

# Cutaneous lymphoma – a patient’s guide

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Adapted, abridged and translated from *A Patient’s Guide to Understanding Cutaneous Lymphoma* (Cutaneous Lymphoma Foundation, 2<sup>nd</sup> edition, 2018, [www.clfoundation.org](http://www.clfoundation.org)).

This translation includes extracts amounting to about 20% of this guide which were originally published on Lymphoma Action’s webpages on skin lymphoma ([www.lymphoma-action.org.uk](http://www.lymphoma-action.org.uk)). Lymphoma Action has granted its approval for the extracts to be included in this publication and translated versions.



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# Cutaneous lymphoma – a patient’s guide

## 1 Introduction

### Scope of this publication

This is a guide for people affected by cutaneous (or skin) lymphoma. It is an amended, adapted and abridged version of information and materials originally produced by other organisations, most notably the Cutaneous Lymphoma Foundation, based in the US, and also by Lymphoma Action, based in the UK. The aim is to create a standard, accessible and universal guide that is available for use and translation in multiple languages throughout Europe.

Although this guide will be useful elsewhere in the world, readers should be aware that it has been designed primarily for use in a European context. Readers in Europe will know that healthcare systems and diagnostic, treatment and care practices vary from country to country. Further to this, Lymphoma Coalition Europe has supplemented the original source materials and text with content on the European context. However, it is beyond the scope of this publication to cover the situation in every European country. This publication takes a generalised approach to cutaneous lymphoma, including when covering access to, and use of, treatments and medical procedures, which may be different in each country.

Some treatments and procedures may be available as routine care in some countries, while others may not. Some may be accessible via clinical trials or compassionate use programmes, while others may simply not be currently approved for use in Europe. Similarly, with the treatments and skincare products referred to in this publication, we have used the generic name wherever possible, while also indicating a known brand name. Readers should be aware that brand names may vary from country to country.

For further information on access to treatments, you are advised to contact your local/national lymphoma or blood cancer support organisation or the Lymphoma Coalition.

### What is cutaneous (or skin) lymphoma

Lymphoma is a cancer that starts in cells called lymphocytes, which are part of our immune system. Lymphocytes are normally found in the lymph nodes (glands). They are also found in other lymphoid tissues, for example, in the spleen, the gut and the skin.

# The lymphatic system

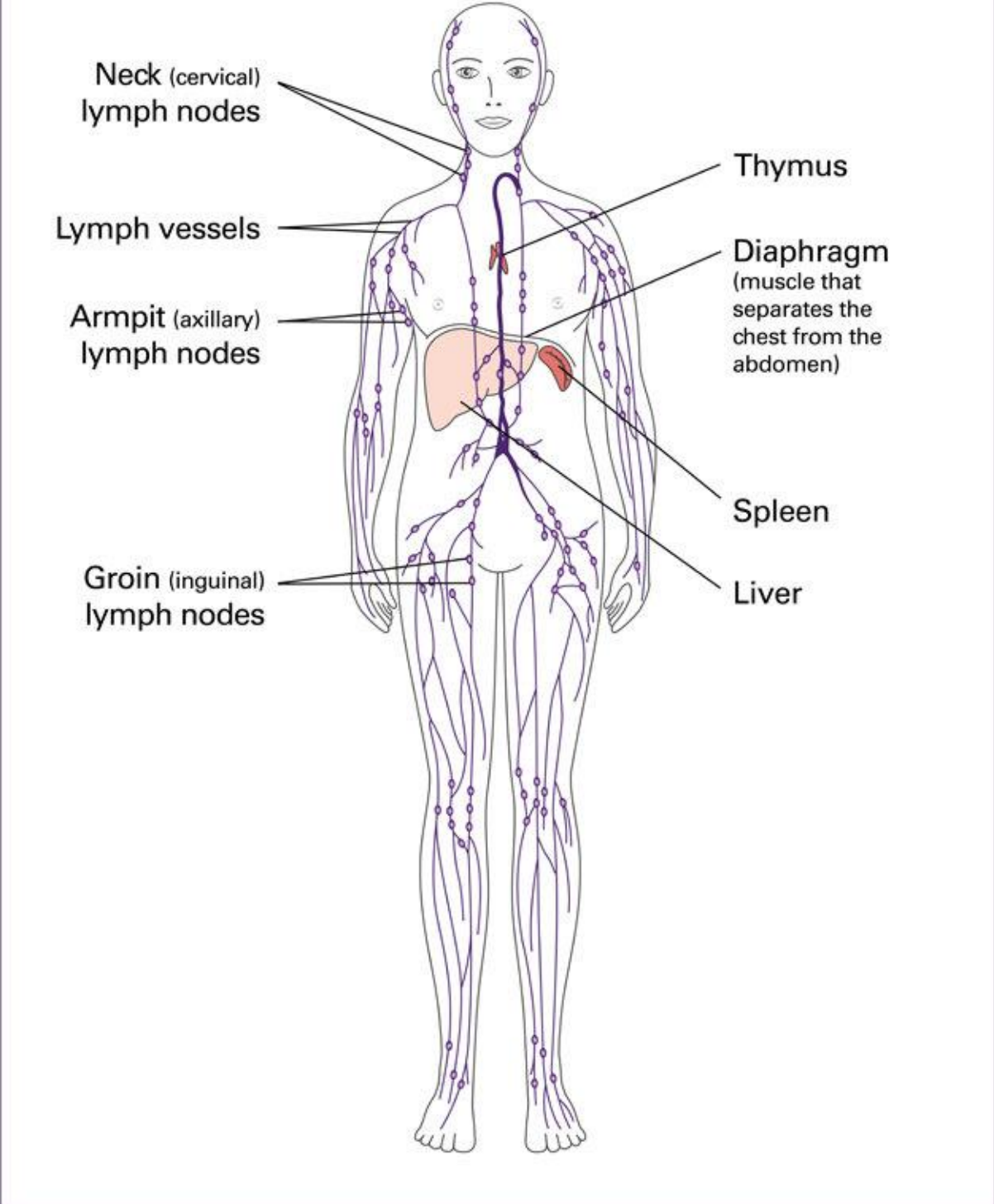


Figure: The lymphatic system (lymph vessels and lymph nodes are shown in purple)  
(Reproduced with permission from Lymphoma Action)

If lymphocytes start to grow out of control, or don't die after their normal lifespan, they can build up and form a cancerous collection of cells. This is a lymphoma. If the lymphoma starts in the lymphocytes in the skin, it is called a 'cutaneous' lymphoma, which means a lymphoma 'of the skin'.

Cutaneous lymphomas are rare. They have an estimated annual incidence of 1 in 100,000 people in Western countries. Although cutaneous lymphomas are a form of cancer, in many cases they are very slow growing and do not affect life expectancy. They behave more like a long-term (chronic) skin condition than like a cancer.

Please note that a lymphoma that starts somewhere else, for example in the lymph nodes, and then spreads to the skin is not a cutaneous lymphoma. Naming a specific cancer is based on the type of cells that are involved and from where it starts, not from where it may travel to. For example, if a patient has breast cancer and it migrates to a lymph node or to the bone, it's still breast cancer, not lymphoma or bone cancer.

## **Types of lymphoma**

There are many different types of cutaneous lymphoma. As with all forms of lymphoma, it is important to know your subtype and use the most specific name possible, so that you can understand the proper course of treatment, what to expect, and potential outcomes, as well as find the best information and support tailored to your subtype. Make sure you ask your doctor about your specific lymphoma subtype so that you can be equipped with the most up-to-date and thorough knowledge possible.

## **Diagnosis and treatment**

Cutaneous lymphomas are often difficult to diagnose because they develop slowly and because they resemble more common skin conditions, such as eczema or psoriasis. It can take years for some people to get their skin lymphoma diagnosed. Fortunately, early treatment is not vital for most of these lymphomas and they respond well to a variety of available treatments.

It is also important to know that cutaneous lymphoma is not contagious – it is not an infection and cannot be passed from person to person.

## **How to use this publication**

In the rest of this guide we cover the following:

- types of cutaneous lymphoma;
- diagnosis and staging;
- the role of the healthcare professionals;
- types of treatment and how to prepare for them;
- side effects of treatment;
- an overview of the differences for children and young adults who have cutaneous lymphoma;
- skin care;
- sexuality.

Finally, at the end of the guide you will find a glossary of the key medical terms that have been used in the text.

**Warning**

This information should not be used for the purpose of self-diagnosis, self-treatment or as an alternative to medical care. If you have any concerns arising out of the information contained in this report, you should consult your own doctor or medical advisor. If you suspect you have lymphoma, seek professional attention immediately.

**About Lymphoma Coalition**

Lymphoma Coalition (LC), a non-profit organisation, was formed in 2002 and incorporated in 2010 with the express purpose of facilitating lymphoma patient organisations around the world to form a community that could support one another's efforts in helping patients with lymphoma receive the best care and support. Lymphoma Coalition is committed to making sure that there is a level playing field of information globally for lymphoma patient organisations and patients, through education, information and advocacy activities. The need for a central hub of consistent as well as reliable current information was recognised as well as the need for lymphoma patient organisations to share resources, best practices, and policies and procedures. LC is made up of 76 patient organisations from 50 countries. The mission of the coalition is to be the global source for lymphoma facts and statistics; improve awareness and understanding of lymphomas; and build capacity for new and existing lymphoma groups.

## 2 Types of cutaneous or skin lymphoma

### Introduction

There are 2 types of lymphocytes: B lymphocytes (B-cells) and T lymphocytes (T-cells). They each have a different job in the immune system. Skin lymphomas can develop from either T-cells or B-cells, so cutaneous lymphomas are classified into two main groups, as follows:

- **cutaneous T-cell lymphomas (CTCLs)** are the most common kind of skin lymphoma. CTCLs often look red and dry like an eczema rash and can affect widespread parts of the body;
- **cutaneous B-cell lymphomas (CBCLs)** more commonly cause lumps in the skin, usually in 1 or 2 areas of the body.

According to the European Society of Medical Oncology's Clinical Practice Guidelines on primary cutaneous lymphoma (published in June 2018), in the western world, CTCLs make up about 75 to 80% of all primary cutaneous lymphomas (with mycosis fungoides (MF) being the most common type) and CBCLs 20 to 25%. However, different distributions are found in other parts of the world. For instance, in South-East Asia, CTCLs other than MF are much more common than in western countries, and CBCLs are much more uncommon.

### Cutaneous T-cell lymphomas (CTCL)

The two most common types of CTCL are:

- mycosis fungoides (MF); and
- Sézary syndrome (SS).

Other forms of CTCL include:

- primary cutaneous CD30+ lymphoproliferative disorders;
- subcutaneous panniculitis-like T-cell lymphoma;
- extranodal NK/T-cell lymphoma, nasal type (very rare in western countries, but more common in Asia and Central and South America).
- primary cutaneous peripheral T-cell lymphoma-not otherwise specified.

Most CTCLs are indolent (ie, chronic) lymphomas – non-curable, but treatable and usually not life-threatening.

