



# **Topical steroid withdrawal reactions: a review of the evidence**

MHRA Public Assessment Report  
September 2021

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# 1. Plain language summary

## Key message

The Medicines and Healthcare products Regulatory Agency (MHRA) and the [Commission on Human Medicines](#) (CHM) has reviewed the available safety evidence for the risk of topical steroid withdrawal reactions, which have been associated with the use of topical corticosteroids.

The review has concluded that when used correctly, topical corticosteroid medicines are safe and effective treatments for skin disorders. However, if used very often or continually for a prolonged time, there have been reports of withdrawal reactions after they are stopped. A particularly severe type of topical steroid withdrawal reaction has been reported with skin redness (or a spectrum of colour changes or change in normal skin tone) and burning worse than the original condition.

It is important to follow the advice provided with topical corticosteroid medicines and to contact your doctor if your skin condition doesn't improve or gets worse, including after you stop using a topical corticosteroid.

## About Topical Corticosteroids

Steroids are natural chemicals produced by the body and also are manufactured to be used as medicines. There are different types of steroids. The most common type used to treat skin disorders are the corticosteroids.

If a corticosteroid is used on the skin, this is known as a topical corticosteroid. These may come in the form of creams, ointments, lotions, mousses, shampoos, gels or tapes.

Topical corticosteroids may be used to treat skin disorders such as:

- [Eczema](#) – a condition that causes the skin to become itchy, dry and cracked
- [Psoriasis](#) – a skin condition causes red, flaky, crusty patches of skin covered with silvery scales
- [Contact dermatitis](#) – a type of eczema triggered by contact with particular substances, such as soaps and detergents

Examples of topical corticosteroid medicines include beclometasone, betamethasone, clobetasol, hydrocortisone, mometasone, and triamcinolone.

## **Reason for the review**

The MHRA received an enquiry from a patient representative to the Yellow Card scheme about the risk of topical steroid withdrawal reactions, which triggered this assessment.

We conducted a comprehensive review of the evidence available. We considered side effects reported to us by patients and healthcare professionals, in addition to information published by researchers and other medicines regulators. We considered whether action should be taken to reduce the risk of these events.

We also sought advice on the review from our experts and from dermatologists and skin charities. The findings and recommendations of the review are summarised in this report.

## **Conclusions of the review**

When used correctly, topical corticosteroid medicines are safe and effective treatments for skin disorders. Correct use includes using these medicines to treat certain skin conditions for short periods of time, or with short breaks in treatment over an extended period.

There is growing evidence of topical steroid withdrawal reactions if they are used continually for a long time. We are unable to estimate the frequency of these reactions. However, given the number of patients who use topical corticosteroids, we understand that these effects occur very infrequently, however they can be debilitating and long lasting.

Information about these reactions will be added to the product information provided to healthcare professionals and patients. We have also produced additional materials for patients and healthcare professionals about the best way to minimise the risks of these reactions with topical corticosteroids and what to do if they occur.

## 2. Introduction

The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for regulating medicines and medical devices in the UK. We continually review the safety of all medicines in the UK and inform healthcare professionals and the public of the latest updates. The [Commission on Human Medicines](#) (CHM) advises government ministers and the MHRA on the safety, efficacy and quality of medicines.

The aim of our Safety Public Assessment Reports is to discuss evidence-based assessments of safety issues for a particular drug or drug class.

The following report provides a summary of the review of available safety data regarding topical steroid withdrawal reactions, which have been associated with topical corticosteroid medicines.

A [glossary](#) is provided for an explanation of the terms used in this report.

We received an enquiry to the Yellow Card scheme regarding 'red skin syndrome', which triggered this assessment. Red skin syndrome is a term used by patients for side effects seen after stopping topical corticosteroids that were used for prolonged periods of time. These reactions are also referred to as steroid addiction, topical steroid withdrawal, red burning skin, and steroid dermatitis. In this report, we use the term topical steroid withdrawal reactions.

