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.

For the treatment of recurrent GBM, Optune is indicated following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

Please see the Optune Instructions For Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions at Optune.com/IFU.
Identifying dAEs

Identifying the types of dAEs patients may experience

The most common side effect associated with Optune® is skin irritation beneath the transducer arrays. This is primarily due to continuous contact between the transducer arrays and the scalp for prolonged periods. The time from initiation of therapy to onset of a dAE may range from 2 to 6 weeks. Most dAEs can be prevented, and those that do occur are typically mild to moderate and reversible with treatment without discontinuing Optune.1

Identifying the type of dAE a patient may be experiencing is important to determine proper treatment and to prevent disruption or discontinuation of Optune.1

<table>
<thead>
<tr>
<th>Type of dAE¹</th>
<th>Description</th>
<th>Potential Cause(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dermatitis</td>
<td>Skin inflammation, presenting with edema or erythema, followed by scaling</td>
<td>Allergic reaction (tape adhesive/hydrogel), chemical irritation (hydrogel, moisture, alcohol)</td>
</tr>
<tr>
<td>Erosions</td>
<td>Moist, circumscribed, depressed lesions from loss of viable epidermis—mild bleeding, pain, and burning are possible</td>
<td>Trauma related to repeated shaving and/or array pressure/removal</td>
</tr>
<tr>
<td>Infections</td>
<td>Pustules (raised epidermal lesions containing pus), possibly friction vesicles (bullae) with clear content or “bullous impetigo” with yellow-greenish content when infection occurs</td>
<td>Secondary bacterial infection</td>
</tr>
<tr>
<td>Ulcerations</td>
<td>Round lesions with well-defined borders, in which the epidermis and the dermis have been destroyed</td>
<td>Decreased perfusion from array pressure</td>
</tr>
</tbody>
</table>

- In the phase 3 pivotal study for recurrent GBM, 16% of patients treated with Optune (n=116) experienced a grade 1/2 medical device site reaction²
- In the phase 3 pivotal study for newly diagnosed GBM, the rate of grade 1/2 medical device site reaction was 52% for Optune + TMZ compared with 0% for TMZ alone³
**Grading dAEs**

**Grading dAEs your patients may experience**

A proposed grading system based on current Common Terminology Criteria for Adverse Events (CTCAE) is used to describe dAEs associated with Optune®. This system is intended to provide more consistent descriptions and grading of dAEs related to Optune, which may help healthcare providers determine appropriate supportive interventions and clinical care for patients.¹

**Proposed grading for device-related dAEs¹,*

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Asymptomatic or mild symptoms; topical therapy indicated</td>
</tr>
<tr>
<td>2</td>
<td>Moderate symptoms; topical and systemic therapy indicated</td>
</tr>
<tr>
<td>3</td>
<td>Severe or medically significant, but not immediately life-threatening; possible treatment interruption; topical and systemic therapy indicated</td>
</tr>
<tr>
<td>4</td>
<td>Life-threatening consequences: urgent intervention indicated; device discontinuation indicated</td>
</tr>
</tbody>
</table>

* A cutaneous, device-related dermatologic event is defined as a disorder characterized by dermatitis, skin infection, erosion, or ulcer related to the noninvasive use of a medical device.
Reducing risks/preventing dAEs

Minimizing dAEs and maximizing time on therapy

Recognizing risk factors associated with dAEs related to Optune®, as well as encouraging patients and their caregivers to take appropriate measures to prevent dAEs, may help ensure that time on Optune is maximized.¹

<table>
<thead>
<tr>
<th>Risk factors associated with Optune dAEs¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Placement of transducer arrays (ie, ceramic discs) overlying scars or craniotomy hardware</td>
</tr>
<tr>
<td>• History of contact dermatitis (eg, from tape adhesive or hydrogel)</td>
</tr>
<tr>
<td>• Excessive sweating from hot, humid weather or occlusive wigs</td>
</tr>
<tr>
<td>• Previous skin exposure to ultraviolet or ionizing radiation</td>
</tr>
<tr>
<td>• High doses or recent change in systemic corticosteroids</td>
</tr>
<tr>
<td>• Concurrent administration of chemotherapy, biologics, or targeted therapies</td>
</tr>
</tbody>
</table>

Do not use Optune in patients that are known to be sensitive to conductive hydrogels like the gel used on electrocardiogram (ECG) stickers or transcutaneous electrical nerve stimulation (TENS) electrodes. 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.
Compliance was a predictor of improved overall survival on Optune® in both the newly diagnosed GBM and recurrent GBM pivotal studies.4,5

• Change the transducer arrays at least 2 times per week (every 4 days at most)
• Avoid “pulling” on the skin when removing the arrays
• Use mineral (baby) oil on the edges of the array for easier adhesive tape removal and to alleviate irritation
• Inform patients to notify their healthcare provider if skin irritation occurs

