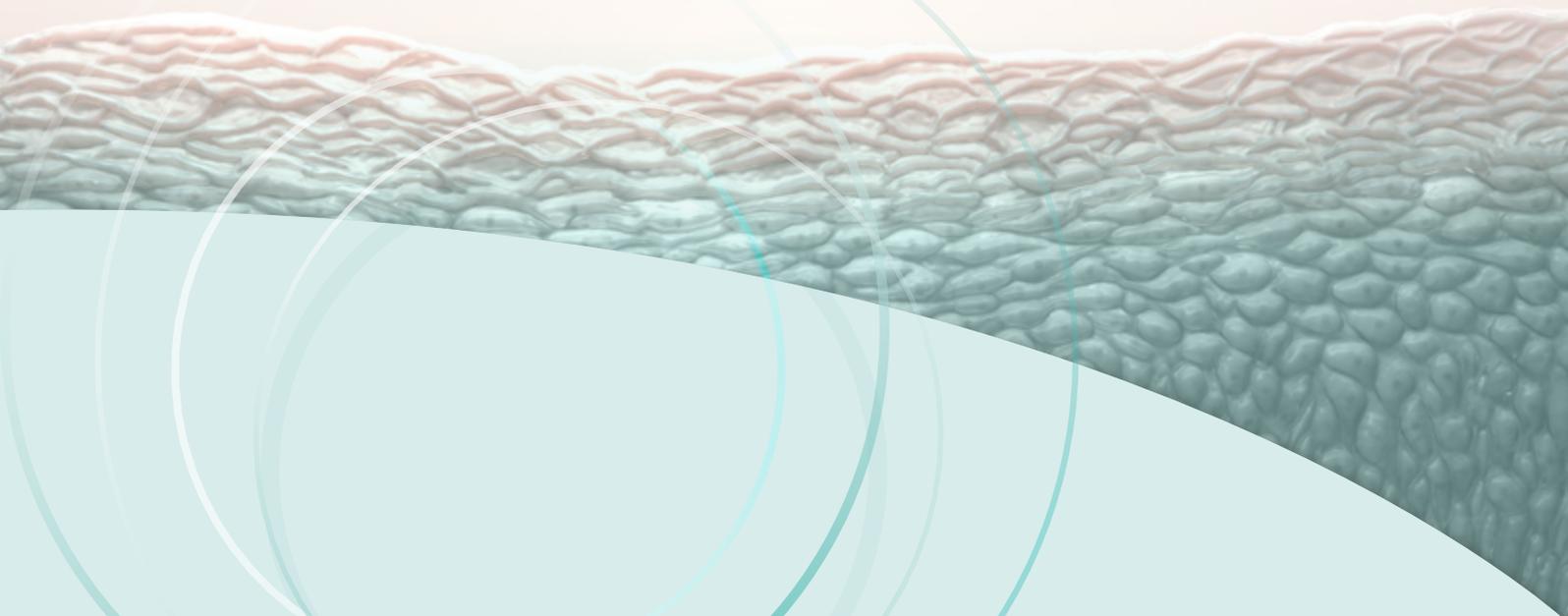


Information Leaflet for Patients

A detailed illustration of a skin cross-section, showing the epidermis and dermis layers. The epidermis is the upper, more textured layer, while the dermis is the lower, smoother layer. The illustration is rendered in shades of teal and light blue, with a soft gradient background. Overlaid on the skin are several concentric, semi-transparent circles in various shades of teal and light blue, creating a sense of depth and focus.

NAIL CHANGES DUE TO ANTICANCER TREATMENTS

The aim of this leaflet

This leaflet is designed to help you understand more about nail changes induced by drugs used against cancer. It informs you about how the drug-induced nail changes look like, which are their causes and how they are diagnosed and treated. It also provides you with practical advices for their prevention and management.

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What are cancer treatment-related nail changes?

Nail changes are a common toxicity that can be caused by a range of cancer therapies. Nail plate, nail bed, and skin around the nail may be affected with a frequency that varies depending on the drug used. Targeted treatments are those most related to nail unit changes. After stopping the treatment, however, the changes gradually disappear.

