Treatments for skin lymphoma

There are many treatments for skin (cutaneous) lymphoma. This page provides information about each type of these treatments. Some of them are not licensed for skin lymphoma in the UK. Your doctor might recommend a treatment off-licence, usually if it is available for another form of lymphoma or if it is used to treat other forms of skin disease. Some are experimental and you might get them as part of a clinical trial.

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How are skin lymphomas treated?

Many skin lymphomas are slow-growing and may never progress beyond an early stage. If this applies to you, your specialist may decide to keep an eye on your lymphoma during regular check-ups in the clinic. This is called ‘watch and wait’. You may feel anxious about ‘watch and wait’ because nothing is being done to treat your lymphoma. However, doctors know from research that the potential benefit of treating some early skin lymphomas is smaller than the risk of side effects from treatment.

Your doctor might recommend treatment for your symptoms, such as moisturising emollient creams or mild medications that you apply to the skin. They help to manage symptoms, eg relieve dryness and itching, and improve the appearance of the skin. However, they do not get rid of the lymphoma.

We have more information about coping with symptoms of skin lymphoma, which you can read on our website at www.lymphomas.org.uk. You can also print this information at home or, if you prefer, our helpline can send you copies. Please email at information@lymphomas.org.uk or call on 0808 808 5555.

If your skin lymphoma is more troublesome or widespread, your doctor may suggest topical treatments, which are applied directly to your skin (skin-directed therapies). These treatments aim to control the skin problems with as few side effects as possible.
If a skin lymphoma is advanced when it is diagnosed, or is not responding to topical treatments, your doctor is likely to suggest a **systemic treatment**. Systemic treatments are treatments that affect the whole body.

Many people with skin lymphoma have symptomatic, topical and systemic treatments over the course of their lymphoma, either one at a time or in combination. Any treatment your doctor offers you is tailored to you. You shouldn’t be concerned if your treatment is different from the treatments given to other people you meet in the clinic. Try not to worry if your doctor advises no treatment at all. Sometimes ‘watch and wait’ can be the best option.

**How does a medical team decide which treatment to use?**

Several specialists are likely to be involved in planning your treatment, including a dermatologist (skin consultant), an oncologist (cancer consultant), a pathologist (specialist doctor who examines and tests skin biopsies in the laboratory) and a clinical nurse specialist. This **multidisciplinary team** take several factors into account when discussing and planning treatment, such as:

- the appearance of the affected skin and the type of skin lymphoma you have
- how troublesome your symptoms are
- how much skin is involved and whether or not the lymphoma has spread to your lymph nodes or internal organs (the stage of your skin lymphoma)
- whether you have already had treatment for skin lymphoma and how you responded.

Your medical team should discuss all the options with you before they advise on the treatments they think are best.

Skin lymphomas are rare. If your local hospital does not have much experience with skin lymphoma, they might refer you to a centre with more expertise to ensure you get the best treatment. You can also request to be referred elsewhere.

Doctors use topical and systemic treatments for skin lymphomas. Some of these treatments are not yet licensed in the UK. Before a drug can be used widely or funded by the NHS, it must first be licensed. A licence is given when a drug has undergone testing and it has been shown that its benefits outweigh its risks for a given condition.

As skin lymphoma is rare, it is difficult for drug companies to conduct clinical trials that are large enough to show that a drug is beneficial and to allow it to be licensed. Many treatments used for skin lymphoma are used off-licence. They are often medicines that are licensed for another form of lymphoma or another form of skin disease. Some treatments are experimental and might only be available in a clinical trial.
What are ‘topical’ treatments?

Topical treatments are applied directly to the skin areas affected by lymphoma. They are usually used for early-stage skin lymphoma. The aim of these treatments is to control the lymphoma with as few side effects as possible.

Topical treatments include:

- steroids,
- chemotherapy (page 3),
- light treatment (PUVA and UVB) (page 5),
- radiotherapy (page 6).

Steroids on the skin

Steroid drugs are related to the hormone cortisol, which the body produces naturally. They are particularly helpful if the skin is itchy or inflamed. Topical steroids come as creams, ointments and gels. In the UK, they are classified into 4 categories of ‘strengths’: mild, moderate, potent (strong) and very potent.

