

TAF MEK melanoma - Mechanism of action - HCP

[Prescribing information](#)

Image



Image



Mechanisms of action of TAFINLAR® (dabrafenib) + MEKINIST® (trametinib)

TAFINLAR in combination with MEKINIST is indicated in adult patients with unresectable or metastatic melanoma with a *BRAF* V600 mutation.^{1,2}

TAFINLAR in combination with MEKINIST is indicated for the adjuvant treatment of adult patients with Stage III melanoma with a *BRAF* V600 mutation, following complete resection.^{1,2}

For the full safety profile, please refer to the Summary of Product Characteristics (SmPC) for [TAFINLAR](#) and [MEKINIST](#).

Adverse event reporting: Details of how to report adverse events are available at the bottom of the page. Please refer to the respective SmPC for all licensed indications.

TAFINLAR + MEKINIST target two distinct points on the mitogen-activated protein kinase (MAPK) pathway to provide concomitant inhibition^{1,2}

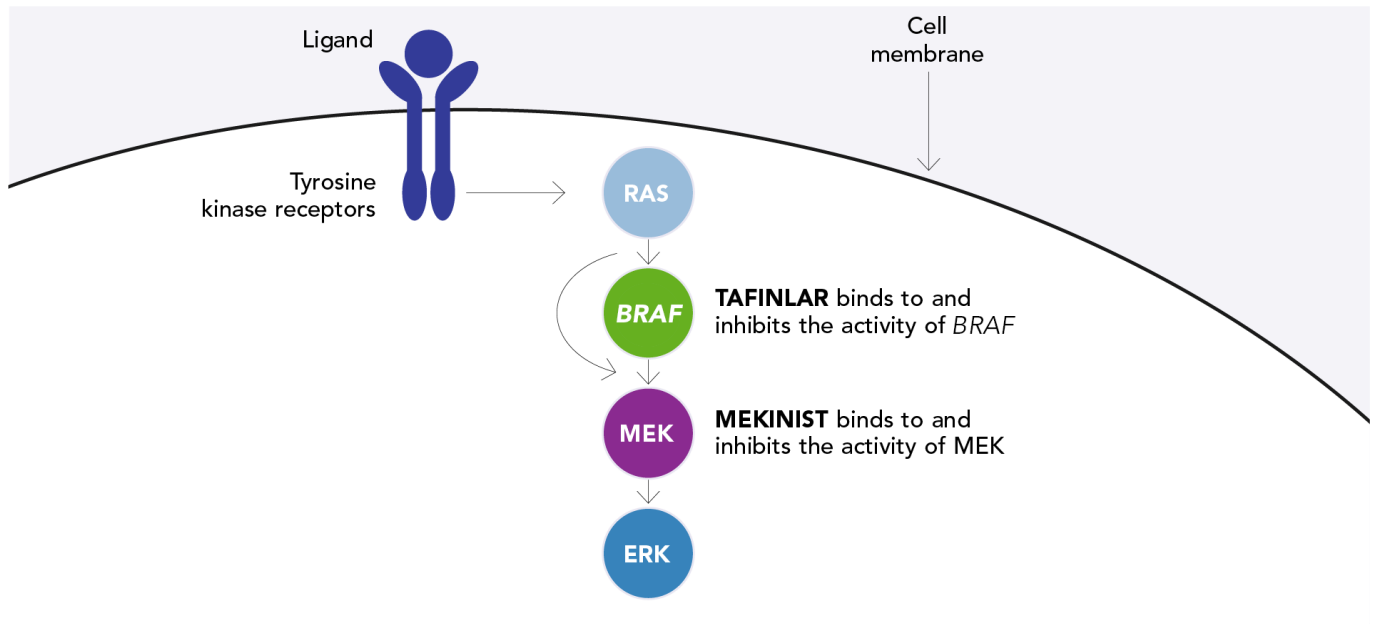
BRAF V600 mutations result in constitutive activation of the MAPK pathway, which plays a key role in regulating the growth, proliferation and survival of normal cells, including melanocytes, which are the cells from which melanoma originates.^{3,4} As many as 50% of patients with melanoma harbour mutations of the *BRAF* V600 gene.⁵

In melanoma cells with a *BRAF* V600 mutation, the *BRAF* V600 and mitogen-activated extracellular signal-regulated kinase (MEK) proteins send signals that cause melanoma cells to grow and increase uncontrollably. TAFINLAR + MEKINIST work together to block these signals.^{1,2}

TAFINLAR, in combination with MEKINIST, is designed to target the oncogenic driver of *BRAF* V600-positive melanoma. TAFINLAR is an inhibitor of the mutated *BRAF* V600 kinase¹ and MEKINIST is a reversible and highly selective inhibitor of MEK 1 and MEK 2, which sit downstream of *BRAF*.² Based on pre-clinical research, combined inhibition of *BRAF* and MEK reduces extracellular signal-related kinase (ERK)-driven gene expression that can cause tumour growth.

Schematic of the MAPK signalling pathway showing where TAFINLAR and MEKINIST act^{1,2}

Image



Further information about *BRAF* V600 mutations, the *BRAF* pathway, and the importance of *BRAF* testing in melanoma can also be found [here](#).

Benefits of blocking MEK, in addition to BRAF

Combining TAFINLAR + MEKINIST results in greater inhibition of tumour growth versus either drug alone in *BRAF* V600-positive melanoma^{1,2}

Blocking MEK, in addition to *BRAF* in *BRAF* V600-positive melanoma:

- Prolonged inhibition of tumour growth with TAFINLAR + MEKINIST vs TAFINLAR alone (median progression-free survival was 11.0 vs 8.8 months, respectively [hazard ratio=0.67; 95% CI: 0.53-0.84, p= 0.0004])⁶
- Is thought to reduce the risk of treatment resistance vs *BRAF* inhibitor alone, based on pre-clinical research^{1-3,7-10}

Cutaneous malignancies are a special warning associated with TAFINLAR + MEKINIST. Please refer to the SmPC for the full guidance.

BRAF V600, mutation of the *BRAF* gene in which valine (V) at amino acid 600; CI, confidence interval; ERK, extracellular signal-related kinase; MAPK, mitogen-activated protein kinase; MEK, mitogen-activated extracellular signal-regulated kinase; RAS, rat sarcoma; SmPC, summary of product characteristics.

References

1. TAFINLAR (dabrafenib) Summary of Product Characteristics.
2. MEKINIST (trametinib) Summary of Product Characteristics.
3. Nijenhuis CM, et al. *Cancer Treat Rev* 2013;39:305–312.
4. Melanoma UK. What is melanoma? Available at: <https://www.melanomauk.org.uk/pages/category/what-is-melanoma> [Accessed March 2025].
5. Ascierto PA, et al. *J Transl Med* 2012;10:85.
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7. Hauschild A, et al. *J Clin Oncol* 2013;31(suppl): abstract number 9013.
8. Robert C, et al. *Pigment Cell Melanoma Res* 2018;31:201.
9. McArthur GA, et al. *Lancet Oncol* 2014; 15: 323–332.
10. Greger JG, et al. *Mol Cancer Ther* 2012;11:909–920.

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Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Novartis online through the pharmacovigilance intake (PVI) tool at www.novartis.com/report, or alternatively email medinfo.uk@novartis.com or call 01276 698370.

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