Although nail changes are not life-threatening, they can cause discomfort and pain. They may impair your daily activities and have a negative impact on your quality of life. Certain preventive and therapeutic measures can ameliorate this sometimes difficult-to-treat adverse event.

Which cancer treatment can cause nail changes?

A large number of chemotherapeutic agents and targeted therapies can induce nail changes. The onset ranges from 1-2 weeks to several months after treatment initiation.

The table below provides a list of the most common anticancer medications and the corresponding nail changes that they may cause.

Loosening of the nail plates (detachment)	capecitabine, docetaxel, doxorubicin, eribulin, etoposide, ixabepilone, mercaptopurine, methotrexate, mitoxantrone, paclitaxel, immune checkpoint inhibitors, FGFR inhibitors
Loss of the nail plate	docetaxel, paclitaxel, FGFR inhibitors
Bleeding under the nail plate	docetaxel, paclitaxel, sorafenib, sunitinib, cabozantinib
Discoloration of the nail plates	bleomycin, cyclophosphamide, dacarbazine, daunorubicin, docetaxel, doxorubicin, erlotinib, etoposide, fluorouracil, gefitinib, idarubicin, imatinib, lapatinib, melfalan, paclitaxel, vincotaxel, panitumumab, topirostatin...
Infections	docetaxel, eribulin, erlotinib, gefitinib, lapatinib, paclitaxel, panitumumab, cetuximab, osimertinib, afatinib
Redness and swelling of the periungual tissues	eribulin, erlotinib, gefitinib, lapatinib, panitumumab, trametinib, cetuximab, osimertinib, afatinib, binimetinib, ibrutinib
Nail fragility	all chemotherapeutic agents
Nail plate surface abnormalities (fissures, ridges, depressions)	immune checkpoint Inhibitors

What are the signs and symptoms of cancer treatment-related nail changes?

Different changes may affect one or more nails at the same time and can also co-exist in the same nail.

1. Nail fragility: certain anticancer drugs can modify nail growth. This results in a

slower nail plate growth and/or a weak nail plate that is less elastic and crumbles and splits easily. Usually, this type of nail change is otherwise not painful and harmful. After treatment cessation, the nails gradually recover.

- 2. Ridges or lines in the nail plate:** some anticancer drugs can cause ridges and/or transverse lines (Beau's lines) in the nail plate. This is a harmless side-effect, resulting from a temporary and partial interruption of nail plate growth. Ridges and lines will eventually disappear a few months after the end of the treatment.
- 3. White discolorations in the nails:** some anticancer drugs can hinder the nail matrix from properly forming the nail plate. The latter results in white transversal bands or spots. This is a harmless side-effect. Bands and spots will gradually disappear after treatment cessation, following the outwards growth of the nail.
- 4. Dark spots under the nail:** some chemotherapeutic agents can cause dark pigmentation of the nail unit. Usually, this discoloration is temporary, but it can also be permanent. It may involve a part or the entire nail plate.
- 5. Bruising under the nail:** small bruises may appear in the nail bed. These are visible as small red lines along the nail plate (splinter hemorrhages). Larger areas of subungual bleeding, accompanied by pain can be also present. In this scenario, there is also a risk of infection.
- 6. Loosening of the nails:** the nail plate is loosely attached to the nail bed (onycholysis). This is temporary but can be painful. There is also an increased risk of infection.
- 7. Loss of the nail:** some anticancer drugs can result in complete loss of the nail plate. This is temporary but can be painful. There is also an increased risk of infection.
- 8. Inflammation of the periungual tissues:** redness or swelling of the skin around the nail of the finger or toe (paronychia or perionyxis). This can be very painful and can limit your normal daily activities.
- 9. Pyogenic granuloma:** a benign vascular tumor that often occurs in the lateral nail fold, usually of the great toenail. It can grow quickly and give discomfort and oozing.
- 10. Nail plate surface abnormalities (fissures, ridges, depressions):** surface abnormalities: tiny depressions in your nails (called "nail pits"); white, yellow, or brown discoloration; crumbling nails; nail(s) separating from your finger or toe; buildup beneath your nail and blood under your nail.