## 3. Background

### About topical corticosteroids

Topical corticosteroids are used to treat the symptoms of many skin disorders, such as eczema, dermatitis, and psoriasis. Topical corticosteroids may also be combined with other medicines to treat bacterial or fungal infections.

Examples of topical corticosteroid medicines include beclometasone, betamethasone, clobetasol, hydrocortisone, mometasone, and triamcinolone.

Topical corticosteroids are available in multiple forms including creams, lotions, gels, mousses, ointments, or solutions. They are commonly used treatments for many dermatological conditions and are generally considered very safe and effective.

Mild corticosteroids, such as hydrocortisone, can be bought over the counter from pharmacies for use in older children and adults, whereas stronger or more potent types of corticosteroids are only available on prescription. Corticosteroids for skin problems in children younger than 10 years are available only on prescription.

### About topical steroid withdrawal reactions

Topical steroid withdrawal reactions have been reported in long-term users of topical corticosteroids after they stop use (Rapaport and Lebwohl, 2003; Hajar and others, 2015; Gust and others, 2016; Sheary 2016 and 2018). Symptoms noted include redness of the skin, a burning sensation, and itchiness. This may then be followed by skin peeling (Gust and others, 2016), which appears to be distinct from a flare-up of the underlying condition.

At the time of the review, topical steroid withdrawal reactions were not acknowledged as a side effect of corticosteroids in commonly used UK clinical materials and patients described to the MHRA encountering difficulties with diagnosis

### Reason for our review

Topical corticosteroids are safe and highly effective treatments when used [correctly](#). As with any medicine, topical corticosteroids can cause side effects, although not everybody gets these.

We conducted a comprehensive review to assess the evidence available. We considered data from Yellow Card reports, in addition to information from the published literature and other medicines regulators. The review considered whether regulatory action was needed to minimise the risk of these events.

We sought advice and endorsement on the assessment from the [Gastroenterology, Rheumatology, Immunology and Dermatology](#) and [Pharmacovigilance](#) Expert Advisory Groups of the [Commission on Human Medicines](#). Clinical experts in dermatology and skin charities were invited to participate in these discussions.

The findings and recommendations of the review are summarised in this report.

## 4. Review of Yellow Card data

The [Yellow Card scheme](#) run by the MHRA is the UK system for collecting and monitoring information on safety concerns such as suspected side effects involving medicines. Suspected side effects are reported by health professionals and the public, including patients, carers and parents. All Yellow Card reports received are entered onto the MHRA's adverse drug reaction database so that they are available for [signal detection](#).

We aimed to identify suspected spontaneous reports of topical steroid withdrawal reactions associated with topical corticosteroids on the Yellow Card database.

It is important to note that a reported reaction or case does not necessarily mean it has been caused by the drug or vaccine, only that the reporter had a suspicion it may have. Underlying or concurrent illnesses may be responsible and such events can also be coincidental. Additionally, it is also important to note that the number of reports received via the Yellow Card scheme does not directly equate to the number of people who suffer adverse reactions, and therefore cannot be used to determine the incidence of a reaction. Adverse drug reaction reporting rates are influenced by the seriousness of these reports, their ease of recognition, the extent of use of a particular drug or vaccine and may be stimulated by promotion and publicity about a drug or vaccine.

### Case search

Identifying cases in the database was challenging because there is no official recognition of topical steroid withdrawal reactions and the MedDRA clinical coding system does not currently include topical steroid withdrawal reactions or other related terms. Therefore, we searched for possible cases in association with a number of different topical corticosteroids (beclometasone, betamethasone, clobetasol, hydrocortisone, mometasone, triamcinolone) using the below MedDRA search criteria:

- System Organ Class: Skin – all cases were reviewed
- High Level Terms: Allergic conditions not elsewhere classified (NEC), "Allergies to foods, food additives, drugs and other chemicals", Application and instillation site reactions, Immune and associated conditions NEC, Inflammations, Substance related and addictive disorders, Therapeutic and nontherapeutic responses, Withdrawal and rebound effects

The search included Yellow Cards reported between 1963 (inception of the database) and 29 January 2020.

