Opdualag™ (nivolumab and relatlimab-rmbw)

Pronounced: nye-vol'-ue-mab and rel-at-li-mab

Classification: Programmed death receptor-1 (PD-1) blocking antibody (nivolumab) and a lymphocyte activation gene-3 (LAG-3) blocking antibody (relatlimab).

About Opdualag™ (nivolumab and relatlimab-rmbw)

This medication is a combination of the programmed death receptor-1 (PD-1) blocking antibody nivolumab and the LAG-3-blocking antibody relatlimab. It is used for some types of skin cancer.

The immune system works by creating antibodies, which are proteins that attach to antigens found on the surface of a cell. The antibody “calls” the immune system to attack the cell it is attached to, resulting in the immune system killing the cell. Monoclonal antibodies are created in a lab to attach to the antigens found on specific types of cancer cells. These antibodies can work in different ways, including stimulating the immune system to kill the cell, blocking cell growth or other functions necessary for cell growth. Nivolumab and relatlimab are both monoclonal antibodies.

- Nivolumab is a type of monoclonal antibody therapy, which works to stimulate the immune system to destroy cancer cells. T-cells are a type of white blood cell that are very important to the normal functioning of the immune system. Nivolumab works as a form of immunotherapy by binding to the "programmed death receptor" (PD1) found on T-cells to stimulate the immune system to find and kill cancer cells.
- Relatlimab targets lymphocyte-activation gene 3 (LAG-3), a cell-surface receptor found on some T cells.

Targeting LAG3 along with PD1 may help restore T-cells and can help with an anti-tumor immune response.

How to Take nivolumab and relatlimab-rmbw

Nivolumab and relatlimab-rmbw is given by a single intravenous (into a vein) infusion (both medications are mixed together and given at the same time). The dose and how often you receive the medication will be decided by your care team.

Make sure your care team is aware of all medications (including prescription and over-the-counter), supplements, and vitamins you are taking. Steroids should be avoided while on immunotherapy unless directed by your care team.

Tell your care team about all your medical conditions, including those that are autoimmune in nature (Crohn’s disease, lupus, rheumatoid arthritis, etc.) as these can get worse with immunotherapy. You should also notify your provider if you have had or plan on having an allogeneic stem cell transplant as this medication can worsen a side effect of the transplant called graft-versus-host disease.

Possible Side Effects of Nivolumab and relatlimab-rmbw

There are a number of things you can do to manage the side effects of nivolumab. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

Muscle or Joint Pain/Aches

Your healthcare provider can recommend medications and other strategies to help relieve pain.

Fatigue
Fatigue is very common during cancer treatment and is an overwhelming feeling of exhaustion that is not usually relieved by rest. While on cancer treatment, and for a period after, you may need to adjust your schedule to manage fatigue. Plan times to rest during the day and conserve energy for more important activities. Exercise can help combat fatigue; a simple daily walk with a friend can help. Talk to your healthcare team for helpful tips on dealing with this side effect.

**Low Red Blood Cell Count (Anemia)**

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the red cell count is low, you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing or pain in your chest. If the count gets too low, you may receive a blood transfusion.

**Low White Blood Cell Count (Lymphocytopenia)**

White blood cells (WBC) are important for fighting infection. A lymphocyte is one kind of white blood cell. While receiving treatment, your WBC count can drop, putting you at a higher risk of getting an infection. You should let your care team know right away if you have a fever (temperature greater than 100.4°F or 38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn’t heal.

**Tips for preventing infection:**

- Washing hands, both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bath daily and perform frequent mouth care.
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with, has any vaccinations.

**Rash and Itchy Skin (Pruritis)**

Some patients may develop a rash, scaly skin, or red itchy bumps. Use an alcohol-free moisturizer on your skin and lips; avoid moisturizers with perfumes or scents. Your oncology care team can recommend a topical medication if itching is bothersome. If your skin does crack or bleed, be sure to keep the area clean to avoid infection. Be sure to notify your oncology care team of any rash that develops, as this can be a reaction. They can give you more tips on caring for your skin.

**Electrolyte Changes**

This medication can affect the level of sodium (and possibly other electrolytes) in your body. Your levels will be monitored using blood tests. If your levels become too low, your care team may prescribe specific electrolytes to be given by IV or taken by mouth. Do not take any supplements without first consulting with your care team.

**Less common, but important side effects can include:**

- **Immune Reactions:** This medication stimulates your immune system. Your immune system can attack normal organs and tissues in your body, leading to serious or life-threatening complications. It is important to notify your healthcare provider right away if you develop any of the following symptoms:
  - **Diarrhea / Intestinal problems (colitis, inflammation of the bowel):** Abdominal pain, diarrhea, cramping, mucus or blood in the stool, dark or tar-like stools, fever. Diarrhea means different things to different people. Any increase in your normal bowel patterns can be defined as diarrhea and should be reported to your healthcare team.
  - **Skin reactions:** Report rash, with or without itching (pruritis), sores in your mouth, blistering or peeling skin, as these can become severe and require treatment with corticosteroids.
  - **Lung problems (pneumonitis, inflammation of the lung):** New or worsening cough, shortness of breath, trouble breathing, or chest pain.
  - **Liver problems (hepatitis, inflammation of the liver):** Yellowing of the skin or eyes, your urine appears dark or
brown, pain in your abdomen, bleeding or bruising more easily than normal, or severe nausea and vomiting. Your oncology care team may monitor for liver problems using blood tests called liver function tests.

- **Brain and/or nerve problems:** Report any headache, drooping of eyelids, double vision, trouble swallowing, weakness of arms, legs, or face, or numbness or tingling in the hands or feet to your healthcare team.

- **Hormone abnormalities:** Immune reactions can affect the pituitary, thyroid, pancreas, and adrenal glands, resulting in inflammation of these glands, which can affect their production of certain hormones. Some hormone levels can be monitored with blood work. It is important that you report any changes in how you are feeling to your care team. Symptoms of these hormonal changes can include: headaches, nausea, vomiting, constipation, rapid heart rate, increased sweating, extreme fatigue, weakness, changes in your voice, changes in memory and concentration, increased hunger or thirst, increased urination, weight gain, hair loss, dizziness, feeling cold all the time, and changes in mood or behavior (including irritability, forgetfulness and decreased sex drive).

- **Eye problems:** Report any changes in vision, blurry or double vision, and eye pain or redness to your healthcare team.

- **Kidney problems (kidney inflammation or failure):** Decreased urine output, blood in the urine, swelling in the ankles, loss of appetite.

- **Heart problems:** Inflammation in the heart muscle can happen in rare cases. If you develop any of these symptoms, report them to your provider right away: chest pain, shortness of breath, trouble breathing when lying down or waking up gasping for air, heart palpitations (feeling like your heart is racing or skipping a beat), swelling in your feet or legs, lightheadedness or fainting.

- **Infusion-Related Side Effects:** The infusion can cause a reaction that may lead to chills, fever, low blood pressure, nausea, and vomiting. Reactions are most common during the first week of therapy, including the evening after the infusion. Your oncology care team will tell you what to do if this happens.

- **Allogeneic Stem Cell Transplant Reactions:** Patients who receive this medication before or after having an allogeneic stem cell transplant can be at an increased risk of graft vs. host disease, veno-occlusive disease, and fever syndrome. Your providers will monitor you closely for these side effects.

### Reproductive Concerns

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Even if your menstrual cycle stops or you believe you are not producing sperm, effective birth control is necessary during treatment and for 5 months after stopping treatment. You should not breastfeed while taking this medication or for five months after the end of treatment.