SUBMISSION FOR THE RECLASSIFICATION OF SODIUM PICOSULPHATE FROM PRESCRIPTION MEDICINE TO PHARMACY MEDICINE

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Part A.

1. International non-proprietary name of the medicine

Sodium picosulphate.

2. Trade name

Dulcopearls

3. Name of company requesting reclassification

Boehringer Ingelheim (NZ) Limited

4. Dose form and strength

2.5 mg soft gel capsules.

5. Pack size and other qualifications

Various

6. Indications for which change is sought

Laxative use

7. Present classification of the medicine

Sodium picosulphate, when used as a laxative, has recently been reclassified from a Pharmacy Medicine to a Prescription Medicine

8. Classification sought

Pharmacy Medicine

9. Classification status in other countries

Boehringer Ingelheim sodium picosulphate preparations are registered and marketed in many countries worldwide. The status in key markets is as follows:

Country	Classification	Comments
Argentina	OTC	
Armenia	OTC	
Australia	OTC	General Sale
Austria	OTC	Pharmacy-Only
Belarus	OTC	
Belgium	OTC	Pharmacy-Only
Brazil	OTC	
Czech Republic	OTC	Pharmacy-Only
Denmark	OTC	General Sale
Ecuador	OTC	
Estonia	OTC	
Finland	OTC	Pharmacy-Only
Germany	OTC	Pharmacy-Only
Georgia	OTC	
Hungary	OTC	
Ireland	OTC	Pharmacy-Only
Italy	OTC	Pharmacy-Only
Korea	OTC	Pharmacy-Only
Luxembourg	OTC	
Mexico	OTC	
Netherlands	OTC	Pharmacy-Only
Norway	OTC	Pharmacy-Only
Peru	OTC	
Philippines	OTC	
Portugal	OTC	
Russia	OTC	
Slovakia	OTC	
Spain	OTC	Pharmacy-Only
Sweden	OTC	Pharmacy-Only
Switzerland	OTC	Pharmacy-Only
Ukraine	OTC	
Uruguay	OTC	
Venezuela	OTC	
UK	OTC	General Sale

10. Extent of usage in New Zealand key markets and elsewhere, and dates of original marketing consent

Country	Approval Date
New Zealand	1999
Australia	2000
Belgium	1972
Denmark	1995
Brazil	1966
Austria	1971
Netherlands	1971
Portugal	1996
Switzerland	1991
UK	1993

Worldwide sales of Boehringer Ingelheim sodium picosulphate products for the period 1 January 1993 to 1 January 1998 are:

Liquid 0.1% 82,638,823 litres

Drops 0.75% 79,178,233 litres

Tablets 2.5/5 mg 325,702,162,440

which amounts to an estimate of 295,327,621 patient years exposure.

11. Draft labelling for the proposed presentation

The draft Consumer Medicine Information and packaging are the same as that registered for the Pharmacy Medicine scheduled product.

12. Proposed warning statements if applicable

No additional warnings are proposed if reclassification to Pharmacy Medicine is approved.

13. Other products which would be affected by the proposed change

There are no other sodium picosulphate products registered in New Zealand with an indication for use solely as a laxative.

Part B.

1. Benefits to both the consumer and the public expected from the proposed change

With the recent reclassification of sodium picosulphate to Prescription Medicine patients are now faced with the need to obtain a doctor's prescription in order to obtain this laxative product. Re-instatement of a Pharmacy Medicine status would overcome this barrier to consumer awareness and access and also provide consistency of classification for laxative products.

2. Ease of self diagnosis

It is well established that constipation is a condition that can be easily recognised by patients, and does not need medical attention for diagnosis, and hence the need for laxatives to be easily accessed by patients is necessary. Nevertheless, Boehringer Ingelheim agrees that the risk of abuse is always present with any laxative. Our Company's experience, both locally and overseas, as well as data from literature reviews, do not indicate that oral sodium picosulfate products present a significant risk for laxative abuse.

3. Relevant comparative data for like compounds

World-wide use of oral dosage forms of sodium picosulfate over many years has shown that these products are very well tolerated, and safe for use by self-selection in pharmacy and on general sale. Only minor gastro-intestinal disturbances may occasionally occur. There are no significant safety concerns that warrant the scheduling of sodium picosulfate for laxative use.

Sodium picosulfate products for laxative use should continue to available for self-selection at pharmacy or general retail outlets for the convenience of all patients, especially those in remote or isolated areas. The excellent safety profile of sodium picosulfate for laxative

use strongly supports the availability of sodium picosulfate as a Pharmacy Medicine.

4. Local data or special conditions relating to New Zealand

The recommendation to change the classification of sodium picosulphate from Pharmacy Medicine to Prescription Medicine was made at the 28th meeting of the Medicines Classification Committee. This recommendation was made to foreshadow recommendation of the NDPSC. However the NDPSC did not ratify the decision and has decided to keep the general sale classification for sodium picosulphate when used as a laxative. Thus there is a great disparity of classifications for laxative use of sodium picosulphate between Australia and New Zealand.

5. Interactions with other medicines

The concomitant use of diuretics or adreno-corticosteroids may increase the risk of electrolyte imbalance if excessive doses of Dulcopearls are taken.

Electrolyte imbalance may lead to increased sensitivity to cardiac glycosides.

Concurrent administration of broad spectrum antibiotics may reduce the laxative action of Dulcopearls.

6. Contraindications

Dulcopearls are contraindicated in patients with ileus, intestinal obstruction, acute surgical abdominal conditions like acute appendicitis, acute inflammatory bowel diseases, and in severe dehydration.

Dulcopearls are also contraindicated in patients with known hypersensitivity to substances of the triarylmethane group.

7. Possible resistance

Not applicable.

8. Adverse events

Rarely, abdominal discomfort and diarrhoea have been reported,

9. Potential for abuse or misuse

Abuse

Boehringer Ingelheim accepts the possibility that any laxative may be subject to abuse by a small number of patients. Although this issue involves laxatives generally, the Periodic Safety Update Report provided in Appendix 1 indicates that there have been no reports of abuse of sodium picosulphate for laxative use.

From a recent literature review[1] of the types of abused laxatives, no cases of laxative abuse involving sodium picosulphate were reported. In regard to the dependence potential, experiments in rats[2] revealed no habituation to sodium picosulphate. After a treatment period of 75 days using up to 57 times the human therapeutic dose, a laxative effect occurred at the same dose as in untreated rats[3]. The results of animal experiments were confirmed by several clinical trials. In studies over a long treatment period, often a dose reduction could be achieved, or the initial dose was at least maintained, indicating no dependence potential.[4, 5, 6] Tests in more than 200 patients, over periods of two to four years, did not reveal any drug dependence, as cited by Bruch et al.[7]

Misuse

Boehringer Ingelheim have not received any reports of misuse of sodium picosulphate laxatives taken in the mistaken belief that it would help weight control.

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