe Label Statements Database the 'excessive use' statement is not generally required as a warning on the outer pack in other drug classes such as dextromethorphan and pholcodine which are more likely to be associated with abuse and misuse.

Medsafe's response

Stimulant laxatives are general sale or pharmacy-only medicines and, therefore, there may be limited input from healthcare professionals at the point of purchase. The classification of dextromethorphan and pholcodine (in December 2022) as pharmacist-only medicines means that the pharmacist must be involved in the sale of these products and provide information to the consumer about how to safely use them.

[1] Roerig JL, Steffen KJ, Mitchell JE, et al. 2010. Laxative abuse: epidemiology, diagnosis and management. *Drugs* 70(12): 1487-503. DOI: 10.2165/11898640-000000000-00000.

10. Outcome: Stimulant laxative statements to be included in the Label Statements Database

Table 13 shows the conditions, statements and required time frame for implementation.

The Label Statements Database will be updated on 1 September 2022. Affected products are required to have these statements by 1 March 2024.

Table 13: Stimulant laxative statements for Label Statements Database

Medicine/Group/Class	Conditions	Statement	Required by
Stimulant laxatives Examples include: • Bisacodyl • Glycerol • Sennosides/senna • Sodium picosulfate	When for oral or rectal use (except glycerol for rectal use only). Excludes bowel cleansing preparations.	• Does not help with weight loss • Excessive use can be harmful • If symptoms persist seek medical advice	1 March 2024