In CTCL, malignant T-cells travel to the upper layers of the skin, causing a rash, which leads to diagnosis. CTCL is sometimes wrongly referred to as a skin cancer because it affects the skin, but this is not a precise use of the term “skin cancer”. Skin cancer is the designation for cancers that develop from other, non-lymphoid cells of the skin, including epidermal cells (which lead to squamous cell carcinoma) and melanocytes or pigment cells (which lead to melanoma).

### **Classic mycosis fungoides (MF)**

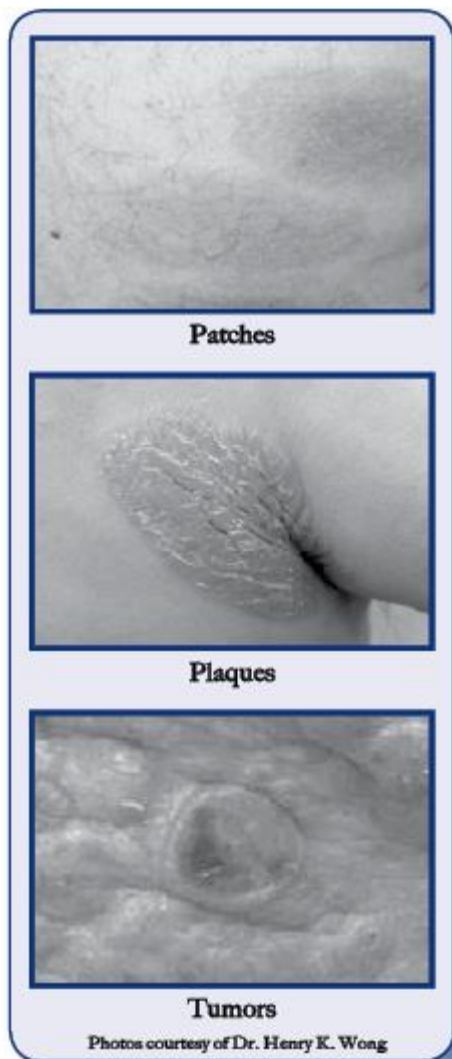
Mycosis fungoides is the most common form of CTCL. It is an indolent type, following a slow, chronic course, often over many years or decades, and very often does not spread beyond the skin. Over time, in about 10% of cases, it can progress beyond the skin. Most people will have the classic form of MF, but there are several rarer forms. Many patients lead normal lives while treating their disease, some remaining in remission for long periods of time.

MF can appear anywhere on the body but tends to affect areas of the skin protected from sun by clothing. Classic MF will usually start in the form of irregularly shaped, oval or ring-like (annular), dry or scaly patches (usually flat and either discoloured or pale). The patches vary in how they behave; disappearing suddenly, staying the same shape and size or gradually enlarging. They can appear anywhere on the body but will generally be found on the torso or buttocks.

It can also appear as thicker and slightly raised areas of skin, called plaques, which can itch and sometimes ulcerate (break down/weep). These will tend to appear on the buttocks or in the folds of the skin, and may cause hair loss in affected areas. In rarer cases, larger nodules or raised lumps may appear, called tumours, which can ulcerate or weep and be painful.

In a very few people, erythroderma may develop, where the skin becomes red, thickened and sore all over.

While it is possible to have all these types of lesions at the same time, most people who have had the disease for many years experience only one or two types of lesions, generally patches and plaques (see photograph).



Although generally an indolent, chronic disease, the course of MF in individual patients is unpredictable. It can be slow, rapid or static. Most patients will only experience skin symptoms without serious complications. About 10% will see the disease progress with serious complications. Unlike types of skin cancer, chiefly melanoma, MF almost never progresses to lymph nodes and internal organs without showing very obvious signs of progression in the skin.

#### *Rarer forms of mycosis fungoides*

Apart from the classic form of mycosis fungoides there are 3 other, rarer forms that behave slightly differently and look different under a microscope:

- **folliculotropic mycosis fungoides** affects hair follicles in particular. It commonly affects the head and neck and can cause hair loss. There may just be one patch, plaque or



tumour but most people have several. There may be small cysts or blocked pores. These are sometimes called ‘comedones’ (whiteheads) or ‘milia’ (milk spots) as they look like white bumps on the skin. Topical therapies, such as PUVA and chemotherapy ointments, don’t work well for this type of skin lymphoma. The suggested treatment may be total-skin electron beam therapy, PUVA combined with retinoid drugs, interferon or radiotherapy.

- **pagetoid reticulosis (Woringer-Kolopp disease)** usually shows up as a single scaly plaque, often on an arm or leg. It never spreads beyond the skin. It may be treated with surgery or a low dose of radiotherapy.
- **granulomatous slack skin (GSS)** is an extremely rare form of mycosis fungoides. Loose folds of skin develop in the armpits and groin. There is no agreed standard treatment for this type of CTCL. Surgery, radiotherapy, PUVA, steroid creams or interferon may be suggested.

For more information on treatments, see Section 5 of this guide.

### **Sézary syndrome (SS)**

Sézary syndrome is a less common but more aggressive type of CTCL that is related to MF but presents with very severe itching, total body redness (erythroderma), intense scaling of the skin and frequent hair loss. People with SS often lose large amounts of skin during the night and may find their bedding covered with skin flakes in the morning. They may also feel tired, have a fever and have enlarged lymph nodes. The malignant T-cells found in the skin are also seen circulating in the bloodstream.

SS is the only type of CTCL that always affects the skin and the blood. The skin may be hot, sore, extremely itchy, occasionally flaking and burning. Oozing of clear fluid from the skin is common. Because much heat is lost through the skin, people often feel cold. Symptoms may be accompanied by changes in nails, hair or eyelids.

### **Primary cutaneous CD30-positive lymphoproliferative disorders (PCCD30+LPD)**

There are two main types of these disorders, accounting for almost one-third of all diagnosed CTCLs:

- lymphomatoid papulosis (LyP); and
- primary cutaneous anaplastic large-cell lymphoma (PCALCL).

In both types a CD30 protein is found on the surface of the abnormal lymphocytes. Both disorders can be well-managed and have an excellent prognosis, with a 10-year survival of 100% for LyP and 90% for PCALCL.

#### *Lymphomatoid papulosis (LyP)*

Lymphomatoid papulosis (LyP) manifests itself with self-healing small red-brown bumps and spots on the skin (papules) that come and go. Lesions can be unnoticed or itchy and painful, taking 2-3 months to run their course. It can be persistent with frequent, recurring eruptions or it can disappear for an extended period of time before showing up again. Stress is often reported to trigger the breakouts.

LyP is usually classified as non-malignant or as a CTCL precursor (ie, about 1 in 20 people with LyP will go on to develop another lymphoma such as PCALCL, MF or Hodgkin lymphoma), though some experts say it is a very low-grade form of CTCL.

The disease can happen at any time in life – from early childhood to middle age, affecting both genders equally. Black-skinned individuals seem less affected than other racial groups.

#### *Primary cutaneous anaplastic large cell lymphoma (PCALCL)*

Primary cutaneous ALCL (PCALCL) is an indolent, slow-growing type of CTCL, with characteristic features that include single or multiple raised red skin lesions and nodules, which do not typically crust and have a tendency to ulcerate. These lesions may appear anywhere on the body and grow very slowly, so they may be present for a long time before being diagnosed.

### **Rare types of cutaneous T-cell lymphoma**

There are several rare types of CTCL, including:

- **Subcutaneous panniculitis-like T-cell lymphoma (SPTCL)** is slow-growing and can occur at any age. It is slightly more common in women. It starts in the fatty layer of the skin, just below the surface. There may be one or more plaques or nodules, often on the legs. Other more general symptoms may be present, such as fevers, low blood counts and weight loss. This condition responds very well to steroid tablets, which may be the only treatment needed. If further treatment is required, this may be in the form of local

radiotherapy (only to the affected area) or chemotherapy with doxorubicin. If the SPTCL is faster growing, suggested treatment may be a combination of chemotherapy drugs such as CHOP or even a stem cell transplant.

- **Extranodal NK/T-cell lymphoma, nasal type**, is a fast-growing type of lymphoma that is very rare in western countries but more common in Asia and Central and South America. It is sometimes seen in the skin, but can also start elsewhere and involve the skin. People with this type of lymphoma usually test positive for Epstein-Barr virus (EBV). In most cases, this type of lymphoma is treated with a systemic (whole body) chemotherapy regimen, such as SMILE (dexamethasone, methotrexate, ifosfamide, L-asparaginase and etoposide), combined with radiotherapy for localised disease.

#### *Primary cutaneous T cell lymphoma-not otherwise specified*

The ESMO Clinical Practice Guidelines include the following cutaneous lymphoma subgroups within the category of primary cutaneous T cell lymphoma-not otherwise specified:

- **primary cutaneous CD4-positive small/medium T-cell lymphoma** is a slow-growing lymphoma with a good prognosis (outlook). It usually appears as a single plaque or nodule on the face, neck or upper torso. Treatment is usually to remove the plaque or nodule surgically or attack it with radiotherapy. If the lymphoma is more widespread, suggested treatment may be either a chemotherapy drug called cyclophosphamide or an immunotherapy drug, interferon alpha.
- **primary cutaneous gamma/delta T-cell lymphoma** is a faster-growing type of skin lymphoma that usually occurs in adults. It most commonly shows up as patches and plaques on the arms or legs. Symptoms may also include night sweats, fevers and weight loss. Some people develop low blood counts and an enlarged liver and spleen. Suggested treatment is most likely to be a combination of chemotherapy drugs, or, in some circumstances, a stem cell transplant.
- **primary cutaneous CD8-positive aggressive epidermotropic cytotoxic T-cell lymphoma** is a faster growing lymphoma that occurs mainly in adults. It appears as widespread spots (papules), plaques and tumours on the skin. Affected areas may ulcerate. It can also affect the lining of the mouth. Your doctor is most likely to suggest treatment with a combination of chemotherapy drugs, or, in some circumstances, a stem cell transplant.

For more information on treatments, see Section 5 of this guide.

## **Cutaneous B-cell lymphomas (CBCL)**

The three primary types of CBCL are:

- primary cutaneous follicle centre lymphoma (PCFCL);
- primary cutaneous marginal zone B-cell lymphoma (PCMZL); and
- primary cutaneous diffuse large cell lymphoma, leg type (also known as PCLBCL-LT).

PCFCL and PCMZL are slow growing, indolent types with a good prognosis (10-year survival exceeds 90%), while PCLBCL-LT has a more unfavourable prognosis (with a disease-related 5-year survival of approximately 50%).

### **Primary cutaneous follicle centre lymphoma (PCFCL)**

PCFCL is the most common type of CBCL, most often being found on the head, neck or upper torso. Lesions are pink or red nodules, or slowly-developing tumours. They rarely become open sores or ulcers. Some patients find nodules in many locations on the body, but more often it is a single tumour or small group of nodules.

