Appendix 1

Reclassification of a Medicine for consideration by the Medicine Classification Committee

This form should be completed in conjunction with the directions in the guidance: How to change the legal classification of a medicine in New Zealand.

Once completed, this application should be sent to committees@moh.govt.nz by the deadline indicated on the Dates and Deadlines page on the Medsafe website.

By submitting this form, you are confirming that all information is true and accurate, and understand that this information and any appendices and/or supporting information that is not considered commercially confidential under the Official Information Act 1982 criteria will be published on the Medsafe website.

Part A

1. **International Non-proprietary Name of the medicine.**
   Phenol

2. **Proprietary name(s).**
   Note that this submission is being made by the Podiatrists Board of New Zealand (PBNZ), the Responsible Authority (RA) and regulator of registered podiatrists under the HPCA Act 2003 and Podiatry New Zealand, the Professional Association, not by the sponsor or supplier of a medicine in New Zealand. We are aware that there are several phenol products available internationally, such as Podopro Swab-It, Phenol EZ Swabs,

3. **Name and contact details of the company / organisation / individual requesting a reclassification.**

   Podiatrists Board of New Zealand (PBNZ).

   [redacted]. Tel: [redacted] Mobile: [redacted]

   Email: [redacted]

   Podiatry New Zealand.

   [redacted]. Tel: [redacted]

   Email: [redacted]

   Note: Contact details will be removed from the form prior to publication on the Medsafe website.

4. **Dose form(s) and strength(s) for which a change is sought.**
   As an example, for Podopro Swab-It; Each ampoule contains between 0.15 – 0.2 ml USP Phenol, which is applied using a swab. Ampoules are individually wrapped, pack size of up to 30 units.

5. **Strength**

High concentration phenol for nail chemical matrixectomy (current products available contain 89% liquid phenol).

6. **Pack size, storage conditions and other qualifications.**
   Up to 30 ampoules in each pack, to be stored below 25 Degrees Celsius.

7. **Indications for which change is sought.**
   Nail chemical matrixectomy only

8. **Present classification of the medicine.**
   Prescription; for injection.

   Pharmacy only; in medicines other than for injection containing more than 3%

   General sale; in medicines other than for injection containing 3% or less.

9. **Classification sought.**

   Prescription; for injection; except when specified elsewhere in this schedule; except when supplied in a manufacturers original pack that has received consent from the Minister or Director-General to a podiatrist registered with the Podiatrists Board of New Zealand (PBNZ), for chemical matrixectomy.

   Pharmacy only; in medicines other than for injection containing more than 3%, other than for chemical matrixectomy.

   General sale; in medicines other than for injection containing 3% or less.

10. **Classification status in other countries (especially Australia, UK, USA, Canada).**

    These products are medicines under New Zealand legislation. However, in many other regions they are medical devices, with unrestricted access:

    UK-Class IIa medical device, MHRA (April 2022), Australia- Class IIa medical device TGA,

11. **Extent of usage in New Zealand and elsewhere (eg, sales volumes) and dates of original consent to distribute.**

    Phenol in liquid form (88-89%) has been used in New Zealand for the last 40 years by podiatrists, general practitioners and surgeons and is the gold standard for the treatment of ingrown toenail with chemical matrixectomy (Andre et al, 2018) due to it's associated low rate of ingrown toenail recurrence, and its haemostatic, antiseptic and analgesic effect. Therefore, reducing the risk of infection, pain and bleeding post operatively (Shaikh et al 2008, Canedo et al 2013).

    Ref:

    Andre M-S, Caucanas M, Andre J, Richert B (2018) Treatment of Ingrown Toenails with Phenol 88% or trichloroacetic acid 100%: A comparative, prospective, randomised, double – blind study, Dermatol Surg, Vol 44 (5) pp 645-650.

    Canedo F, Sanches N, De Troya M (2013) Chemical Matricectomy with Phenol, Actas Dermosifiiogr (Spain), Vol 104 (1), pp 79-80.

Shaikh, F.M, Jafri M, Giri S.K, Keane R (2008) Efficacy of wedge resection with phenolisation in the treatment of in grown toenails, Journal Podiatric Medicine Association, Vol 98 (2), pp118-22.

12. **Local data or special considerations relating to New Zealand (if applicable).**

    As above, phenol swabs are typically considered medical devices by overseas regulators but are medicines under New Zealand legislation.

13. **Labelling or draft labelling for the proposed new presentation(s).**

    There are no phenol swab products approved in New Zealand. Labelling of any phenol swab product will be evaluated by Medsafe as part of the medicine approval process.

14. **Proposed warning statements (if applicable).**

    None required as per Medsafe label statement database.

15. **Other products containing the same active ingredient(s) and which would be affected by the proposed change.**

    The classification needs to be worded to ensure that medicines containing over 3% phenol remain pharmacy only medicines (some ear drops containing phenol are approved).

