Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

One Wales Medicines Assessment Group Recommendation
Nivolumab (OPDIVO®) concentrate for solution for infusion and ipilimumab (YERVOY®) concentration for solution for infusion (OW35)

Date of advice: March 2026
AWTTC reference number: OW35

Using the agreed starting and stopping criteria nivolumab plus ipilimumab (OPDIVO® plus YERVOY®) can be made available within NHS Wales for the neoadjuvant treatment of patients with resectable macroscopic stage III melanoma with ≥1 pathologically proven lymph node metastasis and up to 3 in-transit metastases.

The risks and benefits of the off-label use of nivolumab plus ipilimumab (OPDIVO® plus YERVOY®) for this indication should be clearly stated and discussed with the patient to allow informed consent.

Providers should consult the relevant guidelines on prescribing unlicensed medicines before any off-label medicines are prescribed.

There is a simple discount patient access scheme (PAS) for both nivolumab (OPDIVO®) and ipilimumab (YERVOY®).

This recommendation has been endorsed by the All Wales Medicines Strategy Group (AWMSG) and ratified by Welsh Government.

This recommendation will be reviewed after 12 months or earlier if new evidence becomes available.

Clinician responsibility
Clinicians will be obliged to collect and monitor patient outcomes. Evidence of clinical outcomes will be taken into consideration when reviewing the One Wales Medicines Assessment Group decision.

Health board responsibility
Health boards will take responsibility for implementing One Wales Medicines Assessment Group decisions and ensuring that a process is in place for monitoring clinical outcomes

One Wales advice assists consistency of access across NHS Wales and will be disseminated to the service following ratification by Welsh Government.

AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Starting and stopping criteria for nivolumab plus ipilimumab (OPDIVO® plus YERVOY®) for the neoadjuvant treatment of patients with resectable macroscopic stage III melanoma with ≥1 pathologically proven lymph node metastasis and up to 3 in-transit metastases

Developed in collaboration with oncologists in Wales.

Starting criteria
Patients must satisfy all of the following criteria. Treatment may be considered in adult patients who:

- have cytologically or histologically confirmed resectable stage III melanoma of cutaneous or unknown primary origin
- have one or more macroscopic lymph node metastases (clinically detectable), that can be biopsied
- have a maximum of 3 additional resectable in-transit metastases. A concurrent resectable primary melanoma is allowed.
- have not received prior radiation therapy, immunotherapy targeting CTLA-4, PD-1 or PD-L1, nor targeted therapy targeting BRAF and/or MEK
- have an Eastern Cooperative Oncology Group (ECOG) or World Health Organization (WHO) performance status of between 0 and 1
- Have not received immunosuppressive medications within 6 months prior to treatment (steroids equivalent to prednisolone ≤10 mg is allowed)
- are not pregnant. Patients of childbearing potential must be willing to use an adequate method of contraception during treatment and for at least 5 months after the last cycle.

A full list of precautions is included in the Summaries of Product Characteristics (SmPC)[1,2].

Nivolumab plus ipilimumab should always be initiated by an experienced oncologist following a multidisciplinary team (MDT) discussion.
Patients who satisfy the eligibility criteria will be prescribed nivolumab plus ipilimumab following consultation with the patient and/or carer after consideration of potential adverse effects, cautions, contraindications and an explanation of alternative treatment options. This consultation should be recorded in the patient's notes.

The recommended dose for stage III melanoma is 240 mg nivolumab plus 80 mg ipilimumab by intravenous infusion every 3 weeks for a total of two cycles prior to surgery. Dosing delay or discontinuation may be required based on individual safety and tolerability. Recommended modifications to manage adverse reactions are provided in the SmPCs[1,2].

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Adjuvant treatment is indicated in patients who do not achieve a major pathological response to neoadjuvant treatment.

Monitoring

- Full blood count
- Urea and electrolytes
- Liver function tests
- Thyroid function test
- Phosphate and calcium
- Blood glucose
- Clinical evaluation of side effects, refer to SmPC[1,2]

The above tests should be done at baseline and before each cycle of treatment. Refer also to local protocols on scheduling tests.

Whilst on treatment the following investigations are required:

- Baseline electrocardiogram (ECG)
- Computerised Tomography (CT) scan after treatment
- Pathology reporting of residual tumour

This list is not exhaustive. Any other monitoring should be in accordance with the SmPC for nivolumab and ipilimuamb[1,2].

Stopping criteria

- evidence of clinically significant disease progression or symptomatic deterioration as agreed in the MDT
- toxicity; dosing delay may be considered, follow the guidance in the SmPC[1]
- patient request
- after 2 cycles of nivolumab plus ipilimumab

Only one course of treatment may be issued in accordance with this advice. Requests for repeat courses in the neoadjuvant indication should be explored through funding mechanisms such as the individual patient funding request process.

Outcomes

It is important that outcomes are collected for this patient cohort and the outcomes will be reviewed by the One Wales Medicines Assessment Group after 12 months and the periodically. Clinicians will be asked to complete a Blueteq form prior to starting treatment and a follow up reporting the following outcomes: pathological response, requirement for adjuvant treatment, adverse events.

Other considerations

- Patients should be provided with an alert card stating that they have been treated with nivolumab and ipilimumab and advised of the symptoms of immune reactions that should prompt urgent medical care. Link to alert card.
- AWTTC patient information leaflets on understanding unlicensed medicines in English and Welsh and an easy read format, these can be accessed here.
- Clinicians may wish to use one of the Cancer Research UK consent forms for SACT (Systemic Anti-Cancer Therapy) to help ensure your patient is fully informed when consenting to SACT.
- The Strategic Clinical Network for Cancer standard is that all patients receiving SACT should be given the All Wales Cancer Treatment Alert Card with the treating team being responsible for ensuring that the details of which treatment type and name is clearly indicated on the card and the patient is given supporting information and explanations. Further information can be found here: Systemic Anti-Cancer Therapies (SACT) - NHS Wales Executive

References

1. Bristol Myers Squibb Pharmaceuticals limited. OPDIVO 10 mg/mL concentrate for solution for infusion. Summary of Product Characteristics. January 2026. Available at: https://www.medicines.org.uk/emc/product/6888/smpc#gref. Accessed February 2026.
2. Bristol Myers Squibb Pharmaceuticals limited. YERVOY 5 mg/ml concentrate for solution for infusion. Summary of Product Characteristics. July 2025. Available at: https://www.medicines.org.uk/emc/product/4683/smpc. Accessed February 2026.