Mild and moderate topical steroids are available over the counter from pharmacies. They can be safely used for many months to control symptoms such as redness and itching. They rarely clear a patch of skin lymphoma completely.

Stronger topical steroids have to be prescribed by your GP. Potent or very potent topical steroids can clear up patches of skin lymphoma after 4–6 weeks of use. The effect may last for weeks or months after a course of treatment. Treatment can be repeated should the patch come back. For some people with early stage skin lymphoma, this is the only treatment they ever need.

If you use topical steroids for a long time, particularly the ones of more potent strengths, you can get side effects such as thinning of the skin, dilated blood vessels or an acne-like rash. You should be prescribed the lowest strength needed to control your symptoms to avoid developing these side effects.

Steroids should be tapered off as soon as possible. You can usually have another course of treatment if your lymphoma comes back. Steroids are safe if used carefully. Please talk to your doctor or clinical nurse specialist if you have any concerns about how to use topical steroids.

Chemotherapy on the skin

Chemotherapy drugs target lymphoma cells and either kill them or stop them from dividing. In early-stage skin lymphomas this kind of drug can be applied directly to the skin each day, or every other day, as a lotion or an ointment.
Always follow instructions about where to apply the treatment, how much to use and how often. Your doctor may advise you to wear gloves because chemotherapy can harm normal skin. If you develop a reaction to your drug, your doctor might switch you to another one. You can’t use topical chemotherapy if you are pregnant.

Topical chemotherapy has to be made up by specialised pharmacy departments in a controlled environment. Your hospital will arrange it for you.

**Carmustine** (also known as BiNCU®) is a topical chemotherapy drug that is used off-licence for skin lymphoma. It works well for early-stage skin lymphomas; most people have a good response (no evidence of lymphoma).

Apply carmustine only to the affected parts of your skin. Your doctor is likely to only prescribe this for 3–4 months because it can get into the bloodstream and cause a drop in numbers of circulating blood cells (your blood counts). Your blood counts should be regularly monitored during your treatment.

Reddening of the skin can occur. In some people, the patches and plaques can become more intensely discoloured during treatment with carmustine. You might notice fine dilated blood vessels appearing in the treated areas. They usually go away once the treatment has finished.

You might hear about a topical chemotherapy drug called **nitrogen mustard** (also called mechlorethamine or Mustargen®). It is not currently available in the UK. A topical gel containing nitrogen mustard (Valchlor®) is now used in the US, and may be available in the UK in the future.

**Other unlicensed topical creams and gels**

Several other topical creams and gels are starting to be used for people with skin lymphoma. Although they are not licensed for skin lymphoma in the UK, some of them are available for other kinds of skin cancer and inflammatory conditions. Your dermatologist can advise whether they could benefit you. They are particularly useful when only limited areas of your skin are affected by lymphoma and topical steroids have not helped.

Retinoids are related to vitamin A. They disrupt the growth and division of lymphoma cells. Bexarotene (Targretin®) is usually used as a systemic retinoid treatment for skin lymphoma in the UK. It is also available as a topical gel in the US but not yet in Europe. Other topical retinoids that may be relevant to you are: Tazarotene (Tazorac®, Zorac®) gel and isotretinoin gel. They are usually used to treat psoriasis or acne, but may also help people with skin lymphoma.

Imiquimod (Aldara®) is an immunomodulatory drug. It triggers your immune system to form a response that recognises and destroys abnormal cells. It is available as a cream to treat genital warts and some cancerous and pre-cancerous skin conditions. Studies have shown that it can help some people with skin lymphoma too.
Efudix is a chemotherapy cream. It is used to treat some types of skin cancer and pre-cancerous skin lesions. Studies suggest it may help some people with skin lymphoma.

Tacrolimus is an immunomodulatory ointment that is normally used to treat eczema. It is classed as a non-steroid eczema treatment. It may help reduce inflammation in skin lymphoma. It is sometimes used when steroid side effects are a concern, such as for treatments of the face or of body folds.

**Light treatment (phototherapy)**

The ultraviolet part of sunlight slows down the growth of skin cells and reduces inflammation. It has long been known to help with many skin conditions, including psoriasis. It also works well for skin lymphomas, especially for plaques and large areas of skin affected by early-stage disease.

