

One Wales Medicine Assessment Group summary of decision rationale

Medicine: **Trametinib**

Indication: **Treatment of recurrent low grade serous ovarian carcinoma (LGSOC) which has progressed following at least 1 previous platinum-based regimen**

Meeting date: **12 May 2025**

Criteria	OWMAG opinion
Clinical effectiveness and safety	<p>OWMAG note that the clinical effectiveness evidence for the use of trametinib to treat recurrent LGSOC which has progressed following at least 1 previous platinum-based regimen is from the open-label, randomised GOG 281/LOGS phase II/III study. This study demonstrated clinical benefit of trametinib treatment in this population compared to patients receiving standard of care treatments (paclitaxel, pegylated liposomal doxorubicin, topotecan, tamoxifen, letrozole). Median progression-free survival in the trametinib group was 13.0 months compared with 7.2 months in the standard-of-care group. OWMAG note that three of the five standard-of-care treatments used in the study are treatments routinely used in Wales to treat LGSOC that has progressed after at least one previous platinum-containing regimen. OWMAG also note that the characteristics of patients treated in the study in terms of age, ECOG status and stage of disease is reflective of the population to be treated in Wales. OWMAG consider that the study results are likely to be generalisable to the patient population in Wales.</p> <p>OWMAG note that no new safety signals have been observed for the use of trametinib to treat LGSOC, although note that the majority of patients required dose reductions whilst receiving trametinib.</p> <p>OWMAG consider that the evidence provided demonstrates clinical effectiveness for using off-label trametinib to treat recurrent LGSOC which has progressed following at least 1 previous platinum-based regimen.</p>
Cost-effectiveness	<p>OWMAG note one published analysis evaluating cost-effectiveness of trametinib vs standard-of-care from a US payer perspective based on results from the GOG 281/LOGS study. OWMAG consider that this has very limited generalisability to the UK based on differences in treatment and service costs and the assumptions used in the model. In addition, the absence of direct comparative efficacy between trametinib and comparative standard-of-care treatments used in NHS Wales means the actual cost-effectiveness of trametinib for this indication remains unknown.</p> <p>OWMAG note the results of a cost comparison assessment of trametinib versus the standard-of-care comparators used</p>

	<p>in NHS Wales undertaken by AWTTTC. After taking into account the limitations of the cost comparison analysis, OWMAG consider that treatment with trametinib is likely to be both more effective and more costly than standard-of-care treatments. Based on the costs provided, OWMAG consider trametinib to be reasonable value for money for NHS Wales.</p>
<p>Budget impact</p>	<p>OWMAG consider the clinical estimate of patient numbers reported to be reasonable although note that it is slightly higher than would be predicted using published incidence data which may cause the presented budget impact to be overestimated.</p> <p>The group note that additional monitoring, administration and adverse event costs have been included in the budget impact calculations although these may be subject to uncertainty.</p> <p>OWMAG note that the majority of patients receiving trametinib in the GOG 281/LOGS clinical trial required dose reduction. Therefore, the acquisition costs for trametinib may be lower than those presented.</p> <p>OWMAG consider that the base case provided in the report is a reasonable estimate of the associated cost to NHS Wales.</p>
<p>Resource use</p>	<p>OWMAG agree that there is likely to be a reduction in use of NHS services as trametinib is an oral therapy taken at home unlike standard-of-care chemotherapy which require patients to attend a clinic or hospital to receive treatment by intravenous infusion. OWMAG acknowledge that some additional monitoring is required during treatment with trametinib.</p>
<p>Other factors</p>	<p>OWMAG acknowledge the evidence provided by clinical experts at the meeting, who reported that there is no standard treatment pathway for recurrent LGSOC in Wales as it seldom responds to available standard-of-care treatments. Trametinib offers a potentially clinically-effective treatment option for this cohort of patients; it was also reported that the American Society of Clinical Oncology recently issued an alert recommending trametinib as standard-of-care for LGSOC, a recommendation which is increasingly becoming adopted worldwide. OWMAG note that the European Society of Clinical Oncology (ESMO) and US National Comprehensive Cancer Network (NCCN) both recommend using trametinib to treat recurrent LGSOC. Clinicians also highlighted that it is mainly younger women affected by LGSOC who are more likely to be of working age and have</p>

	<p>dependents in comparison to women with high-grade ovarian cancer which tends to occur in older populations.</p> <p>OWMAG note the patient perspectives as outlined in the submissions received from Ovarian Cancer Action and Target Ovarian Cancer, and how knowledge that recurrent LGSOC does not respond well to current standard-of-care treatments causes a sense of uncertainty and anxiety in patients that is difficult to live with. Knowing trametinib was available would reduce anxiety around recurrence for them, and their families and carers. OWMAG also note that trametinib, taken as an oral tablet at home, leads to less disruption of day-to-day life than some standard-of-care treatments currently offered in Wales which are delivered intravenously in a clinical setting. Patients also highlight that the improvements in progression-free survival that trametinib may give would help them to return to a more normal routine like work and spending time with friends and family.</p> <p>OWMAG note that trametinib is routinely commissioned by NHS England to treat recurrent LGSOC which has progressed following at least 1 previous platinum-based regimen and is also supported for use in NHS Scotland for this patient cohort. Clinicians and patients highlight this inequity of access for patients in Wales and the distress this may cause.</p>
<p>Final recommendation</p>	<p>OWMAG recommend the use of trametinib as an off-label treatment of recurrent low grade serous ovarian carcinoma (LGSOC) which has progressed following at least 1 previous platinum-based regimen.</p> <p>This recommendation is subject to the development of appropriate start/stop criteria.</p>
<p>Summary of rationale</p>	<p>There is clinical evidence to support the use of trametinib as an off-label treatment of recurrent low grade serous ovarian carcinoma (LGSOC) which has progressed following at least 1 previous platinum-based regimen. OWMAG is of the opinion that the use of trametinib treatment offers this patient cohort increased progression-free survival compared to current standard-of-care treatments and consider the associated cost to be a reasonable use of NHS resources. Real world data will be captured to assess the benefit of this treatment for this cohort of patients.</p>