## Case criteria

The criteria for narrowing down these cases to definitive cases of topical steroid withdrawal reactions are difficult since many of the symptoms are listed individually for topical corticosteroids and some cases may be not related to these reactions. Additionally, rebound psoriasis is listed and although similar, this term does not fully capture topical steroid withdrawal reactions, which also occur outside the context of psoriasis. Therefore, only cases that have a clear timeline of worsening symptoms or increasing use of stronger steroids or multiple symptoms were included.

There may be more cases within the MHRA Yellow Card database that are potentially topical steroid withdrawal reactions, but due to a lack of information we cannot determine them as such at this time.

For the purposes of this review, cases that were considered indicative of topical steroid withdrawal reactions were referred to as 'probable' cases by the lead MHRA reviewers. There are also some cases that could be considered topical steroid withdrawal reactions but lack sufficient information to be determined as 'probable' and so these have been classed as 'possible' cases. It should be noted that this does not refer to whether the reactions were directly caused by the medicine.

We identified 55 reports categorised as 'probable topical steroid withdrawal reactions' in the Yellow Card database and a further 62 cases of 'possible topical steroid withdrawal reactions'.

**Table 1: Yellow Card reports identified as probable or possible cases of topical steroid withdrawal (TSW) reactions**

<b>Corticosteroid</b>	<b>Probable TSW cases</b>	<b>Possible TSW cases</b>
Beclometasone	1	0
Betamethasone	30	33
Clobetasol	3	9
Hydrocortisone	12	8
Mometasone	9	12
Triamcinolone	0	0

It is important to note that some of the cases may be listed for multiple steroids as often patients are switched by healthcare professionals from one product to another in increasing strength to try and resolve the symptoms. As a result, the numbers of cases for each steroid medicine in Table 1 are not directly comparable, and a higher number of reports should not be interpreted as a larger risk being present for individual steroid medicines.

Assessment of information provided by these reports is provided in Discussion.

## 5. Literature review

### Search Strategy

We aimed to identify relevant published scientific studies or reports about topical steroid withdrawal. To identify relevant papers, the PubMed search engine was used to identify citations from MEDLINE, life science journals, and online books published up to February 2020.

Search terms used were 'red skin syndrome', 'burning skin', and 'topical corticosteroids, withdrawal'. Dates of inclusion were studies published up to February 2020. No other date limiters were used. Only papers referring to reactions on withdrawal of topical corticosteroids were reviewed; all other papers were excluded. Only English-language papers were reviewed.

There are difficulties in identifying information on topical steroid withdrawal reactions within the published literature due to different terminologies being used and a lack of recognition of the issue. This is perhaps to be expected as topical steroid withdrawal reactions may be under-recognised.

The following papers were identified:

### Rapaport and Lebwohl (2003)

Rapaport (1999) had previously reported on 100 patients with chronic eyelid dermatitis, which did not resolve until all topical and systemic corticosteroids had been discontinued. All patients had been treated with topical corticosteroids in the long term, often with escalating dosage and frequency of application. In many cases a severe burning sensation was the main characteristic reported. Patch testing did not reveal any allergens.

In their 2003 paper, Rapaport and Lebwohl present cases in which other body areas were affected, including cases of burning face syndrome, red scrotum syndrome, and chronic eczema. The authors concluded that in all of these cases, corticosteroids had been applied long term and resulted in a characteristic pattern of 'corticosteroid addiction'.

The authors state that when dermatitis first developed, many of the patients self-prescribed over-the-counter 1% hydrocortisone cream or ointment. For those who sought medical consultation, many had been given moderate-strength corticosteroids initially, but in the recent years before publication, potent corticosteroid preparations were commonly prescribed at the outset. When pruritus or rash persisted or when rash recurred, stronger corticosteroids or more frequent application had been recommended.