You may have treatment with either ultraviolet B light (UVB) or ultraviolet A light (UVA), which is often combined with a light-sensitising tablet called psoralen. The combination of psoralen and UVA is often called PUVA. UVB therapy is more widely available, but PUVA is also available at most large or regional skin departments in the UK.

To have **PUVA treatment**, you take a psoralen tablet 1–2 hours before the light treatment, which you have in an air-conditioned, walk-in cabinet containing long fluorescent light bulbs. It is a bit like a sun-tanning booth. You usually have 2 treatments a week; you spend more time in the cabinet each time. You start with a short exposure and gradually build up to several minutes. You usually carry on with treatment until your skin is clear or much improved, which usually takes 20–30 treatments.

Usually, all your skin is exposed to the UVA. You should be given goggles to protect your eyes and male genitals should be shielded. If your face is not affected, your doctor might ask you to wear a face shield.

When your treatment is finished, your doctor continues to monitor your condition in the clinic. If the treatment is successful, you may be free of lymphoma (in remission) for up to 5 years. If the lymphoma comes back, you can have another course of phototherapy.

Some people find that psoralen pills make them feel sick. Should it happen to you, your doctor can give you antiemetics (anti-sickness tablets) to take before your psoralen pill. In a few centres in the UK, ‘bath PUVA’ is available to avoid sickness. Instead of taking a tablet, ‘bath PUVA’ involves soaking in water containing psoralen for 15 minutes immediately before your UVA treatment. You can only have ‘bath PUVA’ if you don’t have lymphoma on your face, head or neck.

Temporary side effects of PUVA include reddening of the skin, itching or a rash. Some people get dizzy, others have headaches. PUVA can reactivate cold sores. If you get them, put sunblock on the affected areas before each treatment.
Skin is very sensitive to the sun for up to 24 hours after PUVA. Avoid exposing your skin to excess sun during this time. You should wear sunglasses for 12–24 hours after each treatment because psoralen sensitises the eyes to ultraviolet light, as well as the skin. Follow usual sun precautions at other times.

UV light can damage the skin. This treatment could increase your risk of other types of skin cancer in the future. For this reason, there is a lifetime limit on the number of PUVA treatments you can have and on the amount of light energy you can have in total (usually around 250 sessions or 1,500 joules of light energy).

**UVB phototherapy** (also known as narrowband UVB) is similar to PUVA, but you don’t take a drug to sensitize the skin first. UVB works as well as PUVA for treating patches, but it is less effective for treating thickened plaques. It is typically given 3 times weekly in a type of cabinet similar to that used in PUVA.

Side effects of UVB are similar to those of PUVA, but UVB is thought to carry a lower risk of developing a second skin cancer later on. This is why it is sometimes chosen instead of PUVA. You also don’t need to take a dryg to sensitize your skin beforehand, or wear sunglasses to protect your eyes after treatment.

You can find more information on phototherapy from the British Association of Dermatologists on their website at: www.bit.do/bad-phototherapy.

**Photodynamic therapy** is used to treat some forms of skin cancer as well as other types of cancer and abnormalities. It may help people with skin lymphoma too. This treatment uses a light sensitising drug that is only activated by a certain wavelength of light. The drug is applied to the affected area as a cream. When the correct wavelength of light shines on the treated area, it activates the drug, which causes damage to the nearby cells.

You can find more information on photodynamic therapy from the British Association of Dermatologists on their website at: www.bit.do/bad-photodynamic.

**Radiotherapy**

Radiotherapy uses high energy X-rays and electrons to destroy abnormal cells. Skin lymphomas are usually very sensitive to radiotherapy. You may have local radiotherapy (to treat individual areas of lymphoma) or total skin electron beam therapy (to the whole skin surface).

**Local radiotherapy** is used in low doses to treat small, localised plaques, ulcerated (broken down) plaques or tumours, or for clearing up any areas of skin that haven’t responded to other treatments (such as PUVA). It is particularly useful for treating the face or parts of the body that aren’t well exposed to UV light in a PUVA or UVB cabinet (such as skin folds). You usually need 2–5 radiotherapy treatments to clear areas of affected skin.

