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PrescQIPP Community Interest Company

Rubefacients and miscellaneous topical analgesics

This bulletin focuses on rubefacients and other miscellaneous topical analgesics (benzydamine, mucopolysaccharide polysulphate and cooling gels/sprays) for the treatment of soft-tissue disorders and topical pain relief. It provides the rationale for discontinuing supply of such products on NHS FP10/GP10/WP10 prescriptions. In England, Scotland and Wales in excess of £2.5 million is spent annually on these products. Medicines optimisation projects in this area focus on discontinuing rubefacient and miscellaneous topical analgesic treatments that are not supported by clinical evidence, and where appropriate, offering an evidence-based alternative with self care if appropriate.

The recommendations in this bulletin do not apply to the prescribing of rubefacients for relieving muscle pain associated with methadone withdrawal or the prescribing of topical non-steroidal anti-inflammatory drugs (NSAIDs) or capsaicin cream.

Recommendations

- People prescribed rubefacients and miscellaneous topical analgesics (benzydamine, mucopolysaccharide polysulphate and cooling gels/sprays) should have their therapy reviewed.
- Discontinue prescribing these products on FP10/GP10/WP10.
- Provide people with information about the reasons behind this change i.e. the lack of clinical evidence that they are effective.
- Do not automatically substitute with topical NSAID preparations.
- Ensure that people with ongoing symptoms have the opportunity to have a review to discuss alternative management options that are based on the best available evidence and the latest guidance.
- If people still wish to use a rubefacient (or one of the specified miscellaneous products), they should be advised that they can purchase an over-the-counter (OTC) product as self care with the support of the community pharmacist.
- Do not initiate new prescriptions for these products.
- No routine exceptions have been identified.

Background

A wide range of topical pain relief products are available. They contain a variety of substances which are proposed to relieve local pain via several different mechanisms.[1] The evidence base for these products differ, so it is important they are sub-grouped (which in some cases is not straightforward) rather than considered as a single homogenous category of 'topical pain relief'. Product types include:

- Rubefacients
- Capsaicin cream
- Topical NSAIDs[2,3]
- Local anaesthetics
- Miscellaneous products: benzydamine, mucopolysaccharide polysulphate and cooling gels/sprays.[2,3]

This bulletin focuses on rubefacients and the miscellaneous products benzydamine, mucopolysaccharide polysulphate and cooling gels/sprays. The other groups are discussed briefly to provide context.

Rubefacients are topical preparations intended to relieve local pain in muscles, joints and tendons. Their application causes hyperaemia (redness due to the dilation of blood vessels) or irritation of the skin, which is associated with a soothing feeling of warmth. It is proposed that they work as a counter-irritant, helping to inhibit the transmission of pain signals.[1,4] Topical rubefacient preparations may contain nicotinate and salicylate compounds, essential oils, and camphor.[5] Despite their relation to aspirin and NSAIDs, salicylate-based products are classified as rubefacients rather than NSAIDs as their mode of action topically is considered to be counter-irritation rather than inhibition of cyclooxygenase (COX) enzymes. Furthermore, there are important differences in the clinical evidence base for these different groups.[4]

Topical capsaicin (the active component of chilli peppers)[4] may also be referred to as a rubefacient.[5] However, topical capsaicin is thought to have a different mode of action to counter-irritant rubefacients, which does not rely on vasodilation of the skin.[1] The recommendations of this bulletin regarding rubefacients do not apply to topical capsaicin products as the evidence base for them differs.

Topical non-steroidal anti-inflammatory drugs (NSAIDs) are a further, distinct group of pain relief preparations. The rationale for their use is based on the ability of NSAIDs to inhibit the cyclooxygenase enzymes (COX-1 and COX-2) locally and peripherally, with minimum systemic uptake.[4] Inhibition of COX enzymes results in inhibition of prostaglandin synthesis, which is largely responsible for the therapeutic effects of NSAIDs.[6,7]

Local anaesthetics such as lidocaine plasters have also been used for topical pain relief and may be helpful for some people with post-herpetic neuralgia. See PrescQIPP Bulletin B200 Lidocaine plasters for further information.

Miscellaneous products that do not fit precisely into other groups include benzydamine, mucopolysaccharide polysulphate and cooling gels/sprays.