The authors described that in the initial phases, the corticosteroids were usually effective, and patients felt relief for weeks to months. However, as time passed many patients required systemic corticosteroids at increasingly frequent intervals, some every 6 to 10 weeks. Daily topical treatment only maintained tolerance of symptoms and mild diminution of the rash. Patients complained that corticosteroids “were not working anymore”. The authors stated that by this point, the initial limited areas of dermatitis had expanded significantly. The itch had mostly disappeared but had been replaced by severe burning, which was only relieved by further topical corticosteroid application. The appearance of the dermatitis changed and was more of a hyperaemia.

### **Cork and others (2006)**

Cork and colleagues reviewed evidence for epidermal barrier dysfunction in atopic dermatitis. They postulated that topical corticosteroids disrupt the epidermal barrier causing an initiation of cytokine cascade followed by an inflammatory response. This was suggested as a possible mechanism of rebound flare in atopic dermatitis, which is not uncommon. The authors cite ‘red burning syndrome’ as an extreme form of rebound flare and that this is further exacerbated by continued use of topical corticosteroids.

The authors proposed a possible mechanism could be that a potent topical corticosteroid causes a thinning of the naturally thin stratum corneum on the face. They postulated that this increased thinning allows more allergens to penetrate, inducing persistent flares of the atopic dermatitis. As a result, the patient uses more topical corticosteroid to treat the flare, but this causes further thinning of the stratum corneum and, consequently, greater allergen penetration, causing more flares. A vicious circle is therefore established.

### **Hajar and others (2015)**

Following an increasing number of patient enquiries to the [US National Eczema Association](#), Hajar and colleagues sought to review the current evidence regarding addiction and withdrawal of topical steroid withdrawal. Cases without a clear temporal association were excluded, as were case series without a definitive number of cases and reviews of expert opinion.

Overall 34 case series were identified, all of which were deemed to be of very low quality, with the oldest article published in 1969 and the most recent in 2013. However, the papers contained information on 1,207 cases of topical steroid withdrawal reactions.

The authors concluded that topical steroid withdrawal generally occurs after prolonged or inappropriate use of topical corticosteroids. They divided topical steroid withdrawal reactions into 2 distinct morphologic syndromes: erythematoedematous and papulopustular.

They reported that the erythematous type develops more frequently in patients who have underlying chronic eczematous conditions such as atopic dermatitis and seborrheic dermatitis; is characterised by erythema, scaling, and oedema; and is generally accompanied by a burning sensation. The papulopustular type is more common in patients who are using topical corticosteroids for pigmentary disorders or acneiform conditions.

They reported that the papulopustular withdrawal subtype is more likely in patients who develop steroid rosacea, but this is not a prerequisite condition for this subtype. The papulopustular variant can be differentiated from the erythematous subtype by the prominent features of pustules and papules, along with erythema, but less frequently swelling, oedema, burning, and stinging.

The authors state that care should be taken since confusing the signs and symptoms of atopic dermatitis for steroid withdrawal could lead to unnecessary withholding of necessary anti-inflammatory therapy. However, they state that a clinician should favour a diagnosis of topical steroid withdrawal over a flare-up of the underlying atopic dermatitis if:

- burning is the prominent symptom,
- confluent erythema occurs within days to weeks of topical corticosteroid discontinuation
- there is a history of frequent, prolonged topical corticosteroid use on the face or genital region

The authors also highlight the issue of nomenclature with the following names used to describe this entity: facial corticosteroid addictive dermatitis, red skin syndrome, topical corticosteroid induced rosacea-like dermatitis, steroid addiction syndrome, steroid withdrawal syndrome, steroid dermatitis, post-laser peel erythema, status cosmeticus, red scrotum syndrome, chronic actinic dermatitis, anal atrophoderma, chronic eczema, corticosteroid addiction, light-sensitive seborrheid, perioral dermatitis, rosacea-like dermatitis, steroid rosacea, and steroid dermatitis resembling rosacea.

### **Juhasz and others (2017)**

Juhasz and others (2017) is a follow-up paper to the review by Hajar (2015); specifically looking at topical steroid withdrawal in children. The study reviewed the literature and social media.

The authors' literature search yielded no studies on or reporting classic topical steroid withdrawal reactions in children. However, periorificial dermatitis, which is generally a steroid-induced disorder in children, was reported in more than 320 cases.