Side effects are skin redness (similar to sunburn) and temporary loss of hair in irradiated areas.
Total skin electron beam therapy (TSEBT)

If you stop responding to skin-directed therapies used for early stage disease (stage 1B or 2A), or start developing tumours (stage 2B), you might be given total skin electron beam therapy (TSEBT). You may also have TSEBT for stage 3 mycosis fungoides or for erythroderma. TSEBT is useful for treating larger areas because it penetrates less deeply into the skin than conventional radiotherapy does. It works very well. Although it is unlikely to keep the lymphoma away forever, should it come back, you can have another course of treatment.

Because other topical treatments, such as chemotherapy and PUVA, also work well for early skin lymphomas, TSEBT is often reserved for treating skin lymphomas that have not responded to these treatments or have come back (relapsed).

TSEBT is only available at specialist centres, so you might have to travel to have treatment. You usually have treatment once a day, 4 or 5 days a week for 2–5 weeks. Each treatment takes about 30–45 minutes.

Side effects of TSEBT include fatigue, itching and peeling of the skin, temporary hair loss in the treatment area and reddening and swelling of the skin. These side effects usually settle down within 4 weeks of finishing treatment, though hair re-growth takes longer.

In the longer term, you may be left with skin dryness, some hair loss, changes in skin pigmentation (colouring) and scattered areas of dilated fine blood vessels. TSEBT can also increase your risk of other types of skin cancers (not the melanoma type) many years later, which are usually easier to treat than the skin lymphoma.

More information on TSEBT is available in a leaflet published by the Clatterbridge Cancer Centre at www.bit.do/TSEBT.

What are ‘systemic’ treatments?

Systemic treatments affect the whole body. You usually have a systemic treatment if your skin lymphoma is advanced when it is diagnosed, or is not responding to topical treatments. The aim is to control your skin lymphoma or put it into remission.

Systemic treatments include steroids, chemotherapy, immunotherapy, drugs called histone deacetylase (HDAC) inhibitors, a type of light treatment called extracorporeal photopheresis (ECP) and, in rare cases, a stem cell transplant.

Steroid tablets

Your doctor may suggest you take prednisolone, or another steroid tablet, for 2-3 weeks. The course of treatment may start with a high dose that then is gradually reduced. Alternatively, you may have a low dose of steroids for a longer period of time.
You may have steroid tablets on their own, for example, if you have a subcutaneous panniculitis-like T-cell lymphoma. Or you may have them alongside chemotherapy treatment, for example, as part of a combination of drugs known as ‘CHOP’.

Steroids have side effects if you take them for a long time. They can cause fluid retention and weight gain, increased blood pressure, raised blood sugar levels, mood changes or sleep disturbance. Note that side effects are less likely with a short course of treatment typical for skin lymphomas.

**Chemotherapy by mouth or injection**

Skin lymphomas can respond well to chemotherapy drugs, but unfortunately the effect tends to last just a few months. You usually have this type of treatment for more advanced skin lymphomas.

You may have some drugs on their own, such as chlorambucil, methotrexate or etoposide, which are all tablets you can take at home. Other chemotherapy drugs used to treat skin lymphoma are given intravenously (by injection into a vein). These include gemcitabine and doxorubicin (in a form known as ‘pegylated liposomal doxorubin’ or Caelyx®). Less often, you may be offered deoxycoformycin or fludarabine. There is no standard order in which these drugs are given. Your doctor decides what drugs are most suitable for you and in what order they should be given depending on your situation.

The British Association of Dermatologists produce a leaflet on methotrexate, which is available on their website at [www.bit.do/bad-methotrexate](http://www.bit.do/bad-methotrexate).

Your skin lymphoma might be treated with several chemotherapy drugs at the same time. The most common combination is CHOP: cyclophosphamide, doxorubicin (hydroxydoxorubicin), vincristine (Oncovin®) and prednisolone. For B-cell skin lymphomas, doctors often give CHOP with the antibody rituximab (R-CHOP). You usually have treatment several times over a few months, with each cycle of treatment taking 3 or 4 weeks.

There is a greater risk of troublesome side effects with combined chemotherapy than with other types of treatment. You are only likely to have combination chemotherapy if you have advanced skin lymphoma or a type of skin lymphoma that needs intensive treatment.

We have information on chemotherapy, which you can read on our website at [www.lymphomas.org.uk](http://www.lymphomas.org.uk). You can also print this information at home or, if you prefer, our helpline can send you copies. Please email at information@lymphomas.org.uk or call on 0808 808 5555.