Part B

1. **Indications and dose**

   - *What is the medicine indicated for, and for which indication(s) is the reclassification application for?*

     Phenol swabs are indicated only for nail surgery – chemical matrixectomy.

   - *What is the evidence that the proposed indication is an OTC indication ie, that the diagnosis and treatment can be understood by the consumer; that the risks of inappropriate treatment can be minimised?*

     Not applicable as the product labelling should ensure that phenol swabs are only available (other than by prescription) to podiatrists registered with the Podiatrists Board of New Zealand (PBNZ). i.e., this will not be an OTC medicine.

   - *What is the treatment population for the indication (age; gender etc.)?*

     An ingrown toenail can occur at any age. There is a slightly higher male to female ratio particularly between ages 14-25 (Shaikh et al, 2008)

     The population ranges from approx. 6- 90 years but not exclusively depending on the severity of the ingrown toenail or nail plate deformity.

     Ref:

     Shaikh, F.M, Jafri M, Giri S.K, Keane R (2008) Efficacy of wedge resection with phenolisation in the treatment of in grown toenails, Journal Podiatric Medicine Association, Vol 98 (2), pp118-22.

   - *What is the dose and dose frequency of the medicine for this indication?*

The dose of the product that has commonly been used in New Zealand is 0.15 - 0.2 ml per ampoule, between 4-6 ampoules per treatment depending on the number of nails to be treated. Application to the nail bed is 2 x 1 min application using 2 swabs (1 swab per application) for optimal patient outcome (Brown, 2002). This is intended to be a one off treatment with a low rate of recurrence.

Ref: Brown J, (2002)Does phenolisation for one minuite provide the best outcome for patients undergoing matricectomy , Poster presentation, Durham School Podiatric Medicine

2. **Presentation**

- *What is the proposed dose form and strength of the medicine to be reclassified? Is this the same for all indications?*

The product that has commonly been used in New Zealand is presented as an ampoule containing 0.15 - 0.2ml 89% USP phenol, with a swab for application. The maximum pack size is 30 units.

- *What disposal considerations need to be made for the medicine?*

No special disposal considerations

- *How practical and easy to use is the proposed presentation?*

The classification proposes use by podiatrists, who are well versed in the use of these products. The Phenol swab is:

1. activated by pushing the applicator downward into the ampoule holding the liquid phenol, to allow the phenol to moisten the cotton bud.

2. carefully remove the applicator and apply phenol to nail matrix.

3. **Consumer benefits**

- *What is the history of this medicine's use for the proposed indication(s) ie, number of users; number of countries used in?*

This product (Swab-It –Podopro) use was increased in the UK following a National Patient Safety Alert (NPSA) which was issued August 2021 for the elimination of bottles of liquid phenol 80% (www.england.nhs.uk/publication/national-patient-safety-alert-elimination-of-bottles-liquified-phenol-80). The Phenol Swab-It ampoule was launched 15 years ago in the UK, and is the primary method of phenolisation after nail matrixectomy in the UK national health service and private surgeries. Also used in Australia, USA, Canada (The product is also sold in the USA under Phenol EZ swabs (89%) liquid phenol made by PediNol McKesson Specialty Health) 72 (3), pp 507-9.

- *To what extent is this medicine used for the proposed indication(s) ie, duration of use; frequency of use?*

The extent of the use: Used widely by podiatrist and GP's for the chemical ablation of the nail matrix for surgical treatment of ingrown toenails (onychocryptosis). Literature review an older and newer paper:

In 1990 Van der Ham et al compared a wedge resection and phenol cauterisation method in a randomised control trial of surgical outcomes of ingrown toenails. They looked at 249 patients. They had a follow up of 97% at 14 months. They found that the

analgesic requirement following the phenolisation was significantly lower. Recurrence rate of the surgical wedge incision was seen in 16 % and in the phenolisation group it was 9.6%.

In a recent paper by Muriel- Sanchez et al (2020) found that the surgical matrixectomy has a shorter healing time with a similar recurrence rate to the chemical matrixectomy. They looked at 34 patients (56 feet) with 112 onchocryptosis. They were randomised and 36 treated with chemical ablation of the nail bed and matrix with phenol and 76 with incisional surgical removal nail bed and matrix The primary measurements were healing time and recurrence. The incisional matrixectomy presented with shorter healing times in days (7.92-8.55 days versus 21.20-22.39 days) with similar recurrence rate to the chemical ablation. Infection rates were similar post operatively, pain was also measured which had no significant difference but was slightly less in the chemical ablation group after day 1.

A systemic review with meta-analysis of the surgical treatments of ingrown toenails in 2023 published in the Journal of Foot and Ankle Research (Exley, 2023) concluded than the use of phenol on the nail matrix reduces the risk of recurrence following nail ablation. They also reported that 1 min appears to be the optimum time for application but there is less certainly around this recommendation.