PCFCL responds well to radiation. You may have radiotherapy if 1 or just a few areas of your skin are affected. Occasionally, you may have surgery if the lymphoma is confined to 1 area. Both treatments work very well.

If the lymphoma is more widespread, treatment depends on how much skin is involved. If you have just a few scattered areas of affected skin, your specialist may monitor it and keep treatment in reserve for when you need it. This is called 'watch and wait'. People often feel anxious about 'watch and wait' because they feel as if nothing is being done to treat them. Rest assured that doctors know from research that the disadvantages of early treatment can outweigh the advantages.

If you have lymphoma in several areas of skin you may receive rituximab. This is an immunotherapy drug that you have intravenously (through a drip into a vein). Some people might have rituximab by subcutaneous injection (injection under the skin). A few people have treatment with a chemotherapy regimen (several drugs), often along with rituximab.

Immunotherapy drugs do not kill lymphoma directly. They stimulate your immune system to recognise the lymphoma cells as foreign to your body and kill them. Interferon alpha is another immunotherapy drug that you may have.

If primary cutaneous follicle centre lymphoma relapses (comes back), it can often be successfully treated with the same treatment you had the first time.

For more information on treatments, see Section 5 of this guide.

### **Primary cutaneous marginal zone B-cell lymphoma (PCMZL)**

PCMZL is the second most common form of CBCL and is related to a type of non-Hodgkin's lymphoma known as extranodal lymphoma of mucosa-associated lymphoid tissue (MALT) type. Patients find pink or red papules, nodules or, less frequently, tumours. It can occur anywhere on the skin but tends to show up on arms, legs or torso.

This is one of the few skin lymphomas with a known cause. Some people with a MALT lymphoma have evidence of a bacterial infection called *Borrelia burgdorferi*. If you have this infection, you have treatment with antibiotics first. When there is no infection, treatment is usually with radiotherapy or surgery, particularly if the lymphoma is only in 1 area.

In other respects, the treatment approach of PCMZL will be the same as for PCFCL (see above), as recommended in the ESMO Clinical Practice Guidelines.

For more information on treatments, see Section 5 of this guide.

### **Primary cutaneous diffuse large cell lymphoma, leg type (also known as PCLBCL-LT)**

PCLBCL-LT is a rare and more dangerous type of CBCL that looks much different under the microscope, and most of the time is found in the lower legs, more commonly in older women, where it can reach a very significant size.

PCLBCL-LT often grows into large tumours that extend deep into the fat of the body, growing quickly and becoming open sores. Unlike slow-growing types of lymphoma, this one has a high likelihood of spreading outside the skin.

Treatment is usually chemotherapy, with or without radiotherapy. The chemotherapy most commonly used is R-CHOP (rituximab together with cyclophosphamide, hydroxydaunorubicin, vincristine (Oncovin®) and prednisolone). You may have rituximab alone. If the lymphoma relapses, your doctor will probably suggest more chemotherapy.

## 3 Diagnosis

### Introduction

One of the challenges in definitively diagnosing cutaneous lymphoma is that its signs and symptoms are not the same for all patients, combined with the fact that some of the symptoms, especially when they are milder, are commonly confused with conditions like eczema or psoriasis, or fungal skin reactions (such as ringworm), or various skin reactions to drugs, certain substances or allergies.

### Key symptoms

Patches, plaques, papules and tumours are clinical names for a variety of skin presentations (also known as lesions) that can be clues that lead to diagnosis.

Patches are usually flat, possibly scaly, and look like a rash. Plaques are thicker, raised lesions. Papules are small, raised solid areas of skin that look like a rash. Tumours are raised bumps or nodules which may or may not ulcerate. To be called a tumour, generally a nodule has to be at least 1 cm in size, or greater. It is possible to have one or all of these types of lesions. Some people have the disease for years and only experience one.

Some people also have swollen lymph nodes, usually in the neck, armpits or groin.

A common symptom is itching, although some patients do not experience this.

### Process of diagnosis

#### In primary care

Diagnosis of the many subtypes of cutaneous lymphomas can vary and sometimes it takes a long time before it is confirmed. Regardless, the process for diagnosis is similar for all types.

Healthcare systems vary from country to country, hence the exact diagnostic process or system may look different depending upon which country you live in. However, usually someone who may have cutaneous lymphoma is most likely to go to a general practitioner (a doctor in primary or frontline care) if they have red or itchy patches of skin or if they have lumps anywhere. Many skin lymphomas look like more common skin conditions such as eczema or psoriasis. Many of them also develop very slowly, some over as long as 10–40 years. It may take a long time for the primary care doctor to rule out other conditions and then make a referral to a specialist. This might be a specialist in skin diseases

(dermatologist) or a specialist in diseases of the blood and lymphatic system (haematologist).

## **Assessment**

At the hospital or specialist clinic, the specialist will ask how and when the skin problem developed and how it affects you. They will carry out a physical examination, looking carefully at skin patches or lumps. A medical photographer might take pictures of the affected areas of skin. The specialist will also ask about your general health and about any other symptoms, such as weight loss or fevers.

## **Biopsy**

The doctor may suspect what the problem is, but will have to confirm the diagnosis with a skin biopsy. In a biopsy, the doctor numbs an area of affected skin with a local anaesthetic and removes a small piece of the skin. The sample is then examined under a microscope and sent for specialised tests to look at the cells and their genes and proteins in detail. These tests sometimes have to be done in a laboratory at another centre. Results of the biopsy can take 2–3 weeks to come back.

Diagnosing skin lymphoma is not always straightforward, even for a specialist. Further skin biopsies might be needed over the following few weeks or months. In some people, the skin rash does not look typical of lymphoma. In this case, there might need to be several biopsies taken over a few years before a full diagnosis can be made. This can be a frustrating and anxious time. It is important that the doctors make an accurate diagnosis and find out as much as possible about your skin condition so that you can have the most suitable treatment.

## **Tests, scans and examinations**

The history of how and when the skin problem developed, the physical examination and the results of skin biopsies help the medical team to diagnose the lymphoma. To find out more about the lymphoma and how it is affecting your body, you also need to have a full physical examination and blood tests. These tests are needed for 'staging' of the lymphoma.

During the physical examination, the doctor will feel for enlarged lymph nodes in the neck, under the arms and in the groin. No internal examinations will be needed. The blood tests will include blood cell counts and measurements of levels of some chemical substances found in the blood, including lactate dehydrogenase (LDH). This is an enzyme in the body that is used in the process of turning sugar into energy.



Further tests depend on exactly the type of lymphoma that is diagnosed and on the patient's general health. If the diagnosis is of the most common T-cell skin lymphoma, mycosis fungoides, and the physical examination and blood tests are normal, only a chest X-ray is needed.

Scans for T-cell skin lymphomas are not done as often as they are for other types of non-Hodgkin lymphoma. Scans may be needed if other investigations suggest there are lymphoma cells in the blood or lymph nodes (glands).

The most common type of scan for skin lymphoma is a computed tomography (CT) scan of your chest, abdomen and pelvis (area between your hip bones). Some people may have another scan called positron-emission tomography (PET), which may be combined with CT into a PET/CT scan. These scans capture images of the internal organs in great detail. Patients usually have them as an outpatient and they can take anything from 30 minutes to 2 hours. Not all hospitals or treatment centres can carry out PET/CT scans so it may be necessary to go to a larger medical centre rather than a local hospital.

A few people with suspected skin lymphoma have a bone marrow biopsy. A bone marrow biopsy involves taking a small sample of the bone marrow (the spongy tissue in the centre of some of the large bones of the body where blood cells are made) from the hip bone with a needle. The doctor numbs the skin over the bone with a local anaesthetic first. The sample is then examined under a microscope to see if it contains lymphoma cells. Painkilling medication can be taken to help with any discomfort after the procedure.

If the lymph nodes are enlarged, a lymph node biopsy may be necessary, which involves having a node removed under a local or general anaesthetic. This is sometimes called an 'excision biopsy'. The node is then sent to the laboratory to be examined under a microscope.

Some people may also have a fine needle aspirate (FNA) of a lymph node. This is where a fine needle is used to remove some cells from the enlarged lymph node without it being removed. An FNA is sometimes done before referral to the specialist clinic. However, after an FNA, a lymph node biopsy is still likely to be necessary as a FNA only samples some of the cells in the lymph node. This means abnormal cells might be missed.

All these tests are done to find out which parts of the body the lymphoma is affecting. They are also done to make sure that the lymphoma definitely started in the skin rather than spread there from somewhere else. This is important. Lymphomas that start inside the body behave differently to skin lymphomas and need different treatment. Once all the results are back, the medical team can decide on the best course of treatment.

The appearance of the skin, together with the physical examination and other test results usually provide:

- a diagnosis of the exact type of skin lymphoma – whether it is a T-cell or a B-cell skin lymphoma and exactly which type;
- information on whether the lymphoma is a slow-growing (low-grade or ‘indolent’) type or faster-growing (high-grade or ‘aggressive’) type;
- an indication of the stage of the disease.

The type, grade and stage of a lymphoma help the doctors predict how it is likely to behave in the future and decide how best to treat it.

### **What does ‘stage’ mean?**

The stage of the lymphoma describes how far it has grown. The stage guides the medical team when they decide on the treatment you need. There are two ways of staging cutaneous lymphoma that patients may encounter during their diagnosis. The first is the one that has previously been used in mycosis fungoides and Sézary syndrome. As with many other cancers, it has four stages, as follows:

#### *Stage 1*

The lymphoma only affects the skin (patches or plaques):

- Stage 1A means that less than 10% of the skin is affected.
- Stage 1B means that 10% or more of the skin is affected.

#### *Stage 2*

- Stage 2A means that there are patches or plaques on the skin and the lymph nodes are enlarged but they do not contain abnormal lymphoma cells.
- Stage 2B means that there are one or more raised lumps or tumours in the skin and the lymph nodes may or may not be enlarged but do not contain lymphoma cells.

### *Stage 3*

80% or more of the skin is affected, with generalised redness, swelling, itching and sometimes pain (erythroderma). The lymph nodes can be enlarged, but don't contain abnormal lymphoma cells. In addition:

- Stage 3A means there are few or no lymphoma cells in the bloodstream (erythrodermic mycosis fungoides).
- Stage 3B means there are moderate numbers of lymphoma cells in the bloodstream (Sézary syndrome).

### *Stage 4*

In addition to skin problems:

- Stage 4A means there are numerous abnormal lymphoma cells in the bloodstream (Sézary syndrome) or the lymph nodes contain lymphoma cells.
- Stage 4B means there is lymphoma in other organs.

You may also see the stages referred to as Roman numerals: I, II, III or IV.

'Early' stage means anything up to 2A. Most people have this stage of skin lymphoma when they are diagnosed. A few people have more advanced disease (stages 2B, 3 and 4). Very rarely, the blood is affected at diagnosis (stages 3B or 4A, also called Sézary syndrome).

### *TNMB staging*

Different staging systems are used for other, rarer types of cutaneous lymphoma. These systems are usually based on the TNMB staging system. TNMB stands for tumour, node, metastasis, blood. In its Clinical Practice Guidelines, ESMO says that the TNMB staging system should also be used for mycosis fungoides and Sézary syndrome.