**Extracorporeal photopheresis**

Extracorporeal photopheresis (ECP) is a version of PUVA used to treat the body’s white blood cells. You may have it if you have erythroderma or Sézary syndrome. Scientists think that this treatment stimulates the immune system, but they don’t completely understand how it works. It is only available in a few specialised centres in the UK.
To have the treatment, you first have some blood removed from one of your veins. The blood flows through a portable machine that separates out the white blood cells, mixes them with a photosensitising drug similar to psoralen and then exposes them to UVA light.

The treated white blood cells are then put back into the body through the vein. You have this treatment on 2 successive days every 2–4 weeks. People usually cope well with this treatment and it has few side effects.

You usually need between 6 and 9 ECP treatments before your doctor can assess how well it is working. If there isn’t much improvement after a few months, you may have other treatments alongside ECP, such as the immunotherapy drugs interferon or bexarotene. Some centres use ECP with immunotherapy from the very start in people with quicker growing types of Sézary syndrome (stage 4A).

The National Blood Transfusion Service have a leaflet on ECP, which you can access at www.bit.do/PUVA-ECP.

**Immunotherapy**

Immunotherapy stimulates your immune system to attack cancer cells instead of fighting cancer directly (as chemotherapy drugs do). These drugs make your immune system react to the cancer cells as if they were foreign to your body. It is still not clear how some of these immunotherapies work. Researchers believe that they slow down or stop the growth of cancer cells, prevent them from spreading, and allow the body’s immune system to be more effective at killing them.

These treatments are substances that the body produces naturally when it is fighting infections and other foreign invaders, but they can also be made in a laboratory. Examples of immunotherapies used to treat skin lymphomas are interferon alpha, retinoids and antibodies.

Interferon alpha occurs naturally in the body and boosts the immune system. As treatment, you have it as a subcutaneous injection (just under your skin). You can also have it injected directly into nodules and tumours.

Interferon is currently being tried on its own and alongside other treatments (such as PUVA) for skin lymphoma that is advanced or has come back.

Like other forms of treatment for lymphoma, interferon can cause a number of side effects, though nearly all are short-lived. It can cause flu-like symptoms such as fever and chills, nausea and loss of appetite. It can also make you feel very tired. Some people have low mood or even depression as a result of having interferon. If you develop troublesome side effects, the dose can be reduced.
Bexarotene (Targretin®) is an example of a retinoid. Retinoids are substances related to vitamin A. Doctors know that bexarotene can help in all stages of T-cell skin lymphomas, but is only licensed in the UK for people whose lymphoma has shown a poor response to at least one other systemic (whole body) treatment. You can have bexarotene for more advanced T-cell skin lymphoma (stages 2B, 3 or 4). You can have it either on its own or alongside another therapy, such as PUVA.

Bexarotene is a tablet that you take once a day. Most people need to take it for several months before noticing an effect. Side effects include headaches and skin reactions. It is quite common for levels of lipids (fats) to rise in your blood and your doctor should give you drugs to reduce your lipid levels from the start of treatment. Bexarotene can also lead to a drop in thyroid hormone levels. If this happens, you should be given thyroid hormone from the start of treatment. You will have blood tests regularly to monitor these side effects. You can’t take bexarotene if you are pregnant because it can cause birth defects.

You can find detailed information on bexarotene in the electronic medicines compendium at www.bit.do/EMC-bexarotene.

Antibodies are substances that recognise proteins on the surface of lymphocytes, including cancerous ones, and attach themselves to them. This mechanism can trigger the body’s own immune system to destroy the lymphoma cells. Rituximab (MabThera®) is an antibody that works against B-cell skin lymphomas and is used to treat many types of non-Hodgkin lymphoma.

An antibody called alemtuzumab (Campath®) can help some people with T-cell skin lymphoma that is advanced or that has come back after other treatments.

Other antibodies are in development and you may be offered them as part of a clinical trial. An example of such a drug is brentuximab vedotin, which is an antibody that attaches itself to the CD30 protein found on the surface of some skin lymphoma cells. Brentuximab vedotin is being studied in CD30-positive skin lymphomas and mycosis fungoides.

