Always read the label

Christine Clark, a pharmacist with a specialist knowledge of dermatology and a particular interest in the care of people with skin conditions and in medication safety, explains how to interpret the labelling on the packaging of your treatments.

The label on a dispensed medicine can be as brief as 'Use as directed', which can be a bit unhelpful if the prescriber did not give any directions in the first place. However, the package or outside of the tube or container usually carries much useful information. This is the case with both prescribed medicines and emollient products bought over-the-counter – much of the information is required by European Union (EU) law. Sometimes the information requires a bit of decoding. This article gives you some pointers about things to look for.

Information on the box or package

Packaging is carefully designed to draw the reader's eye to the information that the manufacturer considers most important. Where medicines are concerned, some of the information must appear by law – for example, the legal status of the medicine and certain warnings. In this country the requirements for labels, patient information leaflets and packaging of medicines are laid down by the Medicines and Healthcare Products Regulatory Agency (MHRA). The UK regulations conform to European Directive 2001/83/EC, which sets out the regulations for medicines for human use throughout the EU. Certain items are deemed critical for the safe use of medicines and must appear on all packs.

They are:

- name of the medicine;
- expression of strength (where relevant);
- route of administration;
- dose (for items intended for self-medication); and
- warnings.

The EU legislation also requires the name of the medicine to be shown on the packaging in Braille.

Legal status

Many medicines are 'prescription only' products, which can only be supplied against a prescription (e.g. Betnovate Cream), but in the UK some medicines can be purchased from a pharmacy, under the supervision of a pharmacist (e.g. Eumovate Eczema and Dermatitis Cream). Prescription-only medicines (POM) must show on the packaging a box containing the letters 'POM'; pharmacy-only medicines must bear a box containing the letter 'P' for pharmacy. It can be useful to know this if, for example, your supply is running out and you are wondering if you can buy it over the counter. The package must also bear the name of the marketing authorisation holder.

There are some medicines that can be bought over the counter in supermarkets and other retail outlets as well as pharmacies – these are 'general sales list' (GSL) items. For these products the designation 'GSL' appears in a box on the package.

Product licence number or CE mark

The product licence (PL) number of a licensed medicine must appear on its packaging. It appears as 'PL' followed by a number. Many over-the-counter products and a number of prescribed emollients are licensed as medical devices rather than medicines. Although it might seem a bit strange to describe an emollient as a device, since this conjures up images of gadgets and electronics, an emollient (or barrier cream) can be registered as a medical device because its primary mode of action is considered to be physical rather than metabolic, immunological or pharmacological – therefore it falls within the definition of a device. However, it is used for a medical rather than a cosmetic purpose. There are also two important practical points: first, the process for registering medical devices is less costly (and less detailed) than for registering a medicine; and secondly, emollients that are registered as medical devices are listed in the Drug Tariff (only items that are listed in the Drug Tariff can be prescribed at NHS expense). Products that have been registered as devices bear a 'CE' mark on the packaging.

What is a Marketing Authorisation?

A marketing authorisation (MA) (previously called a product licence) is granted to a medicine that meets the required standards of safety, quality and efficacy in the UK. An MA is normally necessary before a product can be prescribed or sold. It covers all the main activities associated with the marketing of a medicinal product.

In order to apply for an MA, a manufacturer must submit a technical dossier containing sufficient information to demonstrate that the product is of adequate quality for its intended use, that it is sufficiently safe and that it is effective. For new, active substances, full toxicological, pharmacological and clinical data would be expected. For other applications, adequate chemistry and pharmacy data together with appropriate toxicological and clinical data must be provided. Technical dossiers must also contain full-colour mock-ups of the packaging and the patient information leaflets (PILs). Technical dossiers are not lightweight documents in any sense – they commonly run to thousands of pages.

The granting of an MA demonstrates that a medicine has gone through a rigorous and thorough evaluation process to validate its safety and efficacy – and this sets it apart from folk remedies and herbal products.

Warnings

Although some of the warning statements may seem obvious, it is important to remember that the purpose of the warning statements on the label is to enable the products to be used safely and to best effect. One might argue that in a dimly-lit bathroom, a warning label might just prevent a mix up between toothpaste and steroid cream.

Thus, a Pharmacy Only (P) medicine that is an embrocation, liniment, lotion, cream, liquid antiseptic or other liquid preparation or gel intended for external use, the statement 'Use this medicine only on your skin' must appear on the label. Other common warning statements are shown in Table 1.

TABLE 1. COMMON WARNING STATEMENTS

■ FOR EXTERNAL USE ONLY

Applied to all medicines intended for use on the skin, in a separate box, for extra prominence.

