Grŵp Strategaeth Meddyginiaethau Cymru Gyfan
All Wales Medicines Strategy Group

One Wales Medicines Assessment Group Recommendation
Dabrafenib (Tafinlar®) and trametinib (Mekinist®) (OW27)

Date of advice: April 2024
Date of last review: October 2025
AWTTC reference number: OW27

Using the agreed starting and stopping criteria dabrafenib (Tafinlar®) and trametinib (Mekinist®) in combination can be made available within NHS Wales for the treatment of inoperable anaplastic thyroid cancer with the BRAF V600E variant.

The risks and benefits of the off-label use of dabrafenib and trametinib for this indication should be clearly stated and discussed with the patient to allow informed consent.

There are simple discount patient access schemes (PAS) for dabrafenib and trametinib.

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

This advice 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 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

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One Wales advice assists consistency of access across NHS Wales.

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Starting and stopping criteria for the treatment of inoperable BRAF V600E variant anaplastic thyroid cancer

Developed in collaboration with oncologists in Wales.

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

- have BRAF V600E mutation-positive anaplastic thyroid cancer confirmed by a validated test through the All Wales Medical Genomics Service (AWMGS)
- have cancer that is deemed to be not operable at the time treatment is commenced with dabrafenib and trametinib*
- an Eastern Cooperative Oncology Group (ECOG) performance status of between 0 and 2.
- are not pregnant. Patients of childbearing potential must be willing to use an adequate method of contraception.

*patients who are down-staged following initial treatment with dabrafenib and trametinib and undergo surgical resection with curative intent will continue to be eligible for treatment.

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

Dabrafenib and trametinib should always be initiated by an experienced oncologist following a multidisciplinary team (MDT) discussion.

Patients who satisfy the eligibility criteria will be prescribed dabrafenib and trametinib 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 total daily dose of dabrafenib is 300 mg (two 75 mg capsules twice a day), and the recommended dose of trametinib is 2 mg once daily[1,2]. Treatment is continued until disease progression or unacceptable toxicity occurs. Dosing delay or discontinuation may be required based on individual safety and tolerability. Recommended modifications to manage adverse reactions are provided in the SmPC[1,2].

Monitoring:

- Full blood count
- Urea and electrolytes
- Liver function tests
- Thyroid function test
- Blood pressure
- ECG (+/- echocardiogram and MUGA scan as appropriate)

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- Clinical evaluation of side effects, refer to SmPC

The above tests should be done at baseline. Repeat blood tests, blood pressure and ECG repeated every four weeks in clinic. Refer also to local protocols on scheduling tests.

Whilst on treatment a computed tomography (CT) will be performed every 3 months, according to response to treatment.

Skin examination should be performed prior to initiation of therapy with dabrafenib and trametinib and monthly throughout treatment and for up to six months following discontinuation of dabrafenib or until initiation of another anti-neoplastic therapy. If patients report new visual disturbances, such as diminished central vision, blurred vision or loss of vision at any time while on dabrafenib and trametinib, a prompt ophthalmological assessment is recommended[1,2].

This list is not exhaustive. Any other monitoring should be in accordance with the SmPC for dabrafenib and trametinib[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.
- patient request

Patients who have received treatment with dabrafenib and trametinib who subsequently undergo surgical intervention to improve local control are likely to need to continue treatment post-surgical resection, unless MDT discussion deems that the adequacy of resection was such that adjuvant treatment with dabrafenib and trametinib is no longer indicated.

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

Other considerations:

- 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.
- 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.

References

1. Novartis Pharmaceuticals UK Ltd. Taflinar®. 75 mg hard capsules. Summary of Product Characteristics. Jul 2023. Available at: https://www.medicines.org.uk/emc/product/7837/smpc. Accessed Oct 2025.

2. Novartis Pharmaceuticals UK Ltd. Mekinist®. 2 mg film-coated tablets. Summary of Product Characteristics. Jul 2023. Available at: https://www.medicines.org.uk/emc/product/5072/smpc. Accessed Oct 2025.

First Review of One Wales Decision – July 2025

Dabrafenib (Tafinlar®) and trametinib (Mekinist®) for the treatment of inoperable anaplastic thyroid cancer that has the BRAF V600E variant (OW27)

This report was prepared by the All Wales Therapeutics and Toxicology Centre in July 2025. It summarises any new evidence available and patient outcome data collected since the One Wales decision in April 2024.