Of 142 social media blogs on topical steroid withdrawal reactions, 26 were blogs discussing children, the majority of these (18) were from the USA, with 4 being from the UK. The review included 27 cases.

Duration of topical steroid use ranged from 2 months to 12 years. 56% of children had been prescribed topical steroids at 12 months of age or younger. Of the 11 types of topical steroids initially prescribed, 73% were of the mid-potency to high-potency class, with 30% being over-the-counter hydrocortisone. Despite signs and symptoms, only 6 cases (22%) reported that a medical provider had given them the diagnosis of topical steroid addiction or topical steroid withdrawal reactions. All caregivers provided their children with treatment for topical steroid addiction or withdrawal symptoms, which included discontinuation of topical corticosteroid use.

The authors concluded that topical steroid withdrawal reactions occur in children and can result from discontinuing topical steroids used for as little as 2 months. The authors reported that resultant signs and symptoms can last longer than 12 months, even with short duration of use. The authors acknowledged the lack of peer reviewed research of topical steroid withdrawal reactions in the paediatric population, nevertheless they concluded that the data indicates a need for guidelines pertaining to the safe use of topical steroids and counselling of patients for the signs and symptoms of topical steroid withdrawal reactions.

## Sheary (2016)

This paper by Sheary reviews some individual cases and the literature, including the review by Hajar above. The author concludes that the issue is under recognised and that most cases are caused by prolonged or inappropriate use of topical corticosteroids. The table below is reported as the common features of topical steroid withdrawal reactions.

**Table 2: Features seen in topical steroid withdrawal (TSW) reactions, adapted from Sheary (2016).**

Red Skin	Can be severe and was present in 92% of patients
Burning pain or stinging	Reported in 95% of patients with the 'erythemoedematous' type of topical corticosteroid withdrawal (most eczema patients fit into this category). In the early withdrawal phase, almost all topical products can 'burn' when applied to the skin
Itch	Can be severe, and present in 45% of all patients
Skin peeling or exfoliation	Said to occur at the end of a 'flare' and occurs in 33% of all patients

Oozing areas	Can take months for serous exudate to 'dry-up'
Oedema	Especially eyelids, ankles and hands
Papulopustules	Seen in over 80% of patients who used topical corticosteroids for pigmentary disorders or acne
Hives	Sign of recovery
Excessive Sweating	Sign of recovery
Depression	Psychological support for these patients is essential and may be required for many months
Insomnia	At least in part due to pain and itch

The author concludes that the safe use of topical steroids is an effective treatment; however, as recommended by the [US National Eczema Association](#), daily use should be limited to 2 to 4 weeks with tapering of use after that.

### **Sheary (2018)**

This paper by Sheary highlighted that concerns about topical steroid withdrawal reactions are leading some patients to cease long-term topical corticosteroid therapy and that diagnostic criteria for this condition do not exist. The author therefore examined the demographics and outcomes in adult patients who believe they are experiencing topical steroid withdrawal reactions following discontinuation of chronic overuse of topical corticosteroids.

This was a retrospective cohort study of patients in an Australian general practice presenting with this clinical scenario between January 2015 and February 2018. Women were 56% of the 55 patients seen, and ages ranged from 20 to 66 years (with a mean age of 32 years; and median age of 30 years). 66% had an original diagnosis of atopic dermatitis. 60% had used potent topical corticosteroids on the face, and 42% had a history of oral corticosteroid use for skin symptoms. Burning pain was reported in 65%; all had widespread areas of red skin; and so-called "elephant wrinkles" or "red sleeve".

The author concluded that patients with a history of long-term topical corticosteroids overuse may experience symptoms and signs described as withdrawal reactions on stopping topical corticosteroids.

### **Guidance from other regulators**

We also considered information to prescribers or patients on topical steroid withdrawal reactions from other regulators.