This is a way of recording cancer stages and describes:

- how many areas of changed skin there are, how big they are and where they are (shown by a 'T' and a number between 1 and 3);
- how many lymph nodes are involved (if any) and which ones are involved (shown by an 'N' and a number between 0 and 3);
- whether any other parts of the body are involved (ie parts that are not skin or lymph nodes, shown by an 'M' and either 0 or 1);

- the extent to which the blood is affected at diagnosis by circulating Sézary cells (shown by a 'B' and a number between 0 and 2).

The TNMB system is useful because it is detailed and can flag up changes in stage over time. This can help doctors to monitor the patient's condition and help determine the best treatment.

## 4 The healthcare professionals

Depending on the country in which you live, a number of different healthcare professionals may be involved in your diagnosis, treatment and care, including the following:

- **Dermatologists** – specialists in skin diseases, with some specialising in cutaneous lymphoma.
- **Haematologists** or **oncologists** – specialists in blood cancers or cancers more generally.
- **Histopathologists, haematopathologists** or **dermatopathologists** – doctors who specialise in examining and testing tissues at the microscopic/cellular level in the laboratory
- **Radiation oncologists** or **radiologists** – doctors who specialise in radiation to treat cancer.
- **Nurse practitioners** – registered nurses with advanced education and training who can help doctors manage the disease, symptoms, and side effects.
- **Clinical nurse specialists** – specialised nurses who focus on patient care in certain conditions or treatment.
- **Clinic coordinators, patient navigators** or **care navigators** – healthcare staff tasked with looking at logistics, helping patients plan their course of treatments and providing guidance to patients as they move through the healthcare system.
- **Social workers** – trained staff who assess and plan for the social, emotional, environmental, financial and support needs of patients and their carers.
- **Pharmacists** – experts in medications who understand and can advise on the use and interactions of medicines, and help doctors review allergies and drug-drug interactions.
- **Psychologists, psychosocial therapists** or **counsellors** – trained professionals who can provide counselling and psychological support for patients so that they can deal with any emotional and mental health difficulties brought on by their diagnosis.
- **Nutritionists** – experts in diet and nutritional health who work with patients to find the right strategies regarding their food, drink and nutrients.

In some countries and hospitals, these professionals (or the majority of them) will work closely together as part of a multi-disciplinary team to coordinate the best treatment and care for individual patients.

Some patients find it comforting to involve a spiritual adviser from their faith community in their support team.

## 5 Treatment

### Before starting treatment

The more knowledge you have about what to expect before treatment, then the better able you will be to determine (with doctors, the treatment team and family/friends) the options you have, the benefits and disadvantages of different treatment approaches and, ultimately, what is best for you. While there is no one perfect pill to make things disappear, a combination of treatments, medications and other approaches – along with a heavy dose of patience – is likely to be your personal remedy. Take into consideration your own capabilities, lifestyle and work demands and other daily details before deciding on a treatment course.

The goal of treatment for cutaneous lymphoma is to put it into remission and clear up all patches, plaques, or tumours; to reduce the number of T-cells in the blood (for Sézary syndrome); and to relieve symptoms such as pain, itching, burning, and redness. However, there have been very few studies done to compare the effectiveness of one therapy for cutaneous lymphoma with another, so it is an individual matter of trial and error until your healthcare team finds the right combination of treatments for you. Furthermore, patients tend to handle treatments better when they maintain a healthy diet and exercise regimen and report any new symptoms or changes to their doctors during treatment.

Treatments vary from patient to patient, depending on symptoms, stage of disease, previous treatments and personal health profile (including your age, lifestyle and any other conditions you may have).

Treatments fall into two categories, either directed at the:

- skin (skin-directed therapies); or
- the entire body (systemic therapies).

For many early-stage patients, skin-directed therapies are effective. Cutaneous lymphoma patients with resistant skin disease or blood and internal organ involvement require systemic therapies. More aggressive therapies become necessary later in the disease, when malignant T-cells depend less on the skin and the disease moves beyond the skin.

In treating cutaneous lymphomas, unlike most other cancers, healthcare providers often use the same treatment more than once, such as phototherapy and radiation over the course of your treatment. What worked once will often work again. Although your doctors should keep a record of the treatments you have received, you may find it useful to keep your own records for personal reference.

To help you decide which treatment pathway is right for you, there are a number of good questions you can ask the healthcare team other than “what are side effects?” and “how well does this treatment work?”, such as:

- How confident are you in my diagnosis of cutaneous lymphoma?  
*[The less confident your doctor is in the diagnosis, the less risk you should take with therapies.]*
- What type of cutaneous lymphoma do I have?  
*[Knowing your subtype is important. Patients with mycosis fungoides should expect different treatment options to patients with Sézary syndrome or cutaneous B-cell lymphoma.]*
- What stage of cutaneous lymphoma am I at and what is my prognosis?  
*[This is an important question. In general, early-stage patients should consider topically-applied medications or ultraviolet light therapy rather than pills and IV medications because they are usually very effective, have fewer side effects, and the prognosis is usually very good. Because more advanced-stage patients have a worse prognosis, these patients may consider taking more risks with therapy choices.]*
- What are the short and long-term side effects? How likely are they? Are they reversible, and how long will they last?  
*[The answers to these questions are a major factor in many patients' decisions about treatment choice.]*
- How inconvenient are the treatment options? (How often? Where? For how long?)  
*[Unfortunately, all treatments create at least some inconvenience for patients, but each patient will view the details of their protocol differently as to how it fits into their life.]*

One way to help you track all the details and information is to create a chart of your options and the factors that are important to you. The tips below may also be helpful:



- If possible, find a doctor or treatment centre that specialises in cutaneous lymphoma or that is able to work or communicate with specialists elsewhere.
- It can be hard to remember what questions to ask when you are in the clinic. Write down questions in advance and record the answers after each visit so you don't forget.
- Take someone with you so you can talk over what the doctor said.
- Get a second opinion. Many people like to get information from several sources so they feel confident before making treatment decisions.
- Take time to consider your options and do not feel the need to rush into any immediate decisions.
- Make sure your healthcare team understands you. Share any and all personal details of your lifestyle, schedule, routine and concerns so that they understand as much about you as possible and what factors will affect your treatment choices. Depending upon your situation, one treatment may be better than another. Ask about all possible treatment options so that you can have full information before making decisions.

## **Relying on friends and family**

For skin-directed treatments, you won't need a friend or relative to drive you home. However, you may find comfort in the support of someone close to you when you go for phototherapies, topical therapies or radiation therapies.

When it comes to systemic treatments, especially for the first cycle before you know how you will react, it is a good idea to bring someone with you. A caring companion can allay nerves or fears and, in the event that you have an allergic reaction to a treatment and need relief from an anti-histamine agent like Benadryl, which can be sedating, you will take comfort in the presence of another person who can help you throughout the treatment experience and bring you home.

Even with chemotherapies, most people are not affected immediately upon receiving treatment. Related nausea, vomiting, and other effects take several days to occur, but it is always comforting to have someone at your side so that anxiety doesn't overwhelm you.

## **Managing anxiety**

Because some treatment methods can be confining or claustrophobic, you may experience feelings of anxiety before or during treatment. Integrative processes like hypnotherapy can be helpful in maintaining calm and equilibrium as you face such challenges. Complementary care is often helpful in achieving balance for your emotions and your physical symptoms.

Consider consulting with a nutritionist, reiki therapist, massage therapist, hypnotherapy expert, acupuncturist, acupressure therapist, yoga teacher, xi gong instructor or others to help you handle stress and maintain a sense of control.

## **Physical limitations during treatment**

Many patients experience fatigue or depression during their treatment. Knowing this is a real possibility helps you prepare for such an outcome by seeking out the help of a therapist to talk with during treatment and altering your schedule to account for reduced energy levels. Pace yourself. Do not overload your schedule with commitments. Try to postpone any non-essential appointments until your treatment course finishes.

Doctors and nurses are likely to ask if you have trouble falling asleep, if you have bad dreams and nightmares, and if you're feeling sad, upset or tired. It's worth knowing that some treatments can actually induce depression, so don't be afraid to seek out anti-depressants or other medications to ease such side effects.

## **Treatment options**

**Introductory note – as access to treatments and therapies will vary between countries, please be aware that not all the treatments listed in this section will be available in all European countries**

### **Skin-directed therapies**

Skin-directed or topical treatments are ones which are applied directly to the skin. They tend to be used for cutaneous lymphoma in its early stages, with the aim of controlling it, managing the symptoms and minimising side effects. Such treatments include:

- steroids;
- chemotherapy;
- phototherapy or light treatment (PUVA and UVB);
- radiotherapy.

For most topical treatments, patients may need to clean and prepare their skin. Patients find better penetration through the skin if their skin is well-moisturised beforehand. Bathing or taking a shower so the skin is well-hydrated before applying medication is a good idea. Many patients associate dry skin with their disease; moisturisers work better if the skin is soaked first and then sealed with emollient.

### *Topical steroids*

Topical steroids are the cornerstone of treatment for a host of skin conditions. They are not cosmetic, but actually kill lymphocytes. These agents possess multiple immune surveillance and anti-inflammatory effects. In early-stage disease, topical steroids can induce and maintain clinical clearing of lesions for extended periods of time. Itching is often markedly improved with the use of these agents. Topical steroids are packaged in a variety of ways including creams, ointments, lotions, solutions and gels. Different countries categorise the strength of topical steroids in different ways, so your healthcare team will advise on whether the treatments are mild, moderate, strong, very strong, etc. Some can be obtained over the counter at a pharmacy, while others will only be available by prescription.

### *Phototherapy/light therapy*

One of the most widely recommended treatments for cutaneous lymphoma, particularly in the early stages, is ultraviolet light therapy (phototherapy). The ultraviolet part of sunlight slows down the growth of skin cells, reduces inflammation and has long been known to help with many skin conditions, including cutaneous lymphoma. Patients with more extensive skin involvement (more than 30% of total body surface) are often prescribed phototherapy when topical treatments might be impractical.

Phototherapy is delivered as either ultraviolet B light (UVB) or ultra-violet A light (UVA), which is often combined with a light-sensitising tablet called psoralen. Psoralen combined with UVA is often referred to as PUVA. UVB therapy tends to be more widely available, with PUVA available at larger or more specialised treatment centres.