- Although benzydamine can be classed as an NSAID, it has activities which differ from those of the aspirin-like NSAIDs and is only a weak inhibitor of prostaglandin synthesis. Benzydamine is contained in Difflam® cream.[8]
- Mucopolysaccharide polysulphate is described as a non-steroidal drug with anti-inflammatory activity however, it only has a weak inhibitory effect on prostaglandin E2 synthesis based on in vitro studies. Mucopolysaccharide polysulphate is an ingredient in Movelat® products, along with salicylic acid*.[9]

Both drugs are therefore pharmacologically different from those routinely referred to as NSAIDs in current practice (such as ibuprofen and diclofenac). So, it cannot be presumed that the clinical evidence relating to NSAIDs can be extrapolated to benzydamine or mucopolysaccharide polysulphate containing products.

*Information pertaining to salicylate-containing rubefacients is therefore also applicable to Movelat® products.

- Cooling gels and sprays are promoted for application to joints or muscles for soothing/cooling relief, including after injury.[10]

National guidance

NHS England have published guidance for CCGs on items which should not be routinely prescribed in primary care (link). Rubefacients (excluding topical NSAIDs and capsaicin) are included as items that should not be initiated for new patients, and which prescribers should be supported in deprescribing.[11] Similar guidance has been issued in NHS Wales (link).[12] Note that lidocaine plasters are also included in this guidance.[11,13]

NHS England have also published guidance about reducing the prescribing of medicines or treatments that are available to buy over the counter (OTC) without the need to see a doctor (link).[14] It advises that medicines available to buy OTC should not be prescribed for certain conditions, including minor conditions associated with pain, discomfort and/fever (e.g. aches, sprains and back pain). The guidance is therefore relevant to any topical analgesic that is available OTC. There are some exceptions, meaning that prescribing is still appropriate for some people. This includes where treatment is for a long-term condition, where there is greater clinical complexity, or where the person's ability to self care is significantly compromised.[14] This guidance does not apply in Wales, where similar proposals have been rejected.[15] This guidance also does not apply in Scotland or Northern Ireland.

NICE guidance on the management of osteoarthritis states that rubefacients should not be offered as a treatment, as the evidence base does not support their use[16] (see 'Clinical effectiveness' below). This is a NICE 'do not do' recommendation.

Topical NSAIDs and topical capsaicin are both options that can be considered as an adjunct to core treatments for knee or hand osteoarthritis. Core treatments are as follows, and should be discussed with all people with clinical osteoarthritis:

- Access to appropriate information
- Activity and exercise
- Interventions to achieve weight loss if the person is overweight or obese.[16]

Local heat or cold should be considered as an adjunct to core treatments.[16]

SIGN guideline 136 for management of chronic pain states that rubefacients should be considered for the treatment of pain in patients with musculoskeletal conditions if other pharmacological therapies have been ineffective.[17] However, this is based on a Cochrane review, which has since been updated. Although the findings of the review have not changed, the latest version is more cautious in its interpretation of the results. The authors state that evidence does not support salicylate-containing rubefacients for chronic conditions, or for acute injuries (see 'Clinical effectiveness' below).[18]

The Clinical Knowledge Summary on sprains and strains suggests advising on initial 'PRICE' (Protection, Rest, Ice, Compression, Elevation) self-management strategies for the first 48–72 hours after injury. It refers to the careful application of ice wrapped in a damp towel for limited time periods. The recommendation is pragmatic, and it is acknowledged that insufficient evidence is available to determine efficacy. Cooling sprays and gels are not discussed.[19]

Some rubefacient preparations are also listed in Part XVIIIA of the Drug Tariff - Drugs, Medicines and Other Substances not to be ordered under a General Medical Services Contract. Examples include a number of Mentholatum® products: Mentholatum® Balm; Mentholatum® Deep Freeze Spray; Mentholatum® Deep Heat Massage Liniment; Mentholatum® Deep Heat Maximum Strength Rub; Mentholatum® Deep Heat Rub and Ralgex® Cream. These are not permitted on FP10/WP10 and will not be reimbursed by the NHS Prescription Services.[20]

Clinical effectiveness

A number of systematic reviews have considered topical analgesia, including rubefacients, for acute and chronic pain. They generally agree that the available evidence does not support the use of rubefacients (excluding capsaicin).[18,21,22] One older systematic review concluded that topically applied rubefacients may be efficacious in treating acute pain. However, estimates for the efficacy of rubefacients were unreliable because of a lack of good clinical trials.[2]

A Cochrane review published in 2014 investigated salicylate-containing rubefacients for acute and chronic musculoskeletal pain in adults.[18] Six placebo-controlled and one active controlled studies were included for acute pain (n=560 and 137, respectively), and seven placebo-controlled and three active-controlled studies were included for chronic pain (n=489 and 182, respectively). All studies were

potentially at risk of bias, with the greatest risk of bias coming from small study size. The formulations of the interventions varied widely across the studies. All included a salicylate, but additional components were also present, including mucopolysaccharide polysulphate in three of the studies. For both acute and chronic painful conditions any evidence of efficacy came from the older, smaller studies, while the larger, more recent studies showed no effect. The authors concluded that the evidence does not support the use of topical rubefacients containing salicylates for acute injuries or chronic conditions.