Prophylactic management of dAEs1

• Ensure a close shave prior to applying the arrays
• Clean the electric razor after every shave
• Wash scalp with fragrance-free, mild shampoo or seborrheic dermatitis shampoo
• Ensure scalp is dry before applying a new set of arrays

• After shaving and before placing the arrays, wipe scalp with 70% isopropyl (rubbing) alcohol to remove scalp oils and to improve adherence of the arrays
• Avoid areas of skin irritation

• Change the transducer arrays at least 2 times per week (every 4 days at most)
• Avoid “pulling” on the skin when removing the arrays
• Use mineral (baby) oil on the edges of the array for easier adhesive tape removal and to alleviate irritation
• Inform patients to notify their healthcare provider if skin irritation occurs
Managing dAEs that may occur with Optune®

Proper management and treatment of dAEs is essential to help avoid interruptions or discontinuation of Optune.1 Maximizing the amount of time a patient uses Optune each day (≥18 hours) may help improve overall survival (OS).1 Treatment options for dAEs are dependent upon the type and severity of the dAE. The primary treatments for dAEs associated with Optune are topical corticosteroids and topical antibiotics.1

Management intervention1

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dermatitis</strong></td>
<td>Remind patient about shifting arrays (back and forth and not over palpable plates/screws) and evaluating skin at every array exchange</td>
<td>High potency topical corticosteroid (eg, clobetasol)</td>
<td>High potency topical corticosteroid ointments AND avoidance of direct contact of discs/adhesive tape with affected area(s)</td>
</tr>
<tr>
<td><strong>Erosions</strong></td>
<td>Topical antibiotics (eg, mupirocin or polymyxin B/bacitracin [polysporin] ointments)</td>
<td>Topical and oral antibiotics AND avoidance of direct contact of discs/adhesive tape with affected area(s)</td>
<td>Treatment interruption; consider dermatology consult</td>
</tr>
</tbody>
</table>

- Reassess after 2 weeks (either by healthcare provider or patient self-report). If reaction worsens or does not improve, proceed to guidance for next grade.
- Reassess after 2 weeks. Consider resuming Optune once event has recovered to grade 1.
### Management intervention\(^1\) (continued)

<table>
<thead>
<tr>
<th></th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infections</strong></td>
<td>Remind patient about shifting arrays (back and forth and not over palpable plates/screws) and evaluating skin at every array exchange</td>
<td>Culture and then treatment with appropriate topical antibiotic</td>
<td>Culture, then treatment with appropriate oral antibiotic AND avoidance of direct contact of discs/adhesive tape with affected area(s)</td>
<td>Obtain skin culture; oral antibiotics; consider treatment interruption until grade 1; consider dermatology consult</td>
</tr>
<tr>
<td><strong>Ulceration</strong></td>
<td>Open areas require topical antibiotics</td>
<td>Topical and oral antibiotics AND avoidance of direct contact of discs/adhesive tape with affected area(s)</td>
<td>Treatment interruption; consider dermatology consult</td>
<td>Reassess after 2 weeks. Consider resuming Optune(^\circledR) once event has recovered to grade 1.</td>
</tr>
</tbody>
</table>

- Reassess after 2 weeks (either by healthcare provider or patient self-report). If reaction worsens or does not improve, proceed to guidance for next grade.

- Reassess after 2 weeks. Consider resuming Optune\(^\circledR\) once event has recovered to grade 1.

Adapted with permission from Seminars in Oncology; Elsevier Inc.
Prevention and proper treatment of dAEs help maximize time on Optune

Being proactive about management of dAEs is important during treatment with Optune. Encourage your patients to take the preventative steps that can help reduce the risk of dAEs and, if they experience a dAE, to report it at once so that you can clinically manage the event promptly and appropriately. Preventing, identifying, and managing dAEs may help patients maximize their time (≥18 hours per day) on Optune, which is important to achieving a longer OS benefit.\textsuperscript{1,4}

Please refer to the companion brochure for patients, entitled \textit{A guide to scalp care and proper transducer array placement}, as an educational tool to use with your patients and their caregivers.
**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.

For the treatment of recurrent GBM, Optune is indicated following histologically- or radiologically-confirmed recurrence in the supratentorial region of the brain after receiving chemotherapy. The device is intended to be used as a monotherapy, and is intended as an alternative to standard medical therapy for GBM after surgical and radiation options have been exhausted.

**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.

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

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.
Important Safety Information (continued)

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.

The most common (≥10%) adverse events seen with Optune monotherapy were medical device site reaction and headache.

The following adverse reactions were considered related to Optune when used as monotherapy: medical device site reaction, headache, malaise, muscle twitching, fall and skin ulcer.

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.

If the patient has an underlying serious skin condition on the scalp, evaluate whether this may prevent or temporarily interfere with Optune treatment.

Please see the Optune Instructions For Use (IFU) for complete information regarding the device’s indications, contraindications, warnings, and precautions at Optune.com/IFU.