References:

Exley V, Jones K, Ocarroll G, Watson J (2023) A systematic review and meta-analysis of randomised control trails on surgical treatments for ingrown toenails part 1: recurrance and relief of symptoms, Journal of Foot and Ankle Research, pp 3-19.

Muriel- Sanchez J.M et al (2020) The treatment of Ingrown toenail: Chemical Matrixectomy with phenol versus Aesthetic Reconstruction. A single Blinded Randomised Clinical Trail, Journal Clinical Medicine,Vol 9 , pp 845.

Van de Ham A.C, Hackeng C.A, Yo T.I (1990) The treatment of ingrown toenails. A randomised comparison of wedge excision and phenol cauterisation. Journal Bone and Joint Surgery (British) Vol.

There are multiple papers in the literature evidencing excellent patient outcomes following the use of phenol for chemical matrixectomy for the treatment of ingrown toenails

- *What is the evidence that improved access is beneficial for the individual?*

It has been reported that 20% of patients that report to their GP with foot problems have an ingrown toenail (Heidelbaugh and Lee, 2009).

Currently patients have to get a prescription from their GP under a section 29 exemption and take the product to their podiatrists for use, which is logistically very difficult.

Ref:

Heidelbaugh JJ, Lee H (2009) Management of ingrown toenails, American Family Physician, Vol 79, pp 303-8.

- *What is the evidence of improved consumer involvement in their health?*

There are multiple papers in the literature evidencing excellent patient outcomes following the use of phenol for chemical matrixectomy for the treatment of ingrown toenails.

- *What are the benefits from a consumer viewpoint?*

Benefits from a patient (consumer stand) point is that patients will be able to have an effective, safe and relatively noninvasive treatment for their painful ingrown toenails which will improve quality of life.

Currently patients have to get a prescription from their GP under a section 29 exemption and take the product to their podiatrists for use, which is logistically very difficult.

4. **Contraindications and precautions**

- *Precautions: What are the contraindications for the medicine and how easy are they to identify and prevent?*

Contraindications: poor blood supply to the digit, (peripheral vascular disease), diabetics with active foot ulcers

Relative contraindications: pregnancy, paediatrics under 6 years, soft tissue hypertrophy, complex regional pain syndrome.

The Swab-It labelling also includes a warning 'not to be used by patients with diabetes or circulation issues, in particular those patients with diabetic foot ulcers'.

The clinician will make their clinical judgment through a thorough and extensive history and assessment of the patient prior to nail surgery with phenolisation of the nail matrix.

Precautions: handing of phenol by the clinician, to prevent spillage on the clinician / and the patient. Use only in a well-ventilated area.

- *Does the medicine have a low therapeutic index?*

No.

- *What are the precautions for this medicine and how easy are these to understand?*

Precautions – primarily in handling.

- The use of the Swab-It phenol ampoules reducing the risk of spillage,
- excessive application of phenol as the phenol is only contained in the swab,
- fumes are reduced due to single ampoule design,
- leakage is reduced as each ampoule is located within a single foil pouch and is single use,
- after use the swab is put back in the ampoule to be disposed of.

- *What class effects need to be considered and what are the risks?*

None.

- *What are the risks of the medicine being used in an OTC environment?*

The classification will ensure access to podiatrists, who are trained in its use (no consumer access).

- *What other drug interactions need to be considered?*

None known with this topical application to the nail matrix.

- *What food and/or drink interactions need to be considered?*

None known with this topical application to the nail matrix.

- *Are there any other restrictions when taking the medicine i.e., driving restrictions or operating machinery?*

None.

- *Are there any special populations where exposure to the medicine needs to be restricted?*

None.

5. **Undesirable effects**

What are the known undesirable effects and the frequencies of these? Do these vary for special populations?

- *What are the risks and consequences of known undesirable effects?*

Phenol irritation/burn to the skin. To mitigate this effect isopropyl alcohol is sometimes used to dilute the phenol after its full application time and aids in its removal (Cordoba et al, 2012).

Not all clinicians do this, and it's not indicated as an instruction of use for the Swab-It product.

Ref: Cordoba D.D, Losa I, Cordoba D.M, Beccerro de Bengoa V.R (2012) Enhanced removal of phenol with saline solution over alcohol and in vitro study, dermatol Surg, Vol 38 (8), pp 1296-1301.

Risks consequences: phenol burns can occur due to spillage to the surrounding skin. The risk of spillage is reduced with the use of the Swab-It as it is contained within the ampoule.

- *Are there any significant safety concerns for the medicine under review?*

No safely concerns known by the submitters (not the product sponsor).

