Management guidelines for dermatologic adverse events (dAEs)

A healthcare provider’s guide to help prevent, identify, and manage dAEs for patients using Optune® to help maximize time on therapy

Inform your patients to contact you as soon as they experience itching or redness

This brochure does not represent medical advice, but guidance based on clinical trial results and real-world clinical experience. Novocure® cannot give medical advice.
Help prevent dAEs to maximize time on therapy

The most common adverse event associated with Optune® in clinical trials was skin irritation beneath the arrays. For this reason, it is important to monitor not only the patient’s clinical status but also their scalp health. Early prophylactic interventions may decrease the risk and severity of dermatologic AEs.1

**Prophylactic tips for skin AE management**¹

<table>
<thead>
<tr>
<th>Shave and prepare the scalp to maximize the skin’s contact with arrays, and minimize erosions and other factors increasing the risk of infection</th>
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</table>

**Recommendations for patients and caregivers**¹

| • Always wash your hands prior to array application |
| • Shave the scalp completely every time arrays are changed, using gentle but firm circular motions |
| • Use a clean, electric razor to avoid cuts |
| • Apply mineral (baby) oil before shaving to cleanse the skin and help remove bacteria and scale |

<table>
<thead>
<tr>
<th>Remove natural oils and any moisture (sweat) from the scalp before array application</th>
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| • Wash the scalp with mild, fragrance-free shampoo (eg, baby shampoo) or dandruff shampoo |
| • Wipe the scalp with a piece of gauze or a cotton ball soaked in first aid isopropyl alcohol (70%), unless there are signs of skin irritation |
| • Before placing arrays, ensure the scalp is dry |

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Please see Optune Instructions For Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions at Optune.com/Safety.
Additional prophylactic steps that may help to reduce the risk of dAEs

<table>
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<tr>
<th>Prophylactic tips for skin AE management¹</th>
<th>Recommendations for patients and caregivers¹</th>
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<tr>
<td>Careful application and removal of arrays is important to minimize the risk of skin irritation</td>
<td>• Change arrays at least every 3–4 days, or more frequently if they become wet or loosen</td>
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<tr>
<td></td>
<td>• Apply mineral (baby) oil to the scalp to slowly and gently remove arrays. Do not pull the skin or forcefully rub the scalp to remove adhesive, this can lead to skin breakdown and irritation</td>
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<td></td>
<td>• Based on patient experience, arrays may also be removed in a hot shower by rubbing in a body wash containing coconut oil, causing the arrays to slide off the scalp</td>
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<td>• Monitor the skin and scalp for signs of irritation with every array change, and notify your healthcare provider if there are signs of irritation (taking a picture of the affected area is advised)</td>
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<tr>
<td>Regularly reposition arrays to minimize direct pressure on the scalp and ensure avoidance of surgical scar lines</td>
<td>• At each array change, shift array placement by 0.75 inches, ensuring that pairs of arrays are moved together</td>
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<tr>
<td></td>
<td>• Move arrays back to original position at the next change</td>
</tr>
<tr>
<td></td>
<td>• Avoid placing ceramic discs directly over scars or surgical screws</td>
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Recommend breathable headwear to avoid overheating.¹ Visit Optunedailylife.com for a list of head coverings.

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## Identifying key risk factors

<table>
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<th>Key risk factors associated with dAEs¹:</th>
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<tr>
<td>✓ Prior craniotomies, especially those that necessitated scalp reconstruction</td>
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<tr>
<td>✓ Placement of arrays (ie, ceramic discs) overlying scars or craniotomy hardware</td>
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<tr>
<td>✓ Concurrent treatment with high doses of systemic corticosteroids</td>
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<td>✓ Treatment with oral antibiotics</td>
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<td>✓ Concurrent administration of chemotherapy or targeted therapies</td>
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<tr>
<td>✓ Previous skin exposure to ultraviolet or ionizing radiation</td>
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<tr>
<td>✓ Pre-existing skin conditions or a history of contact dermatitis (eg, from tape adhesive or hydrogel)</td>
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<tr>
<td>✓ History of hyperhidrosis (excessive sweating)</td>
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<tr>
<td>✓ Persistent alopecia</td>
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Dermatologic adverse events

- Can potentially be prevented
- Identify patient risk factors
- Educate on proactive and proper scalp care
- Are typically mild to moderate in nature
- Are generally managed with topical therapy without resulting in treatment discontinuation