How to prevent or reduce cancer treatment-related nail changes?

It may not be possible to prevent nail changes, but you can take several actions to prevent the worst damage to your nails and to control minor nail changes. Check your hands and feet every day to see if there are any abnormalities and act to prevent them from getting worse.

Below is a list of tips:

- 1. Keep your skin and nails clean to prevent infections.**
- 2. Keep your nails short and straight:** short nails are less likely to break or "catch" on something (for tips: see below).
- 3. Protect the nails of your hands and feet from damage.**
 - Avoid pressure on the hands and feet: wear shoes that are not too tight and do not wear high heels. Protect your hands by wearing work gloves.
 - Avoid activities with a lot of effort for the hands, such as cleaning, odd jobs, or hobbies that can damage your skin and nails.
 - Protect your skin from frequent contact with moisture; wear vinyl gloves when cleaning the house, washing dishes, or gardening. For additional protection,

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use vinyl gloves one size larger and wear white cotton gloves underneath to absorb sweat and protect the skin.

- Wear 100% cotton socks and change them often. Cotton socks help absorb moisture and can help prevent fungal infections and skin maceration.
 - Dry your fingers and toes well after washing dishes, swimming, or taking a bath/shower to prevent infections.
 - Avoid hot hand and foot baths.
 - Do not expose your hands and feet to extreme cold: wear gloves and slippers to protect your hands and feet from the cold.
 - Avoid sun exposure and regularly use sunscreen on your skin and on your nails.
- 4. Moisturize your hands, nails, and cuticles regularly with a hydrating cream**
 - 5. Pay special attention to your cuticles:** the cuticle is a thin layer of dead tissue riding on the nail plate that protects your nails from harmful bacteria and fungi, do not damage them by biting or cutting them.
 - 6. Prevent the development of hangnails:** a hangnail looks like a 'mini nail' next to your normal nail. A hangnail occurs when the cuticles are very dry and cracked. As a result, a piece of hardened skin can stick up. It occurs on

both toenails and fingernails. A hangnail can be quite annoying and painful. If there are hangnails, do not pull them off, but carefully secure them with medical tape with micropores.

- 7. Protect exposed nail bed:** exposed skin from the nail bed can be covered with non-adherent moisturized gauzes in the form of the defect.
- 8. Avoid polishing your nail plates:** do not polish your nail plates with a file. Polishing the nail plate thins the brittle nail plate, which can cause damage and infections.
- 9. Avoid nail polish removers and nail enamel with toxic ingredients:** use natural nail polish removers without acetone and ethyl acetate; favor nail polishes marketed as non-toxic.
- 10. Use water-based nail lacquers on nails that are ridged, fragile, or splitting:** this water-based nail polish strengthens and protects the nails. Water-based nail lacquer is ideal because it contains the least amount of chemicals.
- 11. Avoid artificial nails, nail silk wraps:** an infection can grow under wraps and artificial nails; do not apply gel nail polish, as it can only be removed with acetone.
- 12. Do not use acrylic nails:** acrylics tend to weaken your natural nails and make them brittle.

How to manage cancer treatment-related nail changes?

Early recognition, prevention, and treatment of nail changes are important to ensure an unimpeded anticancer therapy, avoiding dose modification or discontinuation.

Carefully assess the nails of your hands and feet and act if early changes or any of the below-mentioned signs/symptoms appear around or under your nail(s):

1. Loosening of the nail plates

2. Bleeding under the nail plates

3. Purulent discharge around and under the nails (drainage, bad smell)

4. Nail fungus

5. Easily bleeding growths on the nail walls

6. Skin and nail(s) that is warm, hot, or hard to the touch

7. Pain and discomfort

Your doctor may prescribe topical medications to treat nail changes. Topical medications are those applied on your nails and may include:

- Steroids
- Moisturizers
- Anti-microbial or anti-fungal medications (medications that kill germs)
- Liquid bandage to close any open skin on your hands or feet

If your symptoms do not resolve with a topical medication, your doctor may prescribe oral medications (medications you take by mouth, such as antibiotics or pain killers).

Occasionally it may be necessary to perform a partial removal of the nail plate or a more complex surgical procedure. ■