- *Have there ever been any withdrawals of the medicine or other regulatory actions taken for safety reasons (during a time period or in a specific jurisdiction)?*

No withdrawals known by the submitters (not the product sponsor).

- *Are there any withdrawal effects following cessation of use of the medicine?*

Not applicable (topical, single use product).

6. **Overdose**

- *Is there a potential for overdose of the medicine?*

- *What are the consequences of overdose of the medicine?*

- *Are there any reports of overdose of the medicine?*

None.

7. **Medication errors and abuse/misuse potential**

- *Would reclassification affect the risk of unnecessary use?*

In principle, classification would improve access to podiatrists. However, this product has been used by podiatrists for many years (there has been a misunderstanding in the sector that this is a medical device), this is not a new medicine to podiatrists and there is not expected to be an increase in unnecessary use compared to historical use.

- *Is the medicine provided with necessary tools to allow correct dosing eg, liquids supplied with a measuring device?*

The Swab-It comes with pre-loaded dosages in each ampoule 0.15 - 0.20 ml, so no other measuring device would be needed and there is consistency in dosage of each ampoule.

- *What are the reported medication errors post-market?*

No medication errors post market known to the submitters. Note that the submitters are the Podiatrists Board of New Zealand (PBNZ), who regulate podiatrists under the HPCA Act 2003 and the Professional Association, Podiatry NZ, who would be well aware of medication errors.

- *What are the reported cases of abuse/misuse/accidental overdose?*

Reported cases of abuse or misuse or accidental overdose – none with Swab-It to date.

- *How would reclassification affect import considerations?*

Classification statement should ensure that only approved medicines should be able to be accessed by podiatrists (i.e., include 'supplied in a manufacturers original pack that has received consent from the Minister of Health).

- *What is the addiction potential of the medicine?*

None.

8. **Communal harm and / or benefit**

Not applicable

- *What are the possibilities of community harm resulting from wider use of the medicine in question (e.g., the development of antibiotic resistance in bacteria or increased immunisation rates)?*

Not applicable.

- *What are the possibilities of community benefit resulting from wider use of the medicine in question (eg, greater herd immunity as a result of improved access to a communicable disease vaccine)?*

Not applicable.

9. **Integrated benefit-risk statement**

- *A summary of the reclassification benefits*
- *A summary of the reclassification risk of harm*
- *A summary of the need for the medicine at the classification proposed*
- *Precedent – how are other medicines in the same class classified?*

Benefit considerations of the reclassification of liquid phenol (Swab-It ampoules) for the treatment of ingrown toenails include improved access to registered podiatrists in New Zealand to perform this important procedure. This will enable podiatrists to improve clinical outcomes for their patients who suffer from ingrown toenails. This procedure reduces the risk of potential prolonged infection for the patient with the offending ingrown nail therefore the need for antibiotics (increasing risk of antibiotic resistance), and an appointment to the GP. In severe cases it may cause severe infection (sepsis) requiring a hospital stay. See Benefit risk assessment **–** value tree framework (separate document).

Other medicines are currently classified to enable access to podiatrists, e.g.:

1193:
Lignocaine; for injection except when used as a local anaesthetic in practice by a nurse whose scope of practice permits the performance of general nursing functions or by a podiatrist registered with the Podiatrists Board or by a dental therapist or oral health therapist registered with the Dental Council; for ophthalmic use except when used in practice by an optometrist registered with the Optometrists and Dispensing Opticians Board; for oral use except in throat lozenges in medicines containing 30 milligrams or less per dose form; for external use in medicines containing more than 10%; except in throat sprays in medicines containing 2% or less; except when specified elsewhere in this schedule.

10. **Risk mitigating strategies.**

- *Are there any risk mitigation strategies required? If so, what ris mitigation strategies are required eg, healthcare professional education; integration of care; consumer information to be provided etc?*

Risk mitigating strategies include:

1) Education videos and seminars for podiatrists on how to use the Swab-It product safely and effectively.

2) Thorough, clear medical history and physical assessment (which is standard) of each patient preoperatively to assess suitability for nail surgery with chemical matrixectomy with Swab-It ampoules.

3) Clear preoperative information sheets and verbal explanation for patients with risks and benefits of nail surgery with chemical matrixectomy with Swab-It ampoules so they can make an informed decision and consent to their treatment.

4) Use of mupirocin or petrolatum (vaseline) to protect surrounding skin from phenol burn if there was a perceived risk.

- *What is the evidence that these proposed risk mitigation strategies would be effective?*

There is a long history of safe use of this product in New Zealand.

- *What post-market surveillance activities would be carried out?*

No additional activities.

Is the proposed reclassification supported by professional bodies?

The proposed reclassification is supported by the Podiatrists Board of New Zealand (PBNZ), Podiatry New Zealand, the Royal New Zealand College of General Practitioners (RNZCGP).