- UVB (also known as narrowband UVB or broadband UVB) refers to a shorter spectrum of ultraviolet light that causes sunburns. In a controlled environment, UVB phototherapy can produce marked improvements in patch and plaque stage lesions as well as control symptoms of itch. This form of UV light treatment does not require the administration of an oral medication. UVB can be delivered in private dermatology practices or hospital settings. Most patients receive 3 treatments per week, increasing in length of time from a few seconds to a few minutes. As the disease improves and remission is reached, the frequency of UVB treatments diminishes over time to 1 per week.
- PUVA refers to ultraviolet A (the longer spectrum of ultraviolet light) plus psoralen, a compound that makes UVA light biologically active in skin cells. PUVA treatment penetrates deeper into the skin and is helpful in managing patients with thicker

plaques or who have cutaneous lymphoma involvement at the hair follicle level. Similar to UVB therapy, PUVA is administered in a dermatology practice or hospital setting. Patients take the prescribed psoralen medication 1 hour before exposure to UVA light. Protective eyewear is worn for 12-24 hours after treatment ends. Once a patient has achieved clinical improvement with PUVA, a gradual taper in the frequency of treatments takes place with a goal of treatment delivery every 4-8 weeks.

### Preparing for PUVA

For patients receiving PUVA treatment, eye care is essential. There exists a theoretical, though minimal, risk of patients developing cataracts due to exposure to UVA lights. With that in mind, it's a good idea to have an eye exam prior to the start of treatment to determine that your eyes are healthy. Also, make sure you have protective eyewear, UVA-blocking wrap-around sunglasses, to wear on the days of your PUVA treatments until sundown.

Because you will be sensitive to light after undergoing PUVA, if possible you'll want to arrange your treatment sessions accordingly. Getting PUVA first thing in the morning may not be a wise choice as you'll likely spend the rest of the day going in and out of sunlight. Discuss your specific lifestyle demands and routines with your doctor to determine the best time of day to schedule light treatments.

Also discuss with your doctor the potential side effects of this or any treatment (which can include nausea) because certain natural remedies may alleviate such symptoms.

### *Topical chemotherapy*

Mechlorethamine (Mustargen®), also known as nitrogen mustard, is a cytotoxic (cell-killing) chemotherapeutic agent that is used topically in early-stage cutaneous lymphoma. This drug has demonstrated very good results when used in patients with limited or extensive skin involvement and recalcitrant disease after other skin-directed therapies have been attempted. A specialty pharmacist, also known as a compounding pharmacist, prepares the nitrogen mustard usually by mixing it with an ointment or gel. Valchlor® or Ledaga®, a pre-formulated nitrogen mustard gel, may also be prescribed. Topical nitrogen mustard is not absorbed systemically, so it does not cause nausea or hair loss. It can make subtle lesions more visible but this is not a sign of worsening disease. It should not be applied to the face or genitals. It can frequently cause irritation or an allergic reaction so you may be asked to apply the medication to a small area for 7-10 days to check for these side effects before wider use.

### *Bexarotene (Targretin®) gel*

Bexarotene or Targretin® gel is a Vitamin A derived agent that belongs to a larger class of medicines called retinoids, which activate retinoid receptors. Retinoid X receptors (RXRs) steer abnormal T-cells toward cell death. Targretin® gel is applied as a topical agent in the management of stubborn earlier-stage lesions. During the first few weeks of treatment with this agent, a topical steroid is often used together with Targretin® gel to decrease local site irritation.

### *Tazarotene (Tazorac®)*

Tazarotene cream is another retinoid. It binds to the retinoic acid receptors (RAR), which is believed to have anti-inflammatory effects. This cream may cause local irritation and dry skin.

### *Imiquimod (Aldara®) cream*

Imiquimod cream is an immune-activating agent. It stimulates your immune system to develop a response that identifies and destroys abnormal cells. The cream can only be applied to small areas of skin; as such it is best for isolated or refractory lesions. It may cause inflammation of the skin and in some cases flu-like symptoms.

### *Efudix*

Efudix is a cream used in the treatment of skin cancer and research indicates it may help some people with cutaneous lymphoma.

### *Tacrolimus*

Tacrolimus is an immunomodulatory ointment, classed as a non-steroid treatment for use in eczema. It may reduce inflammation in cutaneous lymphoma and can be used when steroid side effects are a concern.

### *Radiation therapy*

Radiation therapy has a long history in the treatment of cutaneous lymphoma, dating back to the early 20th century. Either photo (x-ray) or more commonly electron forms of radiation are used. Currently there are two forms of radiation:

- localised (also known as “spot”) radiation; or
- total skin electron beam therapy (TSEBT).

Both forms deliver only skin deep radiation with limited side effects.

Spot radiation, which delivers radiation to a limited skin surface area, may be in the form of an electron beam delivered from a distant source of radiation or brachytherapy, which is a form of radiation that is emitted from an applicator that is placed and contoured over the skin. Typically spot therapy is delivered anywhere from 2 to 15 treatments.

Total skin electron beam therapy (TSEBT) has undergone many modifications and advances over the years with the goal of delivering the radiation to the target tissue (skin) and minimising the damage to surrounding tissues. TSEBT is administered in an outpatient setting under the direction of an expert radiation therapist. Typically patients receive TSEBT daily for an approximate 3-10-week treatment cycle. As a skin-directed therapy, TSEBT is highly effective for patients with extensive skin involvement with plaque or tumour stage lesions.

### **Systemic therapies**

Systemic therapies affect the whole body and are usually used in advanced cutaneous lymphoma or where it is not responding to topical treatments.

#### *Extracorporeal photopheresis (ECP)*

Extracorporeal photopheresis (ECP) is an immunotherapy recommended in cutaneous lymphoma patients with an abnormal circulating T-cell population identified in the peripheral blood. During ECP, white blood cells are separated out and exposed (outside the body) to UVA light and psoralen and then re-infused. It is believed that the UVA-exposed white blood cells produce a vaccine-like effect against malignant T-cells. Other treatments (interferons, Targretin®) are frequently used alongside ECP therapy.

Nurses administer photopheresis treatments two successive days every 2-4 weeks in outpatient settings.

The more informed a patient is about photopheresis, the better the procedure will go. Certain blood tests are recommended before beginning photopheresis. Doctors often check a patient's T-cells, red blood cell count, and blood-clotting to have a baseline before beginning this course of treatment.

Eye care is an issue with photopheresis, so make sure you have protective eyewear before beginning treatment. The better hydrated a person is, the easier it will be to access veins for

treatment, so patients should make sure to be well-hydrated for several days before each treatment session. Many doctors recommend that patients tour the photopheresis unit before undergoing treatment and have their veins checked for accessibility.

Because the treatment takes time, bring reading material or films to watch to make the time go faster. You may well develop relationships with others in the treatment unit because many people remain on the same schedule and see familiar faces each time.

### *Steroid tablets*

Steroids are medications used to treat a variety of skin diseases. In cutaneous lymphoma, steroids in tablet form that are taken orally may be used to down-regulate inflammatory cells when the skin disease is extensive and associated symptoms are pronounced.

Examples of steroid tablets include cortisone, prednisone, and methylprednisolone.

Prednisone can be prescribed in tapering doses, reducing from 40-60 mg to 5 mg over the course of a few weeks. In other circumstances, low dose prednisone (10-20 mg) may be administered daily on a long-term basis. Some of the commonly encountered side effects with long-term administration include fluid retention, weight gain, increased blood pressure, increased blood sugar, increased appetite, stomach irritation, mood elevation, sleep disturbance, acne, delayed wound healing, weakened bones and muscles and increased infections.

### *Biologicals/immunotherapies/targeted therapies*

Biologic therapies (or immunotherapies) use the body's own immune system to fight cutaneous lymphoma.

### Interferons

Interferon is a naturally-occurring protein in the body that carries anti-viral, anti-tumour, and immunological properties, and can be manufactured in large amounts for use as a drug. In the management of advanced-stage CTCL, doctors seek immune stimulatory effects. Interferon alfa 2b (Intron A®) and Interferon gamma 1b (Actimmune®) represent two different categories of synthetic interferons used in treating this disease. Interferon is patient-administered by subcutaneous injection mostly 3 days per week. Laboratory tests to monitor complete blood count and liver function are required. Most often interferon is used in combination with other therapeutic modalities such as photopheresis.

### Retinoids

**Bexarotene (Targretin®)** capsules are a Vitamin A derived agent that belongs to a larger class of medicines called retinoids. Retinoid X receptors (RXRs) steer abnormal T-cells toward cell death. Oral bexarotene is a systemic agent approved for all stages of cutaneous T-cell lymphoma. Laboratory monitoring (blood tests) of both lipids and thyroid hormone are required during the course of this therapy.

#### HDAC inhibitors

**Vorinostat (Zolinza®)** is a histone deacetylase (HDAC) inhibitor oral agent for patients with progressive or persistent manifestations of cutaneous lymphoma. HDAC inhibition allows a cell's DNA to be transcribed so that cancer cells may die off. This medication requires frequent blood, electrolyte, platelet count and electrocardiogram (EKG) monitoring for the initial weeks of therapy. Vorinostat is used alone or in combination with other therapies.

**Romidepsin (Istodax®)** is another HDAC inhibitor agent available for patients with cutaneous lymphoma who have received at least one prior systemic therapy. Romidepsin is administered by intravenous infusion over 4 hours every week, for 3 weeks, followed by a rest week. Similar to other HDAC agents, monitoring of blood tests including electrolytes, magnesium and platelets is essential.

#### Proteasome inhibitors

**Bortezomib (Velcade®)** is an inhibitor of proteasomes, which the cells normally use to destroy unwanted proteins. In certain cancers, proteins that might otherwise kill the cancer cell are cleared too quickly. It is given intravenously every 4 days, day 1-11, within a 21-day cycle. Potential side effects include tingling in the hands and feet or changes in your blood counts.

#### Monoclonal antibodies

**Alemtuzumab (Campath®)** is directed against the CD52 antigen (surface marker) found on both B-lymphocytes and T-lymphocytes. It is typically administered in low-dose form by subcutaneous injection or sometimes intravenously 3 days per week for an 8-12 week course. Patients receiving alemtuzumab are prescribed oral antibiotics and antiviral medications to protect the immune system while on therapy and for up to 6 months afterwards.

**Brentuximab vedotin (Adcetris®)** is directed against the CD30 antigen (surface marker) found on some T-lymphocytes and other immune cells, and carries a chemotherapy agent that is released in the cancer cells. It is an intravenous infusion given every 3 weeks. The



most common side effects include tingling in the hands and feet, nausea, low blood counts, fatigue and diarrhea.

**Pembrolizumab (Keytruda®)** binds and blocks the activity of the PD-1 receptor expressed on T lymphocytes and other immune cells. PD-1 signaling inhibits the function of T cells that might otherwise attack cancer cells. Pembrolizumab is a form of immunotherapy as it functions to release the brakes on the immune system. It is an intravenous infusion given every 3 weeks.

**Rituximab (MabThera®)** is used in the treatment of many types of non-Hodgkin lymphoma, and also works in cutaneous B-cell lymphomas. It is increasingly available as a biosimilar (a non-branded version of the originating treatment that is biologically similar).

**Mogamulizumab (Poteligeo®)** targets the CC chemokine receptor 4 and is used for relapsed (come back) or refractory (become immune to a particular treatment) mycosis fungoides or Sézary syndrome.