■ AVOID CONTACT WITH EYES

Often applied to wash products and shampoos where contact with eyes during use is possible and could cause irritation.

■ DO NOT USE AFTER EXPIRY DATE

Emollient products may start to separate or decompose after the expiry date. They may also become contaminated with microorganisms during use and no longer be safe to use.

■ USE WITHIN X MONTHS OF OPENING

May be applied to water-based creams and lotions that could easily become contaminated with microorganisms during use. This could cause deterioration of the products and/or pose a risk of infection to damaged skin.

■ TAKE CARE NOT TO SLIP WHEN LEAVING BATH OR SHOWER

Applied to bath oils and products used immediately after showering or bathing (e.g. Oilatum Gel) that could make surfaces slippery.

■ DO NOT USE IF YOU HAVE AN ALLERGY TO ANY OF THE INGREDIENTS

DO NOT USE IN CASES OF KNOWN SENSITIVITY TO ANY OF THE INGREDIENTS

Applied to many medicines but particularly relevant to topical products for people with eczema. May be difficult to comply with as one does not always know. People with eczema should always err on the side of caution and apply a test patch of any new topical product (e.g. to the forearm) before using it on a large area.

■ FLAMMABILITY RISK.

CAUTION: FLAMMABLE. KEEP YOUR BODY AWAY FROM FIRE OR FLAMES AFTER YOU HAVE PUT ON THIS MEDICINE

Applied to:

- Products containing flammable solvents.
- Products containing flammable propellants (e.g. butane/propane)
- Some products based on white soft paraffin/liquid paraffin.
- Garments soaked in white soft paraffin (Vaseline). Whilst the risk is obvious with flammable solvents and gases, it is not always realised that these garments are also flammable and at least one fatal accident has been reported. This sort of situation can arise when large areas of skin are treated with Vaseline or a 50:50 mixture of Vaseline and liquid paraffin.

TABLE 2. COMMON WARNING STATEMENTS ON TOPICAL STEROID TREATMENTS

Some of the warning messages – such as 'Apply sparingly' and 'Do not use on broken skin' – that appear on the patient information leaflets for topical corticosteroids cause a lot anxiety.

■ APPLY SPARINGLY

It has been argued that the instructions, 'Apply sparingly' or 'Apply thinly' carry hints of economy, caution and even danger.[1] These instructions relate to concerns about the most potent corticosteroids, but they appear on all corticosteroids – even the mildest – and can lead to inappropriate under-use. It is unlikely that manufacturers will take the wording out of their leaflets, but an expert group has recommended that it would be better to say, 'Apply enough to cover the affected areas'.[1]

■ DO NOT USE ON BROKEN SKIN

During a flare-up of eczema, inflamed skin is often broken as a result of scratching. There can be clear scratch marks and points where blood has oozed out. Sometimes people withhold corticosteroids when this happens and that is a pity because topical corticosteroids can reduce the inflammation and itching (and therefore the urge to scratch).

The reason for the warning is that more corticosteroid is absorbed into the bloodstream if the cream or ointment is applied to extensive raw and bleeding areas of skin. Experts agree that this is very different from the small amount of bleeding from scratched eczema.

■ DO NOT APPLY TO THE FACE

This warning appears in the patient information leaflet for topical corticosteroids that are bought over the counter, but not those that are supplied on prescription. This can be confusing if, for example, hydrocortisone cream is prescribed for use on the face. The thinking behind the instruction was to prevent people from using topical corticosteroids long-term on the face where skin-thinning could occur.

As always, the risk is greater with more potent corticosteroids. Hydrocortisone acetate cream or ointment can be used safely on the face. Indeed, it is better to use a mild topical corticosteroid to control a flare-up of eczema (and then step down to emollient alone) than to allow untreated eczema to persist.

Descriptions on packages

When it comes to medicinal products, the MHRA is very particular about what can be said or implied. Some common examples are:

Effective relief - This may be used for all products that are registered as medicines (and therefore have an MA and a product licence number) as the issue of an MA is evidence that the product is effective.

Natural - This statement may only be used where all of the ingredients are natural. If only some of the ingredients are natural, then the term is not permitted.

Herbal - This may not be included unless the active ingredients are 100% herbal. It is not necessary for the excipients to be of plant origin.

Storage instructions

'**Keep out of reach of children**' or '**Keep out of the reach and sight of children**' now appears on all medicines as a matter of safety. Medicines can appear attractive and interesting to young children and may be mistaken for sweets. However, sometimes young children want to copy adult behaviour. In one tragic case a toddler took one of his grandmother's discarded pain-relieving patches from a waste bin and put it on his skin just as he had seen her do. The patch contained enough residual fentanyl (a potent pain killer) to stop the child from breathing and cause his death.