Only Medsafe (New Zealand) had information available to [prescribers on topical corticosteroid withdrawal](#). The information refers to an infrequent rebound effect that can occur once a topical steroid has been discontinued. This reaction can occur after prolonged,

inappropriate, and/or frequent use or abuse of moderate-potency to high-potency topical corticosteroids.

[Corresponding guidance](#) from the New Zealand Dermatological Society lists the symptoms of topical steroid withdrawal and advises that the higher the potency, the longer the period of application (in other words, more than 1 year), and the more frequent the application (more than once a day), the more likely that withdrawal reactions may occur.

## 6. Discussion

We conducted a comprehensive review to assess the evidence available. We considered data from Yellow Card reports, in addition to information from the published literature and guidance from other medicines regulators.

We identified 55 reports in the Yellow Card database that are probable reports of topical steroid withdrawal reactions and 62 further reported reactions potentially indicative of topical steroid withdrawal reactions.

The cases have been reported over a wide time-period, and the majority of reports are from patients. The terms used for reporting are reactions that are already listed in the product information, which impacts how we detect newly emerging safety concerns to medicines. Since the reports are mostly from patients, most cases use colloquial terminology and have been added to the database with the side effects reported in the case rather than with the term topical steroid withdrawal or withdrawal. Most of these side effects are already listed individually for topical corticosteroids.

The lack of a consistent terminology has also been raised within the literature and has potentially led to the condition being under-represented. Many of the reports we have received have the recurring theme that patients found the information on topical steroid withdrawal reactions for themselves rather than receiving a diagnosis from a healthcare professional.

In some patients, the adverse reactions appear to present while the topical corticosteroid is still being used. These cases may not relate to topical steroid withdrawal reactions and may represent allergic reactions (possibly to multiple topical corticosteroids), patients developing a different skin condition or some form of tolerance. However, this cannot be determined from the information available.

Topical steroid withdrawal reactions are thought to result from prolonged, frequent, and inappropriate use of moderate to high-potency topical corticosteroids. It has been reported that these reactions develop after application of a topical steroid at least daily for more than a year. To date, they have not been reported with normal use, such as treating certain skin conditions for short periods of time, or with short breaks in treatment over an extended period (Rapaport and Lebwohl 2003, Hajar and others, 2015, Juhasz and others, 2017, Sheary, 2018).

People with atopic dermatitis are thought to be most at risk of developing topical steroid withdrawal reactions (Hajar and others, 2015).

Juhasz (2017) reported that the signs and symptoms occur within days to weeks after discontinuation of long-term topical steroid treatment.

The signs of the specific type of topical steroid withdrawal reactions reported by Hajar (2015) and Sheary (2016) are:

- worsening of rash and redness of skin (extending beyond the original treatment area) that no longer responds to topical steroids or other treatments
- severe burning sensation of the skin
- dry skin that crinkles easily
- skin depigmentation or dark pigmentation, seen as either white patches on the skin or dark brown/grey areas of the skin, commonly seen near the knees, elbows and on the face, but can occur anywhere topical steroids are used
- stretch marks on the skin
- skin swelling
- pimple-like bumps, nodules or pustules, also known as 'steroid acne' or 'pustular psoriasis'
- extensive wrinkling of skin – especially seen above the knees, arms and hands but it can occur anywhere on the body
- loss or thinning of hair
- cracked skin, especially on the corners of the mouth, lips and hands
- frequent skin infections, including requiring antibiotic treatment
- increased itch

Sheary (2018) postulated that the basis for the skin redness seen in these patients is due to an elevation in blood nitric oxide levels, which widens blood vessels, increasing blood flow to the skin. It has also been proposed that topical corticosteroids disrupt the epidermal barrier causing an initiation of cytokine cascade followed by an inflammatory response (Cork and others 2006). Topical corticosteroids are known to constrict blood vessels in the skin and therefore some reddening of the skin would be expected on withdrawal. However, this specific kind of topical steroid withdrawal reaction could be an extreme form of this reaction.