### *Chemotherapy*

Chemotherapy administered as single agent or in combination may be used to treat the manifestations of advanced cutaneous lymphoma. Combination or multi-agent chemotherapy is usually reserved for advanced stages of disease. The following single-agent chemotherapy drugs are known to be “gentler,” so they do not cause much hair loss or vomiting. With most of these agents, doctors will monitor blood counts and kidney and liver function.

**Methotrexate (Matrex®)** is an anti-metabolite agent used for a host of immune-based diseases. It interferes with folic acid metabolism in cancer cells. In cutaneous lymphoma, this is administered in oral form usually by pill weekly.

**Pralatrexate (Folotyn®)** is used in the treatment of transformed mycosis fungoides and other aggressive non-Hodgkin lymphomas such as peripheral T-cell lymphoma. It is a folate metabolic inhibitor which targets the same pathway as methotrexate. Patients receiving pralatrexate therapy take a daily dose of folic acid and receive Vitamin B12 injections every 8 to 12 weeks. It is delivered intravenously usually once weekly for 3 weeks followed by a rest week.

**Liposomal doxorubicin (Doxil®)** is a special formulation of doxorubicin, a drug that interferes with DNA activity in cancer cells. The liposome, or microscopic sphere of fat surrounding the doxorubicin, minimises side effects and improves activity. Doxorubicin is delivered by intravenous infusion every 2-4 weeks. Certain patients will have an evaluation of heart function performed prior to starting therapy.

**Gemcitabine (Gemzar®)** is a chemotherapy drug that works by interfering with DNA production in cancer cells. It is delivered by intravenous administration in various schedules.

#### *Multi-agent combination chemotherapy*

The use of chemotherapy drug combinations in cutaneous lymphoma should be discouraged because they have never been proven to be more effective than sequential single agents, and they are always much more toxic. Intravenous combinations such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), ESHAP (etoposide, solumedrol, high-dose ara-C, and cisplatin), and GND (gemcitabine, navelbine, and doxil), or oral therapy PEP-C (chlorambucil, cyclophosphamide, etoposide, prednisone), may be used when no other therapy is available, or in rare circumstances as a way to produce brief responses in preparation for a bone marrow transplant.

#### *Stem cell transplant*

Bone marrow or stem cell transplantation is considered in cases for patients with advanced disease. Allogeneic stem cell transplantation is the recommended transplantation method for advanced cutaneous lymphoma patients. However, most cutaneous lymphoma patients will never need to evaluate this option. Allogeneic stem cell transplantation refers to a procedure where healthy stem cells are transplanted from one individual to another. Sources of stem cells include bone marrow, peripheral blood or umbilical cord blood. Hematopoietic stem cells can grow into any of the cells found within the bloodstream. They make blood cells and the components that your immune system needs to function. During a transplant, your body is infused with healthy stem cells which then grow and produce all of the different parts of the blood that both your body and your immune system need.

### **Clinical trials**

The best way to identify effective drugs and find new ways to treat cutaneous lymphoma is through ongoing research and testing including clinical trials. Because this disease is less common than other forms of cancer, scientists depend upon willing participants. Clinical trials are crucial in identifying prognostic strategies and determining optimal doses for patients.

If you are interested in participating in a clinical trial, talk to your doctor about which ones may be appropriate and available for you.

## 6 Coping with treatment side effects

Treatments are intended to relieve the symptoms of your disease, but often the side effects from the treatments may cause discomfort and make daily life challenging. Let your doctor know if you experience any side effects such as:

- skin irritation and inflammation;
- redness, rash, and itching;
- heat, tenderness, or burning sensation (like a sunburn);
- fatigue or depression;
- flu-like symptoms.

Many oral medications and IV chemotherapy can also cause change in appetite or loss of appetite entirely. If you experience chronic nausea, vomiting or weight loss, be sure to seek out a nutritionist to discuss options for increasing nutrient intake in a way that your body can handle and maintain. Other problematic side effects can occur in the gastro-intestinal (GI) tract, for example, diarrhea or constipation. Try altering the time of day when you take the medication, which may alleviate appetite or GI side effects.

Many cutaneous lymphoma patients experience extreme fatigue as a side effect of treatment. If this is the case, try to anticipate it and pace yourself, building rest periods into your day as needed, and adjusting your work schedule wherever possible. Reorganising your life to accommodate the changes that come from this disease and its treatments is important. It is also essential to focus on eating right, getting enough sleep and being kind to yourself rather than checking things off a regular to-do list and pleasing others. Self-care is essential and will affect the outcomes of your treatment and healing process.

If you experience treatment-induced depression, talk with your physician and don't hesitate to request anti-depressants to help boost your mood and energy.

Always maintain hydration. Dietary supplements and protein drinks can help maintain nutrient intake and prevent weight loss.

Generally, side effects may be more or less intense at times, some with cumulative side effects, and some worsening as treatments increase. Patients should understand that each specific treatment protocol leads to its own set of side effects, so communicate with your doctor.

Skin-related issues can be addressed with soothing emollients, extra moisturisation, and increasing fluid intake to keep the skin moist. Apply moisturisers immediately after bathing. Wear non-irritating clothing and protect your skin from the sun. Watch for signs of infection and report any as they appear. Protective clothing and/or protective dressings may help if a particular area is troublesome or painful.

For excessive itching, oral antihistamines and other medications that help with nerve-related itching are available and can offer relief. Good skin care goes hand in hand with healing. Apply topical agents that your healthcare provider prescribes, avoid scratching lesions, and take recommended antihistamines.

If you experience heat or a burning sensation in the skin, there are remedies that can help. Cool soaks, moisturisation, and cooling agents with menthol can be helpful. In addition, consider cold compresses or ice applications for severely affected areas.

Always check with your doctor or a pharmacist or both before using any over-the-counter products or supplements to make sure they do not contain harmful ingredients.

## 7 Children and young adults

Cutaneous lymphoma is a rare disease in general. It is even rarer to find it in children. In Europe and the United States, up to 5% of all cases are diagnosed before the age of 20. However, in some parts of the world, such as the Arab populations in the Middle East, children constitute up to 60% of the patients with mycosis fungoides. Prevalence rates differ greatly among geographic regions and populations.

Many researchers believe that mycosis fungoides, in young people in particular, may have a genetic component and may be triggered by environmental factors. In fact, there may be a link between skin type and early incidence of this disease. For example, African Americans are diagnosed with mycosis fungoides before the age of 40 significantly more often than Caucasians.

Despite the infrequent occurrence of this disease in children, the principles of diagnosis remain the same regardless of age. However, there are some special considerations regarding this age group. For example, physicians devote extra attention to determining a course of treatment for younger patients, weighing the benefit of therapy against any potentially long-term complications more prevalent among the pediatric age group than adults. Phototherapy is the preferred treatment for mycosis fungoides, but if a child is very young, they are technically unsuitable for it.

Among children, the distinguishing features of this disease can be misleading, making it even more difficult to diagnose cutaneous lymphoma in children. Another complicating factor is that the medical community is usually hesitant to perform biopsies on children unless there is absolute indication of the presence of this disease – and biopsy is the best way to firmly diagnose cutaneous lymphoma. For these reasons, diagnosis in children is often delayed much longer than in adults. The prognosis for children is similar to adults.

When children have chronic inflammatory dermatitis, which are ongoing skin conditions that are not classified with a certain diagnosis (an unusual presentation of psoriasis, eczema or atopic dermatitis), physicians must consider the possibility of mycosis fungoides. The challenges of diagnosing and treating such complex and often ambiguous diseases are magnified by parents' concerns, expectations, and a child's own level of understanding.

It has only been in the last several years that investigators have truly begun to understand the characteristics of pediatric presentations of cutaneous lymphoma as more data has become available.

Treatment decisions for pediatric patients are difficult to make because younger patients are more sensitive to the adverse effects of certain therapies. Of particular concern, given their young age, pediatric patients have more time to develop and experience the long-term adverse effects of anti-cancer therapies. When treated with oral/topical psoralen plus ultraviolet A (PUVA) or narrowband UVB phototherapy, local radiation therapy, or total skin electron beam therapy, younger patients are inherently subject to greater risk for developing skin cancers because they have a longer expected lifetime ahead of them.

Similarly, pediatric patients in need of systemic chemotherapy may develop leukemia later in life, and patients taking retinoids such as isotretinoin (Accutane®) are at risk of premature stunting of bone growth. Topical steroids and nitrogen mustard may be among the safer treatments for early-stage disease with less cancer risk. In the end, proper treatment for pediatric cutaneous lymphoma is individualised to the unique occurrence and needs of each patient.

Although rare, some younger adults are diagnosed with cutaneous lymphoma. For patients who are sexually active, this can be a devastating diagnosis. The hardest part, say some patients, is the physical presentation of the disease – especially if you're in an active workplace or engaging in relationships. A facial rash or other obvious outbreak can make you self-conscious.

*“You feel like you're a broken individual, like you're not whole anymore.”*

*Patient*

Treat your diagnosis like any other serious medical diagnosis – this is cancer, after all, and if you put it in those terms to colleagues, friends and partners they may be more understanding.

## 8 Skin care

Cutaneous lymphoma, as well as some treatments for this disease, can make skin dry, itchy, and scaly. Because cutaneous lymphoma occurs in the skin, with effects that can make the skin irritated, the skin care recommendations for patients are similar to those for patients with other chronic skin conditions such as eczema. The following may help with your skin care routine.

### Moisturising

Adequate moisturising is a very important part of keeping skin healthy as it helps thicken the barrier function and keeps our skin feeling comfortable. Keeping skin moisturised and decreasing dryness can alleviate itch, too. A simple and effective way to combat dry skin is to frequently apply moisturisers or emollients.

With so many different moisturisers on the market today, it may be difficult to decide which ones to use. Here are some tips to use when comparing products:

- Ointments and creams provide the greatest moisturising power. They are the best moisturising products to use because they contain a high content of oil that leads to greater penetration and more staying power.
- Avoid lotions as they are made with mostly water and little oil. Avoid gels as they contain alcohol or acetone that can be drying to skin. Avoid moisturisers that contain perfume and dyes.
- Apply moisturisers frequently, at least 2 to 3 times daily, to keep skin from drying.
- You may need to try different products before finding those that work best for you.

Moisturise the skin while damp because moisturising lotions and lubricating ointments can trap water against the skin and provide longer relief from dryness. When skin gets dry and flaky, wet the skin with water then apply a lubricating ointment with lanolin such as petroleum jelly. Patients often need to lubricate and moisturise skin many times. For information on acceptable moisturisers it may be worth contacting a local or national eczema organisation in your own country.

### Dryness

Dryness accompanies almost all presentations of cutaneous lymphoma.



Because of this, dryness (also known as xerosis) is the most common cause of itching, which contributes to a high degree of patient discomfort.

There is, of course, wide variability as to how dryness shows up with cutaneous lymphoma. Some patients have dry patches primarily during colder months when humidity is low. Other patients experience shedding of dry flakes of skin throughout the year as their disease involves more and more of the skin's surface. In patients with extensive skin involvement, especially those with redness (also known as erythroderma), diffuse shedding of skin can occur (also known as desquamation).

