Nifedipine for the treatment of chilblains

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Rationale for compounding nifedipine

Chilblains (perniosis) are an inflammatory condition affecting the extremities. Symptoms include erythema, pruritus, and ulceration; they may be acute or chronic.1

Chilblains are common in cold, damp and windy conditions (wind can increase the cold conductivity).1,2 They are more common in women, people with low body mass and in patients with impaired peripheral circulation, including people with diabetes.2 The lesions present as itchy and painful erythematous purple coloured swellings. They may resolve spontaneously in two to three weeks, but in severely affected patients chilblains may be present throughout the winter and summer and may blister or ulcerate.3

Chilblains do not generally require specific treatment; protection from the cold, smoking cessation, or symptomatic antipruritic treatment (e.g. topical corticosteroids) are often sufficient.1 However, if severe, oral nifedipine has been shown to be effective,3-6 and a 20 mg controlled-release daily dose is generally used.1,2 Oral nifedipine is also the first choice if drug therapy is needed for another vasospastic condition, namely Raynaud’s phenomenon.1,2

The Therapeutic Guidelines also recommend using glyceryl trinitrate 0.2% ointment sparingly topically, once daily initially then titrated to response, for the treatment of chilblains.2 It is suggested that the proprietary product Rectogesic can be used for this indication.2 Rectogesic ointment contains 0.2% glyceryl trinitrate in a base of liquid paraffin, soft yellow paraffin, lanolin and ethanol7 and is used for the treatment and relief of symptoms of anal fissure, to relieve pain and discomfort and assist in wound healing following haemorrhoid surgery7 and thus would not be the most appropriate base to apply to the hands or feet.

Nifedipine applied topically to the affected site would be beneficial in reducing the undesirable systemic side effects associated with the oral
Excipients and formulation considerations

The above preparation (Figure 1) is an example of a nifedipine-containing topically applied preparation. The excipients for this preparation are detailed below. The pharmacist, in consultation with the prescriber, may decide on the use of other bases to meet the requirements of the patient.

**Diethylene glycol monoethyl ether** \((C_{17}H_{18}O_2, MW 134.2)\) is also known as ethoxy diglycol or 2-(2-ethoxyethoxy) ethanol. It is a clear, colourless, hygroscopic liquid\(^{12}\) and is used as a solvent. It is miscible with water, with acetone and with alcohol, miscible in certain proportions with vegetable oils, and not miscible with mineral oils.\(^{12}\)

**Lecithin:** **isopropyl palmitate solution** is a commercially available product and consists of a mixture of lecithin and isopropyl palmitate.

**Lecithin** is a complex mixture of acetone-insoluble phosphatides combined with various amounts of other substances such as triglycerides, fatty acids, and carbohydrates.\(^{1}\) The composition of lecithin, and hence also its physical properties, varies enormously depending upon the source of the lecithin (e.g. egg, soybean) and the degree of purification.\(^{13}\) Lecithin is an emulsifying and stabilising agent used in both the pharmaceutical and the food industries.\(^{1}\)**Isopropyl palmitate** \((C_{19}H_{38}O_2, MW 298.51)\) is a clear, colourless to pale yellow-coloured, practically odourless viscous liquid that solidifies at less than 16°C.\(^{13}\)

It is a non-greasy emollient with good spreading characteristics.\(^{13}\) It is insoluble in water, glycerol, and propylene glycol, and is soluble in alcohol, acetone, castor oil, cottonseed oil and liquid paraffin.\(^{1}\)

**Pluronic 20% gel** is a commercially available product that consists of **poloxamer 407** (also known as **pluronic F127**). The poloxamer polyols are a series of closely related block copolymers of ethylene oxide and propylene oxide.\(^{1,13}\) Poloxamers are used primarily in pharmaceutical formulations as emulsifying or solubilising agents.\(^{13}\) They are used as gelling agents at concentrations of 15 to 50%.\(^{13}\) Poloxamer 407 is freely soluble in water, in alcohol, and in isopropyl alcohol.\(^{1}\) Poloxamer 407 displays thermoreversible properties.
It is important to remember that pluronic 20% gel has a temperature-dependent viscosity, whereby it thickens when heated, becoming less viscous on cooling. Patients may notice that as the preparation is rubbed into the skin and warms up, it may become slightly more viscous and resistant to rubbing.

Packaging and storage
Since nifedipine undergoes photodegradation when exposed to light, it is important that the packaging provides adequate protection from light. Packaging the product into light-resistant (amber) syringes will protect the API and provide a mechanism for accurately measuring a dose. A variety of other packaging options are available including amber glass ointment jars or plastic tubes combined with an appropriate measuring device. Contact your local supplier for packaging options. Patients may also have a preference for a particular packaging type. It is important that patients are counselled on the use, accurate measurement of dose and appropriate disposal of the packaging. The formulation should be stored in a cool, dry place out of reach of children and pets.

Labelling
Compounded products are to be labelled according to regulatory requirements and should include the approved pharmacopoeial name (where applicable) and the name and strength of any preservatives used. All active ingredients and their amounts/proportions should be included if the preparation is not a pharmacopoeial formulation. Ancillary labels should be used to indicate specific storage conditions, provide an expiry date and indicate specific usage conditions. Suitable labels to indicate internal or external use, such as Label K FOR EXTERNAL USE ONLY, should be included.