In a phase 3 clinical trial (EF-14), the rate of grade 1 to 2 medical device site reactions was 52%, and the rate of grade 3 medical device site reactions was 2%.²

Most dAEs are typically mild to moderate. Management with skin care treatment can help to prevent dAEs without discontinuing Optune.¹

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Causes and management of common dAEs

Treatment options for dAEs are dependent upon the type and severity of the dAE. If condition does not improve after intervention, consider dermatology consult.¹

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<th>Adverse Events</th>
<th>Description</th>
<th>Potential Cause(s)</th>
<th>Suggested Interventions</th>
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</table>
| Hyperhidrosis¹ | Excessive sweating of the scalp | • Genetic predisposition  
• Hot/humid climate  
• Intense activity  
• Medications | • Aluminum chloride antiperspirant or topical glycopyrrolate at every array exchange  
• Avoid using ointments and medications that may cause sweating  
• Consider referral to a dermatologist for botulinum toxin injections |
| Pruritus¹ | Dry skin (xerosis), itchy skin (pruritus), or flaky skin (dandruff) | • Genetic predisposition  
• Cold/dry climate  
• Loss of water/oil  
• Medications  
• May be related to contact dermatitis | • Fragrance-free or anti-dandruff shampoo  
• Although part of the standard array change protocol, limit skin contact with alcohol-based products  
• Topical corticosteroids may be prescribed if inflammation is present (eg, betamethasone, clobetasol, fluocinonide)  
• Identify cause and, if possible, reduce or eliminate |
| Contact dermatitis¹ | Contact  
Localized inflammation of the skin. Symptoms include skin rash that may resemble a burn or red bumps that form moist, weeping blisters | • Allergy to specific exogenous allergens, such as adhesive tape and/or hydrogel, that come into contact with the skin causing an inflammatory reaction | • Immediate removal of the irritant/allergen  
• Array removal from irritation/allergen site  
• Topical corticosteroids, such as betamethasone, clobetasol, or fluocinonide  
• Apply a barrier film  
• Consider trimming adhesive or Surgilast® if reaction exists to tape or adhesive |
| Irritant | Irritant  
Localized dermatitis restricted to the area of the irritant. Symptoms include skin redness, mild edema, scaling, itchy or painful rash | • Nonspecific inflammation caused by direct cellular damage upon contact with an inherently harmful substance to cells, such as chemical irritation from hydrogel, moisture, and/or alcohol | • If blistering develops, apply a cold, moist compress 3 times a day for 20 minutes  
• Consider systemic corticosteroids or treatment breaks if condition continues |

Advise patients to avoid putting ceramic discs or adhesive tape over areas affected by a dAE when placing or exchanging arrays

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<td><strong>Skin erosions</strong></td>
<td>Moist, circumscribed, depressed, secondary lesions that involve the epidermis, but do not extend into the dermal layer</td>
<td>• Mechanical trauma from shaving and/or array application or removal • May develop from inflammation or maceration due to sweat, rupture of vesicles, bullae from infection, or epidermal necrosis</td>
<td>• Array removal from site of erosion or ulcer. May consider replacement to avoid hardware exposure • Wound dressing with gauzes, hydrogels, or hydrocolloids • Assess wound and treat with topical antibiotics, such as clindamycin or gentamicin • May consider wound culture • Keep clear of excess discharge and dead skin. Severe cases may require surgical debridement • Return to clinic in 2 weeks. If condition continues, consider an oral antibiotic or treatment break</td>
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<tr>
<td><strong>Skin ulcers</strong></td>
<td>Secondary lesions involving the epidermal and dermal layers, which may result in scarring</td>
<td>• Ischemic injury and/or decreased perfusion produced by array pressure (especially in areas overlying scars, hardware, and prior radiation exposure)</td>
<td>• Assess wound and treat with topical antibiotic, such as clindamycin or gentamicin • Warm compresses with saltwater or Burow’s solution (5% aluminum subacetate) • Take wound culture and potentially refer to dermatologist • Return to clinic in 2 weeks. If condition continues, consider an oral antibiotic or treatment break</td>
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<td><strong>Dermatitis and infections</strong></td>
<td>Inflammation of skin or hair follicle. Presentation includes pus, itching, or burning</td>
<td>• Secondary bacterial infection • If skin is affected by pathogenic bacteria, infection with or without pustules may occur</td>
<td>• Assess wound and treat with topical antibiotic, such as clindamycin or gentamicin • Warm compresses with saltwater or Burow’s solution (5% aluminum subacetate) • Take wound culture and potentially refer to dermatologist • Return to clinic in 2 weeks. If condition continues, consider an oral antibiotic or treatment break</td>
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Skin irritations associated with treatment with Optune® can usually be managed with proper skin care and the use of medications, such as topical corticosteroids and antibiotics, without discontinuing therapy.