This can be concerning for patients. Some feel embarrassed when skin noticeably sheds or flakes in public and at home. These feelings are understandable and completely normal. Patients can cope with these symptoms in a variety of ways including lubricating the skin with thick layers of ointment-based products such as Vaseline® or petroleum jelly, which can reduce shedding and scaling for at least 2-5 hours before needing to reapply.

Adding fragrance-free bath oils to bath water and soaking for 10 minutes several times a week can ease flaking and shedding for some patients. Be aware that this can cause skin to be very slippery so patients should be careful when emerging from the bath.

Over-the-counter products that contain lactic acid can help remove dry flakes from scaly skin. Most of these products are fragrance-free, and contain 12% lactic acid or 10% urea.

## **Itch**

Most people with cutaneous lymphoma experience itching (also known as pruritus) and often are unsuccessful in finding relief from this chronic, aggravating symptom. Little was known or investigated about the basic mechanisms that underlie itch until the past several years.

Patients who experience itch will begin scratching the area that's itching, which sends a signal to the brain and back to the skin to initiate an itching frenzy. It can be helpful to apply an ice pack, bag of frozen vegetables, or crushed ice in a seal-able plastic bag covered in a paper towel and apply it to the itchy area for as long as 10 minutes. This will "put out the fire" so to speak. Think of itching in this disease like a wildfire – if the instance of itch can be eliminated it can be prevented from spreading all over the skin.

For most patients with cutaneous lymphoma, itching can range from a minor irritation to a tormenting sensation that can significantly decrease a patient's quality of life. Cutaneous lymphoma-related itching is particularly troubling since it can start small and take over the body. In a study conducted by the late Dr. Marie-France Demierre of the Boston University School of Medicine in the USA, 88% of cutaneous lymphoma patients ranked itch among the top causes of distress associated with this disease.

Pruritus is a physiological condition at its root, and appropriate treatment is more likely to be prescribed if the degree of suffering is explained in detail to your doctor. When meeting with your doctor, try to describe the severity of itchiness on a scale of 1 to 10, with 1 being little to no itch and 10 being unbearable and preventing smooth daily functioning.

Although a definitive cause for itch has yet to be determined, some treatments are available. A common first-line treatment is antihistamines. Some options include Allegra® and Claritin® for daytime use or Benadryl® and Atarax®, which are more commonly used at night because they have sedative properties. Some of these medications can be obtained over-the-counter while others require a prescription. These medications block redness, swelling, and itch. For most sufferers, itching becomes noticeably greater just prior to falling asleep, so sedative antihistamines can be particularly effective.

There are easy home remedies to alleviate itch, too. Soak for 15 minutes in an oatmeal bath. Apply a cold compress to a particularly itchy area to calm irritation and reduce the urge to itch. Apply open-wet dressings which are a simple, safe and effective way to alleviate itch as well as decrease redness, burning, and weeping of skin lesions. Ask for detailed instructions about how to apply these dressings when you visit your doctor.

There are other medications that help alleviate itch. Some options are:

- Gabapentin (Neurontin®) is an anticonvulsant prescribed for individuals prone to seizures, which has been effective in treating itch.
- Mirtazapine (Remeron®) is an antidepressant prescribed for individuals at bedtime who have difficulty sleeping due to itching.
- Aprepitant (Emend®) is a prescription medication used for preventing chemotherapy-induced nausea and vomiting, which has been shown to be effective in reducing itch.
- Phototherapy is a viable treatment option for patients with mycosis fungoides, especially those suffering with itch.

- Topical steroids may be effective when used in conjunction with other treatment methods but tend to be impractical in treating severe cases due to the large surface area.
- The most effective over-the-counter lotions for less severe cases are those that contain pramoxine, an anesthetic that reduces the transmission of the itch sensation from skin nerves, or menthol as its cooling properties can overpower the itching sensation. Be cautious of using analgesics as they have been shown to aggravate itching episodes.

In addition, some relief of itch has been reported through alternative methods such as acupuncture and biofeedback.

## **Fissures**

A fissure is a straight or linear crack in the skin, which often extends into the second layer of skin, where it causes considerable pain and discomfort. These primarily occur on the palm side of the fingers and hands. These fissures can make it difficult to use fingers for fine motor skills like dressing, writing, cooking, or eating. Fissures can happen at any time, to anybody, particularly during winter and especially in individuals who have thick, scaly skin on their palms because of an illness like cutaneous lymphoma.

Most doctors believe this occurs in patients with scaly skin because a small crack in the skin gets infected with bacteria that causes a crack to widen and become more painful. It happens more often in winter than summer because the humid conditions of the summer minimise fissuring by virtue of increased moisture.

Patients can take preventative measures to avoid fissures by keeping thick, scaly hands and feet moisturised frequently throughout the day with fragrance-free creams or a thick layer of petroleum jelly products. This may include applying a thick layer at bedtime to palms and soles and sleeping with white cotton gloves or cotton socks.

Once fissures form, it's important to clean them at least twice a day with soap and water and apply an antibiotic ointment to cracks or fissures to speed healing. Most dermatologists encourage patients to avoid triple antibiotic ointment (such as Neosporin®) because the neomycin ingredient in it can be an allergen that causes a rash. If fissuring does not improve, patients should consult with their doctor for prescription-strength topical antibiotics.

Occasionally, a fissure is so deep and wide that doctors may instruct patients to use superglue to glue the fissure together. If instructed to do so, patients should clean the fissure

with soap and water and dispense a tiny droplet of superglue in the fissure, pinching surrounding skin together for 60-90 seconds to help close it. It dries very quickly. However, patients need to be careful not to glue their fingers together.

In addition, consider using a product such as New Skin®, an antibiotic solution containing a light adhesive that also provides a barrier over fissures and a mixture of chemicals that creates a polymer layer which binds to the skin, keeping away dirt and germs and retaining moisture. Look for products named liquid band-aid or something similar.

## **Infection**

Skin infections are not uncommon in cutaneous lymphoma patients. Some patients with more extensive skin involvement may find that their skin is colonised with a bacteria called staphylococcus aureus. While some forms of staph bacteria exist normally on our skin, this version is the most common bacteria to infect the skin of patients with cutaneous lymphoma. When they occur, infections usually arise in skin lesions of cutaneous lymphoma. Infection is the greatest concern for cutaneous lymphoma patients because, if left untreated, its consequences can be life-threatening.

With that in mind, it's important to recognise the signs of skin infection and know when to contact your doctor. Signs of skin infection may include the following:

- a red area on the skin that is painful, swollen, and may be scabbed over or weeping fluid;
- tender redness surrounding a skin lesion;
- a skin lesion that does not itch but hurts;
- lesions that develop a thin, yellowish crust.

You should contact your doctor urgently if any of the following occur (which could indicate the beginning of cellulitis or blood infection):

- you develop fever and chills associated with abrupt onset of fatigue and weakness;
- all of your skin lesions suddenly become tender and red, especially with streaks of redness, extending from the lesions toward your trunk (armpits or groin).

## **Bathing and showering**

When bathing or showering, be sure to use lukewarm water – not hot – as hot water tends to melt the natural oils from our skin that keep it hydrated and can leave our skin drier than before. Hot water also causes a surge of blood flow to the skin, which can increase itching once patients emerge from the shower or bath. Excessively hot water may temporarily relieve itch, but it is not recommended because it may aggravate skin and worsen itch long-term.

Keep baths and showers brief, no longer than 15 minutes. Also, the best time to apply emollients is after bathing, when skin is still moist. Applying moisturiser (or topical medication in an emollient) on damp skin helps seal hydration into the skin's outer layers.

You may reduce the amount of itching and skin infections with the use of “bleach baths,” which is like turning your bath into a swimming pool. Bleach baths entail soaking for 15 minutes in a  $\frac{3}{4}$  full bath tub with warm water and  $\frac{1}{4}$  cup of plain household bleach (fragrance free, sodium hypochlorite 6-8%) three times a week. Bleach baths not only may reduce the risk of infection but they have been shown to be anti-inflammatory.

## **Soaps**

With regard to soap, less is better. When patients feel the need to use soap, try a moisturising soap that contains extra oils. Avoid heavily-fragranced soaps because, when a product is infused with fragrance, it must first be dissolved in alcohol, which is drying to the skin. Fragrances can be irritating, as well, and potential allergens. Choose soaps and moisturisers that are labeled fragrance-free. Avoid antibacterial or deodorant soaps as they may be too drying.

## **Laundry detergents**

Laundry detergents can affect skin, too. Be sure to use a fragrance-free detergent. Also, fabric softeners often have fragrances so look for one that is fragrance-free. Fabric softener sheets added to the dryer are often the worst product for patients with sensitive skin because the fragrances directly coat clothing, which comes into direct contact with the skin and can be a constant source of irritation.

## **Sun protection**

Too much sun is damaging to skin. Use sunscreen, wear a hat with a brim, and consider wearing long-sleeves and trousers year-round. If you receive light therapy as part of your treatment, your doctor may advise you to wear UV-blocking sunglasses. However, for some

people with cutaneous lymphoma, abbreviated periods (15-20 minutes) of sunlight may be beneficial for your skin. Discuss this with your healthcare team to determine which protocol is best for you.

## **Other tips**

You can keep your skin comfortable by also following these helpful tips:

- Wear loose-fitting, comfortable fabrics that ‘breathe”. Cotton is best. Avoid rough, scratchy fabrics like wool. Avoid tight-fitting clothing.
- Do not scrub skin or rub harshly.
- Keep fingernails short to prevent infection and skin damage.
- Avoid getting overheated; sweating worsens itch.
- Find ways to manage stress as it can trigger flare-ups in cutaneous lymphoma and increase itching.

# Chapter 14 – Sexuality

## Intimacy

Being intimate can be challenging when you have cutaneous lymphoma for the simple reason that plaques, lesions and rashes can be so uncomfortable that you don't want to be touched. Also, sometimes people with cutaneous lymphoma feel self-conscious or uninterested in being intimate because of changes to their physical appearance. Some symptoms make the skin feel so raw that a physical experience would be aggravating. From itch to burning to lathering up with ointment after a shower, the details of this disease can definitely create an obstacle to intimacy.

Couples work through this. There are times when you just won't be sexual, and hopefully your partner understands this. Other times, when there aren't flare-ups, you'll probably feel as sexual as you normally would. Some younger patients even go on to have children despite their disease.

Just like you need a solid support system around you to help you weather the ups and downs of this disease, you also need a partner whose love and understanding runs deeper than the physical.

*“When you have a disease, any kind of terrible disease, you need a partner who's very, very understanding. It's frustrating, from the care side, to not know what you can do to make the person you love feel better.”*

*Patient*

Communication is vital throughout the course of this disease. Letting your partner know when it's alright to touch and when it's not, explaining gently that it's not a rejection of the other person but a symptom of the condition of your skin, is important.

*“You have to tell your partner, ‘I love you with all my heart, but I can't explain what I'm going through’ and I'm sure the partner will understand, knowing that you love each other.”*

*Patient*

Riding the roller coaster of a chronic disease can actually help you grow stronger in love.