Counselling/instructions for patients
In the preparation of compounded products, the pharmacist should be guided by the professional standards, the prescriber and the needs of the patient. Patient counselling and education may be adapted from CMIs available for commercially available products. Essential information would include:

Directions for use
- Wash your hands well with soap and water before opening any packaging.
- Instructions on how to open the packaging, accurately measure a dose, and correct use of the applicator.
- Spread a thin layer onto clean, dry skin.
- Instructions on how to store the product and to dispose of any applicators or packaging.

Special precautions
- Pharmacists should consider the precautions and adverse effects for oral nifedipine.
- Patients should also be counselled to advise their prescriber should they experience systemic side effects including facial flushing, headache, nausea, tachycardia, dizziness, hypotension and peripheral oedema.

Non-pharmacological support
Patients should be encouraged to create a favourable environment by:
- keeping hands and feet warm by wearing warm but not tight clothing;
- avoiding tight fitting socks and shoes;
- avoiding rapid changes in temperature, especially when warming feet after being in the cold (i.e. warm feet slowly);
- being strongly advised to cease smoking; and
- regularly exercising to improve circulation and consuming a healthy diet, including avoiding alcohol before going out in the cold weather.

Key learning points
- Pharmacists, in consultation with doctors, may decide on the use of various bases to be used for the topical application of nifedipine to meet the specific requirements of the patient.
- Pharmacists should take care in preparing nifedipine topical products extemporaneously and avoid exposure to light as nifedipine degrades readily. In order to prevent this degradation, work as quickly as possible and switch off fluorescent lights in the pharmacy.
- Pharmacists should counsel patients on the appropriate storage of these products and on their use, especially related to potential temperature-induced changes related to the use of pluronic 20% gel as a base.

References
Continuing Professional Development

Questions

1. **Rectogesic** ointment can be used topically for the treatment of chilblains because it contains:
   a) betamethasone dipropionate.
   b) nifedipine.
   c) glyceryl trinitrate.
   d) triamcinolone acetonide.
   e) betamethasone valerate.

2. Nifedipine (1%) in PLO Gel should be stored under the following conditions:
   a) protected from light.
   b) above 30°C.
   c) cool moist place.
   d) a and c.
   e) a, b and c.

3. The role of the lecithin in the nifedipine (1%) in PLO Gel is as a:
   a) gelling agent.
   b) preservative.
   c) solubiliser.
   d) co-solvent.
   e) emulsifier.

4. The following statement(s) about topical nifedipine in PLO gel for the treatment of chilblains is/are FALSE:
   a) Topically applied nifedipine to the affected site would be less beneficial in reducing the undesirable systemic side effects associated with the oral nifedipine.
   b) Crushed commercially available nifedipine tablets should be used to make this product.

5. Pluronic lecithin organogel may be used as a base for the topical application of drugs and as such it contains _________ as a gelling agent.
   a) Diethylene glycol monoethyl ether.
   b) Lecithin.
   c) Isopropyl palmitate.
   d) Poloxamer 407.
   e) 2-(2-Ethoxyethoxy)ethanol.

National Registration and Accreditation Scheme

The introduction of the National Registration and Accreditation Scheme on 1 July 2010 had a marked impact on the registration procedures for pharmacists.

Not surprisingly, the implementation of the scheme caused huge problems as the demand for registration far exceeded expectations with the result that many professionals were left hanging for months awaiting the right to practice. This led to a Senate Committee investigation, at which PSA gave evidence, whose findings were far from complimentary as to how the system was put into place. Even 12 months later problems persisted, albeit to a far less degree, and PSA moved to try to help pharmacists negotiate the process with at least stress as possible.

The new Pharmacy Board of Australia has quickly demonstrated a clear objective of improving professional standards. Its introduction of mandatory levels of continuing education to be completed for reregistration is a watermark initiative which will bring Australia up to date with most of the Western world.

As the Pharmacy Board audits compliance with CPD requirements annually, PSA decided to open its CPD points recording system to all pharmacists, even those not yet members of the Society. We felt it was in the best interests of the profession as a whole to enable all pharmacists, whether members or non-members, to utilise the specially designed PSA tool for to record their points. PSA is also working hard to ensure its position as the premier provider of CPD throughout Australia is strengthened through the provision of a wide variety of quality and practical programs able to be accessed by all members.

So it certainly has been an exciting and productive three years as PSA President – three years that have seen wins and losses, achievements and frustrations. I have been honoured to have had a strong and supportive Board, and the commitment and support of the PSA secretariat and staff. But most importantly, I have been guided by the strength, commitment and dedication to the profession of pharmacy of you, our PSA members. I hope this will be further rewarded in the years ahead.

‘The President says’, continued from page 610.

This Consultation Draft Vision for Pharmacists’ Practice in Australia has been issued to the pharmacy profession for its consideration and feedback and comment has also been sought from each of the 11 participating pharmacy organisation in order to ensure that the Vision guides and informs future practice and that it is embraced by all pharmacists.

For its part PSA has long advocated the need to change the product supply focus of the current business model that has operated successfully in community pharmacy for more than 50 years to one based more on service delivery of professional services and the need to change the product supply focus of the current business model. As a consequence, PSA has been designing how such a model may be delivered successfully in practice and therefore source the required income streams to make it work and develop the necessary tools to help facilitate the practice change. I am confident that this will become a major activity in support of our membership in the years ahead.

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