'**Store below 25°C**' or '**Do not store above 25°C**' appears on many medicine packages. Excessive heat can cause deterioration of some products.

Medicines are tested for stability, and expiry dates are given accordingly. However, most medicines are not designed to be stable above 25°C because they will not normally be exposed to higher temperatures for long periods. In practice, this means that storing medicines on top of a radiator in the bathroom is not a good idea.

Ingredients in emollient products

One of the main areas of interest to patients with eczema is the labelling of emollient products. Since 2003 it has been a requirement (under EU law) for any medicinal product that is injectable, topical or an eye preparation to declare a full list of excipients on the label (pack). Excipients are basically anything in the product that is not the active ingredient. They are necessary to make the dose 'usable' in practice.

Emollients can be licensed medicines, licensed medical devices or cosmetic products that are not registered as medicines. Under current EU legislation, all cosmetic products sold in the EU must display a complete ingredients list. This helps users to identify products with ingredients to which they know they are sensitive. Ingredient names must, by law, comply with European requirements and use the International Nomenclature of Cosmetic Ingredients (INCI). This means that in whatever European country a cosmetic product is bought, the ingredient names will be the same. The Cosmetic, Toiletry and Perfumery Association (CTPA) provides much useful information on this topic. See **www.thefactsabout.co.uk/files/237201013545Allergy_Card.pdf**

Emollients can contain:

- a mixture of natural and/or synthetic oils, fats and waxes;
- water;
- additional active ingredients such as humectants, anti-itch agents, antiseptics;
- emulsifying agents;
- acids or alkalis to adjust the acidity or alkalinity of the product;
- thickeners to adjust the consistency;
- preservatives;
- perfumes; and
- colourings.

TABLE 3. THE 26 FRAGRANCE INGREDIENTS CONSIDERED MORE LIKELY TO CAUSE REACTIONS IN SUSCEPTIBLE PEOPLE

INCI name	Other names
Amyl cinnamal	
Benzyl alcohol	
Cinnamyl alcohol	
Citral	
Eugenol	
Hydroxycitronellal	hydroxy-citronellal
Isoeugenol	
Amylcinnamyl alcohol	amylcin-namyl alcohol
Benzyl salicylate	
Cinnamal	
Coumarin	
Geraniol	
Hydroxyisohexyl 3-cyclohexene carboxaldehyde	hydroxy-methylpentyl cyclohexenecar boxaldehyde
Anise alcohol	anisyl alcohol
Benzyl cinnamate	
Farnesol	
Butylphenyl methylpropional	2-(4-tert-butylbenzyl) propionaldehyde
Linalool	
Benzyl benzoate	
Citronellol	
Hexyl cinnamal	hexyl cinnam-aldehyde
Limonene	d-limonene
Methyl 2-octynoate	methyl heptin carbonate
alpha-Isomethyl ionone	3-methyl-4-(2,6,6-tri-methyl-2-cyclohexen-1-yl)-3-buten-2-one
Evernia prunastri	oak moss extract
Evernia furfuracea	treemoss extract

Source: The Cosmetic, Toiletry & Perfumery Association (CTPA), consumer website www.thefactsabout.co.uk (Allergy advice section).

TABLE 4. EXAMPLES OF INCI NAMES OF INGREDIENTS MORE ASSOCIATED WITH SENSITISATION

INCI name	Chemical name or common name	Trade name(s) examples
Formaldehyde	formaldehyde	
Methylisothiazolinone	MI or MT	
2-Bromo-2-nitropropane-1,3-diol DMDM hydantoin Imidazolidinyl urea Diazolidinyl urea Quaternium-15	formaldehyde releasers	Bronopol Germall 115 Germall II Dowicil 200
Methylchloroisothiazolinone and methylisothiasolinone		Kathon CG Euxyl K100
Lanolin (and derivatives)	lanolin/wool alcohols	Amerchol L101
Methylparaben Propylparaben	parabens methyl 4-hydroxybenzoate propyl 4-hydroxybenzoate	
Parfum	perfume, fragrance	
Colophonium	colophony, rosin	
Tosylamiode/formaldehyde resin	toluene sulfonamide formaldehyde resin	Santolite Resin
p-Phenylenediamine	PPD	
p-Toluenediamine	PTD	
BHT	butylated hydroxytoluene	
Benzophenone-3	oxybenzone	Eusolex 4360
Butyl methoxydibenzoylmethane		Eusolex 9020 Parsol 1789
Octyl dimethyl PABA		Eusolex 6007
Ethylhexyl methoxycinnamate		Eusolex 2292 Parsol MCX
Resorcinol		Jarocol RL Rodol RS

Source: The Cosmetic, Toiletry & Perfumery Association (CTPA), consumer website www.thefactsabout.co.uk (Allergy advice section).