## Fertility

Cutaneous lymphomas are most often chronic illnesses. Because they are chronic illnesses, treatments are often given continuously over many months to years. Both doctors and

patients look for mild, safe, well tolerated, and effective therapies that can treat and control the lymphoma over a long period of time. In fact, when studying new treatments, doctors consider both duration of response (how long the treatment is effective for) and how many people get better to decide if a new treatment is effective.

When it comes to family planning, using even mild therapies for a long period of time can be an issue. Because many therapies only work while they are being given, aspects of family planning often need to be considered when choosing a therapy. This includes fertility (the ability or potential to become pregnant or get someone pregnant), conception (the actual process of getting pregnant and getting someone pregnant), pregnancy, and breastfeeding after pregnancy. These aspects should be considered if a patient or their partner wants to have a baby soon or even in the distant future.

Most therapies are not studied in pregnant women. Much of our knowledge comes from studies in animals, understanding how drugs work, or a few cases where patients conceived or became pregnant while on one of these therapies. As there is limited information and each patient's treatment needs are unique, please use this as general information to start a discussion with your treating physician and not as a specific recommendation for your care.



# Glossary

## **Aggressive lymphomas**

Lymphomas that are fast-growing and generally need to be treated immediately; also known as high-grade lymphomas.

## **Alemtuzumab (or Campath®)**

A monoclonal antibody directed against CD52, an antigen (or marker) found on both B and T lymphocytes. The drug is used in the treatment of advanced CTCL.

## **Allogeneic (stem cell) transplant**

A procedure in which a patient receives bone marrow or stem cells donated by another person.

## **Antibody**

A complex protein made by B-lymphocytes that reacts with antigens on toxins, bacteria and some cancer cells and either kills or marks them for removal.

## **Antiemetic**

A drug that reduces or prevents nausea and vomiting.

## **Antigen**

Identifying proteins located on the surface of all cells. The immune system uses antigens to determine whether cells are a necessary part of the body or need to be destroyed.

## **Autologous (stem cell) transplant**

A type of bone marrow or stem cell transplantation in which a patient receives their own stem cells.

## **BCNU**

A chemotherapy agent that is used topically in CTCL. (Also known as carmustine).

## **Bexarotene (or Targretin®)**

Medications in both capsule and gel forms that have been shown to be effective in treating CTCL.

## **Biologic therapy**

Treatment that uses or stimulates the immune system in directing a response against an infection or disease.

## **Biomarker**

A compound (usually a protein) used to measure the presence of a disease.

## **Biopsy**

Removal of tissue for evaluation under a microscope for diagnostic purposes.

## **Bone marrow**

Spongy material found inside the bones containing stem cells that develop into three types of cells: red blood cells that deliver oxygen to the body and take away carbon dioxide; white blood cells that protect the body from infection; and platelets that help the blood to clot.

## **Campath® - see alemtuzumab**

## **Cancer**

Abnormal cell growth that cannot be controlled by the body's natural defences. Cancerous cells can grow and eventually form tumours.

**Carmustine**

A chemotherapy agent that is used topically in CTCL. (Also known as BCNU).

**Chemotherapy**

Treatment with drugs to stop the growth of rapidly dividing cancer cells, including lymphoma cells.

**Chemotherapy cycle**

Term used to describe the process in which chemotherapy is given, followed by a period of rest in which the body is allowed to recover.

**Chemotherapy regimen**

Combinations of anti-cancer drugs given at a certain dose in a specific sequence according to a strict schedule.

**Clinical trial**

A research study in which a new treatment is given to patients to determine whether it is safe, more effective or less toxic than current therapies. Clinical trials are an important part of the process of understanding diseases and have been instrumental in providing information to the medicines regulators for approval of new therapies.

**Combination chemotherapy**

Several drugs given together to increase response rate of certain tumours.

**CT or CAT (computed (axial) tomography) scan**

This imaging test provides a series of detailed pictures of the inside of the body using an X-ray machine linked to a computer.

**Dermatologist**

A doctor who specialises in the diagnosis and treatment of skin diseases.

**Disease progression**

The terms used if the disease worsens despite treatment (also called treatment failure).

**Electron beam therapy**

A form of radiation therapy that only treats the superficial portions of the skin. It is highly effective in clearing all forms of lesions of CTCL from the skin. It can be used to treat portions of the skin or the entire skin surface. When used to treat all of the skin it is referred to as total skin electron beam (TSEB) therapy.

**Fatigue**

A decreased capacity for activity that is often accompanied by feelings of weariness, sleepiness or irritability.

**Grade**

A method of classifying a tumour on the basis of how aggressively it is growing.

**Haematologist**

A doctor who specialises in treating diseases of the blood and blood-forming tissues.

**Histology**

The study of tissue characteristics that may lead to identifying a specific type of tumour.

**Immune system**

The body's defence mechanisms involved in fighting infections and recognising foreign tissues. All CTCLs and lymphomas are diseases of the immune system.

**Immunological tests**

Blood tests that detect the presence of diagnostic proteins or antigens on a tumour.

**Immunotherapy**

See biologic therapy.

**Indolent lymphoma**

Lymphoma that is slow-growing and has few symptoms. Also called low-grade lymphoma.

**Interferon (or Intro® or Roferon®)**

A systemic therapy that has been shown to be very effective in treating CTCL.

**Interferons**

Naturally occurring compounds that stimulate the immune system in infections and inflammation. Synthetic forms are used to treat viral infections, autoimmune diseases and cancers.

**Intron®A** – see Interferon

**Lactate dehydrogenase (LDH)**

An enzyme measured in the blood and used as a biomarker to measure the extent or spread of cancers.

**Localised disease**

A cancer that is only present in a limited part of the body – for example, the neck or armpits.

**Low-grade lymphoma** – see indolent lymphoma

**Lymph**

The watery fluid in the lymph system that contains white blood cells (lymphocytes).

**Lymph node**

Small bean-shaped glands located in the vessels of the lymphatic system. Thousands are located throughout the body with clusters of them in the neck, under the arms, the chest, abdomen and groin. Lymph nodes filter lymph fluid, trapping and destroying potentially harmful bacteria and viruses.

**Lymphatic system**

The channels, tissues and organs that store and carry lymphocytes that fight infection and other diseases.

**Lymphocyte**

A type of white blood cell. Lymphocytes, carried along by the lymph fluid, are part of the immune system and fight infection.

**Lymphoma**

A cancer of lymphocytes involving lymph nodes, organs and tissues of the lymphatic system (immune system), generally classified into either Hodgkin lymphoma or non-Hodgkin lymphoma.

**Malignant**

Tending to become worse and life-threatening unless treated successfully.

**Matrex®** - see methotrexate

**Mechlorethamine**

A medication used topically to treat CTCL. Also known as topical nitrogen mustard.

**Medical oncologist**

A physician who specialises in the use of chemotherapy, hormone therapy and many other types of biologic therapies to treat cancer.

**Methotrexate (or Matrex®)**

A chemotherapy that is given as a treatment for some types of cancer.

**Monoclonal antibodies**

Antibodies that act specifically against a particular antigen. Scientists can produce large amounts of an antibody that can be directed to a single target (or antigen) on the cell's surface. Monoclonal antibodies are used to classify lymphomas by identifying surface proteins on lymphocytes.

**MRI (magnetic resonance imaging)**

MRI uses magnets and radio frequency waves to produce images of inside the body. MRIs can provide information about tissues and organs that is not available from other imaging techniques.

**Mucositis**

Inflammation of the lining of the tissues and organs. In the mouth, it is characterised by sores or inflammation.

**Mustargen**

A medication used topically to treat CTCL. Also known as mechlorethamine.

**Nitrogen mustard (NM)**

A medication used topically to treat CTCL. Also known as mechlorethamine.

**Non-Hodgkin lymphoma (NHL)**

A group of several closely related cancers that arise from the lymphatic system. Although the different types of NHL have some things in common, they differ in what the cancer cell looks like under a microscope, how the cells grow and how the tumour affects the body. CTCLs are a type of NHL.

**Oncologist**

A doctor who specialises in treating cancer. Some specialise in chemotherapy (medical oncologist), radiotherapy (radiation oncologist) or surgery (surgical oncologist).

**Ontak®**

A medication used in the treatment of CTCL.

**Pathologist**

A physician who specialises in studying disease through microscopic evaluation of body tissues and organs (biopsy). Any tissue suspected of being cancerous must first be examined by a pathologist to confirm the diagnosis.

**Pentostatin**

A medication used in the treatment of CTCL.

**PUVA**

Combining treatment with UVA with psoralen, a drug that promotes sensitivity to light.

**Stage**

The extent of cancer at the time of diagnosis, discriminating between whether it is localised to its site of origin, spread to neighbouring regions or distant sites of the body.

### **Systemic chemotherapy**

A chemotherapy with single agents along with combination chemotherapy is usually reserved for advanced stages (Stage III and IV) that are recalcitrant to other forms of therapy and administered orally or intravenously.

### **Targeted therapy**

A treatment that is directed to specific genes or proteins (targets) unique or abnormally expressed in a cancer cell.

**Targretin®** - see bexarotene

### **Thrombocytopenia**

A shortage of platelets in the blood, which reduces the ability of the blood to clot.

### **Thymus gland**

A gland located behind the sternum (breastbone) that enhances the reproduction and development of lymphocytes. T-lymphocytes are processed in the thymus.

### **Topical**

A medication or treatment that is applied to the skin.

### **Topical steroids**

High potency topical steroids have been shown to have activity in CTCL and induce clearing in early stage disease (Stage I-A and I-B). Topical steroids are easy to apply and are not associated with many complications like those seen with other skin-based treatments for CTCL.

### **Toxicities**

The unwanted side effects of cancer therapies, such as a decrease in blood cells, nausea and vomiting, and hair loss.

### **TSEB (Total skin electron beam)**

A form of radiation therapy that only treats the superficial portions of the skin. It is highly effective in clearing all forms of lesions of CTCL from the skin. Also known as electron beam therapy.

### **Tumour**

An abnormal mass or swelling of tissue. Tumours may occur anywhere in the body. A tumour may be benign (not life-threatening) or malignant (worsening and potentially life-threatening unless treated successfully).

### **UVB, broadband**

A form of phototherapy that uses ultraviolet light involving the entire range of UVB wavelengths.

### **UVB, narrowband**

A form of phototherapy that concentrates ultraviolet output in a narrow range of UVB wavelengths. It can be an effective treatment for patch-stage CTCL as well as other skin diseases.

### **Vaccine**

A substance or group of substances meant to stimulate the immune system to respond. A vaccine can help the body recognise and destroy cancer cells. Lymphoma vaccines often

combine cancer antigens with a substance to stimulate the patient's own natural defenses to fight the disease. These vaccines are custom-made for each patient using a sample of tumour obtained from the patient's lymph nodes.

**X-ray**

Radiation that is used in low doses to provide images of the inside of the body and in high doses to treat cancer.