You have immunotherapy drugs through a drip (intravenous infusion) or sometimes by direct injection into skin lymphoma tumours (intralesional injections). Apart from the side effects that are common to most of the immunotherapy drugs, such as fevers and fatigue, antibodies can also cause a drop in your blood counts. Your blood counts will be closely monitored when you have immunotherapy.

We have information on rituximab, which you can read on our website at www.lymphomas.org.uk. You can also print this information at home or, if you prefer, our helpline can send you copies. Please email at information@lymphomas.org.uk or call on 0808 808 5555.
HDAC inhibitors

It is not quite clear how histone deacetylase (HDAC) inhibitors work. Researchers think that they act on cell genes, affecting the body’s immune response to lymphoma cells. There are 2 HDAC inhibitors that might be relevant to you: vorinostat (given as a tablet) and romidepsin (Istodax®) (given as an injection into a vein). At the moment, these drugs are only available in the UK as part of a clinical trial.

Early results of clinical trials show that these drugs might be helpful in people with skin lymphoma that is difficult to treat or has come back after treatment with chemotherapy or interferon. The main side effects are fatigue, feeling or being sick, diarrhoea, changes to heart rhythm and a drop in blood counts.

Other targeted therapies

Other drugs that act directly on the lymphoma might be available through clinical trials for advanced T-cell skin lymphomas. Check with your doctor to see if there is a trial that is suitable for you.

Stem cell transplant

A few people with advanced T-cell skin lymphoma have a stem cell transplant. This takes several weeks to complete. You need to be in hospital for at least part of that time. Because it is a complicated and relatively risky treatment, it is usually only done in people that are young and fit.

Stem cells are immature cells used by your body to replace damaged cells. When they are put into the bloodstream they travel to the bone marrow, where they develop into new blood cells. A stem cell transplant allows your bone marrow to recover from the damaging effects of chemotherapy drugs, allowing you to have much higher doses than would otherwise be possible. This helps to improve the chances of the chemotherapy successfully treating the lymphoma.

There are 2 types of stem cell transplants. For an autologous transplant, you have your own stem cells collected before you have chemotherapy. These are stored and then given back to you through a drip after your chemotherapy.

People with skin lymphoma usually have stem cells from a donor (allogeneic transplant). In this type of stem cell transplant, not only does the chemotherapy kill most of the lymphoma cells, but the donated stem cells recognise the lymphoma cells as ‘foreign’ and destroy any that are left after your chemotherapy. This is called the ‘graft versus lymphoma’ effect.

We have information on stem cell transplants, which you can read on our website at www.lymphomas.org.uk. You can also print this information at home or, if you prefer, our helpline can send you copies. Please email at information@lymphomas.org.uk or call on 0808 808 5555.
Taking part in clinical trials

Researchers are continually trying to find out which treatment, or combination of treatments, works best for skin lymphomas. Your doctor may ask you if you would like to take part in a clinical trial. Clinical trials allow new treatments to be evaluated and compared with more established treatments. Studying treatments in this way is required for new and hopefully better treatments to become available.

Some trials look into living with diseases. They study the experiences of people with skin lymphoma to find out more what support they need.

When you are enrolled in a clinical trial, you can be assured that you receive modern and appropriate treatments. It is always worth asking your consultant if there might be a trial you could join.

You don’t have to take part in a trial if you are offered one. If you don’t feel comfortable with the idea after discussing all the options with your medical team, you can say no. You will still receive the best current standard treatment and care available.

We have more information on clinical trials, which you can read on our website at www.lymphomas.org.uk. You can also print this information at home or, if you prefer, our helpline can send you copies. Please email at information@lymphomas.org.uk or call on 0808 808 5555.

Sources used

These are a few of the sources we used to prepare this information. The full list of sources is available on request. Please contact us by email at publications@lymphomas.org.uk or phone on 01296 619409 if you would like a copy.


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We continually strive to improve our resources for people affected by lymphoma and we would be interested in any feedback you might have about this information. Please visit www.lymphomas.org.uk/feedback or email publications@lymphomas.org.uk if you have any comments. Alternatively please phone our helpline on 0808 808 5555.

If you have found this information useful and would like to help make it available to other people coping with lymphoma, then please consider making a donation to support our work at www.lymphomas.org.uk/donate. We rely totally on voluntary donations. Thank you.

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