These adverse events are experienced by patients shortly after stopping treatment, with a rebound of the original eczema that then spreads further. A rebound reaction on discontinuation is well recognised in the treatment of psoriasis and this is reflected in the product information of most topical corticosteroids. However, rebound in the context of eczema or atopic dermatitis is not mentioned in the product information of most topical corticosteroids. Rebound reactions may still benefit from treatment with a topical corticosteroid.

In many cases the worsening of the skin condition has been interpreted as a need for stronger topical corticosteroids. It can be difficult to differentiate between a worsening of a condition (which would benefit from the use of topical steroids) and topical steroid withdrawal. However, as stated by Hajar (2015) and identified by our review of the literature, a topical steroid withdrawal reaction should be suspected as distinct from a flare-up of the underlying atopic dermatitis if the following features are present:

- burning is the prominent symptom,
- confluent erythema occurs within days to weeks of topical corticosteroids discontinuation
- there is a history of frequent, prolonged topical corticosteroids use on the face or genital region.

From the reports the MHRA has received, patients have stated that they found the diagnosis themselves and that they had difficulty getting a diagnosis from a healthcare professional. This could be due a lack of awareness or a lack of recognition of the condition. As stated by Rathi and Souza (2012), topical corticosteroids are a vital tool for the treatment of dermatological conditions. However, if they are used inappropriately and without adequate supervision, there is a risk of reduced patient confidence and therefore compliance in the use of these products.

Many of the symptoms associated with topical steroid withdrawal reactions are listed individually within the patient information leaflets for topical steroids. These include inflammation and/or infection of the hair follicles, thinning of the skin, red marks with associated prickly heat, loss of skin colour, burning, stinging, itching or tingling.

Even though the current product information for topical corticosteroids may list some of the individual symptoms of topical steroid withdrawal reactions, there is no mention of reactions occurring after cessation of treatment. Therefore, following confirmation that topical steroid withdrawal reactions are a side effect that patients and prescribers need to be aware of, it was considered appropriate to update product information to better reflect the possible reactions that can be experienced.

## 7. Conclusions

There is a growing body of evidence that reactions associated with topical steroid withdrawal can occur following long-term or incorrect use of topical corticosteroids, particularly those of moderate to high potency. Correct use includes using these medicines to treat certain skin conditions for short periods of time, or with short breaks in treatment over an extended period.

We are unable to estimate the frequency of these reactions. However, given the number of patients who use topical corticosteroids, we understand reports of severe withdrawal reactions to be very infrequent. There are reports of severe withdrawal reactions taking the form of a dermatitis with intense redness (or a spectrum of colour changes or change in normal skin tone), stinging, and burning that can spread beyond the initial treatment area.

The information provided to both healthcare professionals and patients should reflect these reactions, especially with respect to eczema and dermatitis. Therefore, a strengthening of the information within the product information is considered appropriate, together with communication and consultation with other bodies.

After working with experts in the field and patient representatives, we have requested relevant marketing authorisation holders add the following to their product information:

### **Summary of Product Characteristics**

#### **Section 4.4 – Special warnings and precautions for use**

Long term continuous or inappropriate use of topical steroids can result in the development of rebound flares after stopping treatment (topical steroid withdrawal syndrome). A severe form of rebound flare can develop which takes the form of a dermatitis with intense redness, stinging and burning that can spread beyond the initial treatment area. It is more likely to occur when delicate skin sites such as the face and flexures are treated. Should there be a reoccurrence of the condition within days to weeks after successful treatment a withdrawal reaction should be suspected. Reapplication should be with caution and specialist advice is recommended in these cases or other treatment options should be considered.

#### **Section 4.8 – Undesirable effects**

##### **Skin and Subcutaneous Tissue Disorders**

Not known (cannot be estimated from available data) Withdrawal reactions - redness of the skin which may extend to areas beyond the initial affected area, burning or stinging sensation, itch, skin peeling, oozing pustules. (see section 4.4)

## **Patient Information Leaflet (PIL) wording**

### **Prescription only medicines**

#### **Section 2 – What you need to know before use**

If there is a worsening of your condition during use consult your prescriber – you may be experiencing an allergic reaction, have an infection or your condition requires a different treatment.