Background: Anaplastic thyroid cancer (ATC) is a very rare form of thyroid cancer that progresses quickly. For those patients with inoperable disease there are few treatment options. The BRAF V600E variant is present in 25–45% of ATCs. This variant leads to activation of RAS/RAF/MEK/ERK pathway causing cell proliferation and growth and may be associated with a worse prognosis. Based on these mechanisms of action, patients may benefit from treatment with a combination of the BRAF inhibitor dabrafenib and the MEK inhibitor trametinib. Combination treatment with dabrafenib and trametinib is routinely commissioned in NHS England and NHS Scotland to treat inoperable BRAF V600E variant ATC.

Clinicians in Wales submitted dabrafenib and trametinib as a treatment option for ATC with BRAF V600E variant for consideration through the One Wales Medicines process. They considered there was an unmet need in Wales and a cohort of patients who could benefit from this treatment.

Current One Wales decision: supported for use

Licence status: Dabrafenib and trametinib are not licensed for the treatment of inoperable anaplastic thyroid cancer that has the BRAF V600E variant; their use for this indication is off-label.

Guidelines: A 6th edition of Head and Neck Cancer: UK National Multidisciplinary Guidelines was published in 2024. For anaplastic thyroid cancer the guidelines recommend that biopsy tissue should be sent for molecular profiling, including BRAF V600E variant, and that targeted therapy should be considered if a druggable genomic alteration is present.

No relevant updates to other guidelines were identified.

Licensed alternative medicines or Health Technology Assessment (HTA) advice for alternative medicines: No new medicines or HTA advice reported.

Effectiveness: AWTTC conducted a literature search in April 2025 to find new evidence for the use of dabrafenib and trametinib to treat unresectable BRAF-variant ATC. The search excluded articles published before 2024, articles that reviewed evidence previously presented in AWTTC's first Evidence Summary Report, and conference abstracts.

The literature search identified one retrospective case series, and one case report describing two patients. Russell et al. (2024) described a retrospective case series of 17 patients (12 male; mean age 54.9 years [range 10–73 years]) from the USA and Australia. Patients had locally advanced, thyroid cancer considered unresectable or associated with significant surgical morbidity. Dabrafenib plus trametinib was given as first-line neoadjuvant therapy to 2 patients with unresectable BRAF-variant ATC; one patient underwent surgery after treatment. A third patient with unresectable BRAF variant ATC was transitioned to dabrafenib plus trametinib treatment after developing a tracheal fistula when receiving lenvatinib, but their tumour remained unresectable. Results were grouped for other outcomes and it was unclear which related to patients with unresectable ATC treated with dabrafenib and trametinib.

Yamauchi et al. (2024) reported two cases from Japan of unresectable BRAF-variant ATC that were treated with a combination of dabrafenib and trametinib. Both tumours responded and shrank with treatment and one patient then underwent surgical resection of the tumour. The other patient stopped treatment with 150 mg dabrafenib due to adverse events, and restarted treatment on a lower dose (100 mg twice daily). Both patients remained on dabrafenib and trametinib treatment at the time of reporting; no further outcomes were reported.

Safety: No relevant safety analyses identified in the repeat literature search.

Cost-effectiveness: No relevant cost-effectiveness analyses were identified in the literature search.

Budget impact: No information on patient numbers has been provided.

Impact on health and social care services: Minimal

Patient outcome data: No patient outcome data have been received.

Evaluation of evidence

No significant new evidence has been published that challenges the previous evidence presented. AWTTC recommends continuing access to dabrafenib in combination with trametinib to treat inoperable (unresectable) anaplastic thyroid cancer that has the BRAF V600E variant.

Next review date: October 2026

This document includes evidence published since the last review or full assessment of this medicine for the indication under consideration. It does not replace the original full evidence status report. Any previous reviews and the original full evidence status report are available on request by email to AWTTC@wales.nhs.uk.

liability in association with the use of its content. An Equality and Health Impact Assessment (EHIA) has been completed in relation to the medicine and has been published on the AWTTC website.

Information presented in this document can be reproduced using the following citation: All Wales Therapeutics & Toxicology Centre. Evidence Review. dabrafenib (Taflinar®) and trametinib (Mekinist®) for the treatment of inoperable BRAF V600E variant anaplastic thyroid cancer: OW27. 2025.

References: a full reference list is available on request.

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