In practice, the main reasons for looking at the ingredients list are to check for potential allergens or irritants and to check which additional ingredients are present. The substances that are most commonly associated with sensitisation are preservatives and perfumes.

It is important to note that preservatives (such as chlorocresol or phenoxyethanol) are not a bad thing in themselves. They are essential in creams and lotions because these are water-based products that could easily become contaminated with micro-organisms. Once present, micro-organisms can multiply and could then damage the product and/or cause a skin infection and worsening eczema. It is usually recommended that patients with eczema use unperfumed emollients, because many perfume ingredients are commonly associated with sensitisation.

Table 3 shows the 26 fragrance ingredients that are considered more likely to cause reactions in susceptible people.

These must be indicated in the list of ingredients, in addition to the word 'parfum', if their concentration exceeds 0.001% in leave-on products (e.g. a moisturiser) and 0.01% in rinse-off products (e.g. a shampoo). Table 4 shows ingredient substances that are commonly associated with sensitisation.

Sodium lauryl sulphate

All cream formulations contain an emulsifying agent. Sodium lauryl sulphate (SLS) is a chemical substance that makes it possible to mix oils and water together to form a cream. There are numerous emulsifying agents available and they are widely used in the cosmetic industry. When Aqueous Cream BP was first formulated many decades ago, the emulsifying agent chosen was SLS. We now know that this substance can irritate and damage the skin of people with and without eczema. For this reason, The National Eczema Society and the National Institute for Health and Care Excellence (NICE) recommend that Aqueous Cream BP should not be used as a leave-on emollient.

Many lightweight emollients these days are prominently labelled 'SLS-free', reflecting the fact that they have been formulated using an alternative emulsifying agent. Sodium lauryl sulphate is sometimes named as sodium dodecyl sulphate. It is not the same thing as sodium laureth sulphate. *(NB: sodium laurel sulphate is meaningless – it is a typing error).*

Humectants

Humectants are agents that attract water. They are widely used in cosmetics and in pharmaceutical products. Humectants draw water into the epidermis and produce a long-lasting moisturising effect. Common examples include urea, glycerine, polyethylene glycol, lactic acid and sodium pyrrolidone carboxylate. Application of a 10% urea cream can double the water-holding capacity of the stratum corneum.

Lanolin

Lanolin is a good emollient but is popularly believed to be a common sensitiser. In fact, the evidence suggests that lanolin is a weak sensitiser and large studies have shown that the true incidence of lanolin sensitivity amongst the general population is extremely low. Although the incidence of lanolin allergy is higher amongst people with eczema, it is still only about 1% and the majority of these people are able to tolerate products formulated with hypoallergenic lanolin (Medilan®) without difficulty. In fact, hypoallergenic, highly-purified lanolin is used almost exclusively these days. Unfortunately, lanolin's reputation as a sensitiser has gained currency through frequent repetition in textbooks and cosmetic marketing that has emphasised 'lanolin-free' products as a selling point.

Antiseptics

Some emollients are advertised as being 'antimicrobial' creams. They contain sufficient quantities of antimicrobial agents to exert an effect on organisms on the skin when applied. They are usually recommended as treatments to keep the level of skin colonisation low rather than to treat an obvious infection. The substances used are chlorhexidine 0.1% or benzalkonium chloride 0.1%. This is useful to know because a small number of patients have reported reactions to benzalkonium chloride.

Anti-itch products

Macrogols are water-soluble ethylene glycol polymers, which are said to have mild local anaesthetic effects and can be useful in relieving itching. For this reason, lauromacrogol (also known as polidocanol) is included in Balneum® bath oils and Balneum Plus® cream. It is also found in E45 Itch Relief Cream. Colloidal oatmeal is very finely ground oatmeal that forms a hydrophilic matrix. This makes for a cooling application, which also appears to have some anti-pruritic effects. It is the key ingredient in Aveeno products.

Conclusion

It is useful to have an understanding of the information on the packaging and labels of topical medicines. Some of the names of ingredients can be difficult to interpret – not least because some chemicals are known by several different names. Some of the warnings are hangovers from a bygone age and some provide useful and important information.

The fact that ingredients are now listed on dermatological products – both medicines and cosmetics – is a huge and welcome advance. It is sobering to reflect that – within living memory – all ointments and creams were dispensed (by law) with the label, 'The Cream' or 'The Ointment', and no more information about their contents.

Well-designed packs, labels and patient information leaflets are all important in helping people to use medicines effectively to care for their skin.

Reference **1** Bewley A (2008) Expert consensus: time for a change in the way we advise our patients to use topical corticosteroids. British Journal of Dermatology; 158:917–20