If you experience a recurrence of your condition shortly after stopping treatment, within 2 weeks, do not restart using the cream/ointment without consulting your prescriber unless your prescriber has previously advised you to so. If your condition has resolved and on recurrence the redness extends beyond the initial treatment area and you experience a burning sensation, please seek medical advice before restarting treatment.

#### **Section 4 – Possible side effects**

Steroid withdrawal reaction:

If used continuously for prolonged periods a withdrawal reaction may occur on stopping treatment with some or all of the following features: redness of the skin which can extend beyond the initial area treated, a burning or stinging sensation, intense itching, peeling of the skin, oozing open sores.

## **Pharmacy-only medicines PIL wording**

#### **Section 2 – What you need to know before use**

If your condition worsens during use consult a pharmacist or doctor – you may be experiencing an allergic reaction, have an infection or your condition requires a different treatment.

If you experience a recurrence of your condition shortly after stopping treatment, within 2 weeks, do not restart using the cream/ointment without consulting a pharmacist or doctor. If your condition has resolved and on recurrence the redness extends beyond the initial treatment area and you experience a burning sensation please seek medical advice before restarting treatment.

#### **Section 4 – Possible side effects**

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## **Materials for healthcare professionals and patients**

To raise awareness of this issue the MHRA has published a [Drug Safety Article](#) and prepared a [Patient Safety Leaflet](#) for use while patient information leaflets are being updated. The MHRA will continue to monitor reports and provide further updates should they be required.

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## 9. Glossary of Terms

### **British National Formulary (BNF)**

A United Kingdom pharmaceutical reference containing information and advice on prescribing and pharmacology of medicines.

### **Contact Dermatitis**

A type of eczema triggered by contact with particular substances, such as soaps and detergents. Contact dermatitis causes the skin to become itchy, blistered, dry and cracked.

### **Commission on Human Medicines (CHM)**

The [Commission on Human Medicines \(CHM\)](#) advises ministers on the safety, efficacy and quality of medicinal products.

### **Eczema**

Eczema is the name for a group of conditions that cause skin to become dry and irritated.

### **Marketing authorisation holder**

The company or other legal entity that has the authorisation to market a medicine in the UK.

### **Medical Dictionary for Regulatory Activities (MedDRA)**

A dictionary of international medical terminology used by regulatory authorities and medical organisations.

### **Patient Information Leaflet (PIL)**

The Patient Information Leaflet (PIL) is the leaflet included in the pack with a medicine.

### **Product information**

Documents providing officially approved information for healthcare professionals and patients on a medicine. The product information includes the summary of product characteristics, package leaflet and labelling.

### **Psoriasis**

Psoriasis is a skin condition that causes red, flaky, crusty patches of skin covered with silvery scales.

### **Signal**

Drug-reaction combinations that occur more frequently than would be expected when compared to the background frequency of other drug-reaction combinations in the Yellow Card database. The MHRA use specialised software to subject Yellow Card data to statistical analysis to detect signals.

### **Summary of Product Characteristics (SmPC)**

Detailed information that accompanies every licensed medicine, listing its composition and characteristics and conditions attached to its use, which is available at:

<https://products.mhra.gov.uk/>

### **Suspected adverse drug reactions**

Also known as side effects. All medicines or vaccines can cause adverse reactions in some people. Adverse drug reactions reported to the MHRA are looked at and used to assess the balance of risks and benefits of medicines and vaccines.

### **Topical corticosteroid**

A medicine from the corticosteroid family that is used on the skin, for example as in the form of creams, ointments, lotions, mousses, shampoos, gels or tapes.

### **Topical steroid withdrawal reactions**

An adverse reaction relating to the use of a topical steroid after it has been discontinued with some or all of the following features: redness of the skin which can extend beyond the initial area treated, a burning or stinging sensation, intense itching, peeling of the skin, oozing open sores.

### **Yellow Card scheme**

The MHRA's scheme for healthcare professionals and members of the public to report suspected adverse reactions for a medicine or vaccine, as well as medical devices and other products.

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