For their guideline on osteoarthritis, NICE included four RCTs on topical rubefacients, all of which investigated salicylate-containing products. They concluded that the evidence base does not support the use of rubefacients.[16] A surveillance review of this guideline in 2017 did not include any new evidence relating to rubefacients.[23]

A further Cochrane review on topical NSAIDs for acute musculoskeletal pain is also of interest, as three of the 61 studies included related to topical benzydamine (the active ingredient in Difflam® cream). The review found that, whilst a number of topical NSAID formulations demonstrated significantly higher rates of clinical success than placebo, benzydamine did not.[24]

In relation to local heat and cold therapy in osteoarthritis, NICE found the evidence to be scarce. Only evidence relating to cold therapy (in the form of ice massage, cold packs and liquid nitrogen cryotherapy) was found. No evidence relating to cooling sprays or gels was included. The guideline development group felt that local heat and cold are widely used as part of self-management, sometimes as packs or massage, or simply in the form of people using hot baths. Due to the very low cost and safety of such interventions, they felt that a positive recommendation was justified, despite the scarcity of evidence.[16]

Benefits to patients

Reviewing the treatment of people prescribed rubefacients provides an opportunity to review their symptoms and management.

Explain to people that there is a lack of supporting evidence for rubefacients and that they will no longer be prescribed on FP10. This should include miscellaneous products containing benzydamine or mucopolysaccharide polysulphate and cooling sprays/gels. These products are more difficult to categorise, but there is similarly a lack of clinical evidence to support their efficacy.

People wishing to continue using a rubefacient can be advised to purchase a product over the counter. However, for people with troublesome ongoing symptoms it may be more appropriate to arrange a review to discuss personalised management options that are based on the best available evidence and the latest guidance.

People wishing to use thermotherapy for osteoarthritis or sprains and strains should be advised how to do so appropriately and safely. Resources for patients include:

Information on the Patient website about the use of heat and ice treatment for pain. This includes practical information on how to apply such therapies and precautions (including when not to use such treatments).

Information for the public from NICE on Osteoarthritis. This includes information about why rubefacients should not be offered as a treatment.

Costs and savings

There are many different rubefacients on the market and the products vary widely in both composition and cost. Table 1 includes some examples of common branded rubefacients and miscellaneous products (containing benzydamine or mucopolysaccharide polysulphate, and cooling sprays/gels). It lists the ingredients, costs and a calculated price per 30g or 30ml for each product.

Table 1: Examples of common branded rubefacients and other miscellaneous topical analgesics (containing benzydamine or mucopolysaccharide polysulphate, and cooling sprays/gels)