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Instructions for application of topical therapy

Manually update the application directions on the prescription, especially the information in bold below.

**Patient instructions on how to properly apply topical medications:**

- ✔ Remove arrays and clean scalp¹

- ✔ Apply topical agent (eg, steroid or antibiotic) to affected area(s)¹
  - Have patients only apply topical agents when they exchange arrays at least 2 times a week (every 4 days at most)¹,³
  - A thin layer should be applied to the dry scalp¹
  - Allow agent to dry¹

- ✔ Clean scalp with medical (70%) alcohol¹

- ✔ Apply new arrays to a dry scalp, ensuring that arrays are shifted “back and forth” approximately 0.75 inches at each exchange and are not placed over screws or plates¹

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Communication with the patient is key in helping to prevent and manage skin irritation

Please refer to the patient brochure, entitled *A guide to scalp care and proper array placement* (available in both English and Spanish), as an educational tool to use with your patients and their caregivers.

Contact a Novocure representative or go to Optune.com for additional resources, including available styles for head coverings.

Note that neither a Device Support Specialist (DSS) nor a Care Coordinator (CC) at nCompass® can manage skin irritation

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Optune® Indications for Use and Important Safety Information

Indications For Use
Optune is intended as a treatment for adult patients (22 years of age or older) with histologically-confirmed glioblastoma multiforme (GBM).

Optune with temozolomide is indicated for the treatment of adult patients with newly diagnosed, supratentorial glioblastoma following maximal debulking surgery, and completion of radiation therapy together with concomitant standard of care chemotherapy.

Important Safety Information

Contraindications
Do not use Optune in patients with an active implanted medical device, a skull defect (such as, missing bone with no replacement), or bullet fragments. Use of Optune together with implanted electronic devices has not been tested and may theoretically lead to malfunctioning of the implanted device. Use of Optune together with skull defects or bullet fragments has not been tested and may possibly lead to tissue damage or render Optune ineffective.

Do not use Optune in patients that are known to be sensitive to conductive hydrogels. In this case, skin contact with the gel used with Optune may commonly cause increased redness and itching, and rarely may even lead to severe allergic reactions such as shock and respiratory failure.

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Warnings and Precautions
The most common (≥10%) adverse events involving Optune in combination with temozolomide were thrombocytopenia, nausea, constipation, vomiting, fatigue, medical device site reaction, headache, convulsions, and depression.

If the patient has an underlying serious skin condition on the scalp (e.g. ulcers, open wound, broken skin) evaluate whether this may prevent or temporarily interfere with Optune treatment.

Use of Optune in patients with an inactive implanted medical device in the brain has not been studied for safety and effectiveness, and use of Optune in these patients could lead to tissue damage or lower the chance of Optune being effective.

Do not prescribe Optune for patients that are pregnant, you think might be pregnant or are trying to get pregnant, as the safety and effectiveness of Optune in these populations have not been established.

Optune can only be prescribed by a healthcare provider that has completed the required certification training provided by Novocure (the device manufacturer).

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Additional support and resources for your patient

**The Buddy Program**—Connects patients, and/or their caregivers, who have recently started or are considering treatment with Optune® with an ambassador. The ambassador is a patient or caregiver who has experience with Optune and can share how he or she has learned to incorporate Optune into his or her daily life. Call toll free at 1-844-247-1636 for the Buddy Program.

**The nCompass® brochure**—Provides detailed information on the 24/7 support patients and caregivers can expect with Optune at every step of the way. Call toll free at 1-855-281-9301.

**Optune.com**—This online resource gives patients a wealth of information about Optune, including where to find a certified treatment center. Here they can also view a range of videos and download resources.

**Optune Facebook page**—The Optune US Facebook page provides information such as useful tips, answers to frequently asked questions, and information on upcoming events in the glioblastoma (GBM) community.

**Optune YouTube Channel**—Helpful videos present Optune users and their doctors as they discuss GBM, Optune, how it is applied and used, and how it allows for usual daily activities.

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