GSL= General sales List, P = Pharmacy only, MD = Medical device

Product	Content/generic name[25]	Legal category[25]	Size and retail price[25]	Price to the patient for 30g/30ml
Algesal® cream	Diethylamine salicylate 10% w/w cream	P	50g = £2.69	£1.61
			100g = £5.39	£1.62
Balmosa® Cream	Menthol 2%, methyl salicylate 4%, camphor 4%, capsicum oleoresin 0.035%	GSL	40g = £2.99	£2.24
Bell's Muscle Rub	Cajuput oil 0.12% v/w, eucalyptus oil 1.00% v/w, levomenthol 0.5% w/w, methyl salicylate 9.12% v/w[26]	GSL	40g = £2.31	£1.73
Deep Freeze® Cold Gel	Denatured ethanol, purified water, propylene glycol, peppermint oil, diisopropanolamine, carbomer[27]	MD	35g = £2.49	£2.13
			100g = £4.99	£1.50
Deep Freeze® Cold Spray	n-pentane, isobutane/propane/n-butane, peppermint oil, denatured ethanol[27]	MD	150ml = £4.25	£0.85
Deep Heat® Heat Rub	Eucalyptus oil 1.97% w/w, menthol 5.91% w/w, methyl salicylate 12.8% w/w, turpentine oil 1.47%	GSL	35g = £2.59	£2.22
			67g = £3.89	£1.74
			100g = £5.19	£1.56
Deep Heat® Heat Spray	Ethyl salicylate 5%, hydroxyethyl salicylate 5%, methyl nicotinate 1.6%, methyl salicylate 1.0%	GSL	150ml = £5.25	£1.05
Deep Heat® Max Strength	Menthol 8%, methyl salicylate 30%	GSL	35g = £4.79	£4.11
Difflam® 3% cream/ Difflam®-P 3% cream	Benzydamine 3% w/w	P	35g = £5.10	£4.37
			100g = £13.23	£3.97
Mentholatum® Vapour Rub	Camphor 9%, menthol 1.35%, methyl salicylate 0.33%	GSL	30g = £2.65	£2.65
Movelat® cream	Mucopolysaccharide polysulphate 0.2% w/w, salicylic acid 2.0% w/w[9]	P	125g - price range £10 to £12 from various retailers	-
Movelat® gel	Mucopolysaccharide polysulphate 0.2% w/w, salicylic acid 2.0% w/w	P	125g - price range £10 to £12 from various retailers	-
Movelat® Relief cream	Mucopolysaccharide polysulphate 0.2% w/w, salicylic acid 2.0% w/w	P	40g = £4.62	£3.47
			80g = £7.36	£2.76

Product	Content/generic name[25]	Legal category[25]	Size and retail price[25]	Price to the patient for 30g/30ml
Movelat® Relief gel	Mucopolysaccharide polysulphate 0.2% w/w, salicylic acid 2.0% w/w	P	40g = £4.62	£3.47
			80g = £7.36	£2.76
Radian® B Muscle Lotion	Levomenthol 1.4% w/v, racemic camphor 0.6% w/v, acetylsalicylic acid 1.2% w/v, equivalent to ammonium salicylate 1.0% w/v, methyl salicylate 0.6% w/v, equivalent to salicylic acid 0.54% w/v (as methyl and ethyl esters)[28]	GSL	125ml = £3.59 250ml = £5.65	£0.86 £0.68
Radian® B Muscle Pain Relief Spray	Ammonium salicylate 1%, camphor 0.6%, menthol 1.4%, salicylic acid 0.54%	GSL	100ml = £2.85	£0.86
Radian® B Muscle Rub	Camphor 1.43%, menthol 2.54%, methyl salicylate 0.42%	GSL	40g = £2.35	£1.76
			100g = £3.99	£1.20

In England, Scotland and Wales in excess of £2.5 million is spent annually (NHSBSA February to April 2021 and Public Health Scotland January to March 2021) on rubefacients and miscellaneous products (containing benzydamine or mucopolysaccharide polysulphate, and cooling sprays/gels).

The breakdown of the annual spend in England, Scotland and Wales is set out in the table below.

Product	England (NHSBSA February to April 2021)	Scotland (Public Health Scotland Jan to March 2021)	Wales (NHSBSA February to April 2021)
Benzydramine	£9,964	£1,526	£644
Cooling products	£1,692	£12	£0
Mucopolysaccharide	£1,519,608	£207,516	£118,792
Rubefacients	£516,576	£63,688	£35,044
Total	£2,047,840	£272,736	£154,480

Compared to the same period in the previous year, the overall spend is 12% lower. This may reflect changing prescribing practices in response to the publication of NHS England guidance highlighting the lack of evidence supporting the efficacy of these products.

It is hoped that this trend of reducing rubefacient prescribing will continue, releasing further cost savings for the NHS which could be invested in evidence-based treatments and services.

A further 80% reduction in the prescribing of these products could release savings of approximately to £1.8 million across England, Scotland and Wales. This equates to £2,606 per 100,000 patients.

Summary

Rubefacients are topical preparations intended to relieve local pain in muscles, joints and tendons by counter-irritation.[1] The body of evidence for these products does not support their use.[16,18] They are therefore not recommended as a treatment option for osteoarthritis[16] or for prescribing in general.[11] Other miscellaneous topical analgesics containing benzydamine,[24] mucopolysaccharide polysulphate[18] or cooling ingredients also lack a robust clinical evidence base and should not be prescribed.

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Additional PrescQIPP resources

Briefing	https://www.prescqipp.info/our-resources/bulletins/bulletin-287-rubefacients/
Implementation tools	
Data pack	https://data.prescqipp.info/views/B287_Rubefacients/FrontPage?:iid=1&:isGuestRedirectFromVizportal=y&:embed=y

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