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

Equality and Health Impact Assessment

Trametinib (Mekinist®) for the treatment of recurrent low grade serous ovarian carcinoma (LGSOC) that has progressed after at least one platinum-based regimen

AWTTC will fill in an Equality and Health Impact Assessment in parallel with each development stage of our projects. This will help us to follow the five ways of working for public bodies, and work to achieving the wellbeing goals, outlined in the Well-Being of Future Generations (Wales) Act 2015.

Date: 05/03/2025

1.	AWTTC contact details	Tel: 02921 826900 Email: awttc@wales.nhs.uk
2.	State the objectives of the project.	AWTTC will prepare an evidence status report (ESR) for an assessment under the One Wales Medicines process for the use in NHS Wales of trametinib (Mekinist®) for the treatment of recurrent low-grade serous ovarian carcinoma (LGSOC) that has progressed after treatment with at least one platinum-based regimen. The ESR will summarise current use of trametinib in NHS Wales, clinical effectiveness, safety considerations, cost effectiveness, budget impact, and equity of access across Wales and the rest of the UK. AWTTC will request the views of patient organisations relevant to the condition, and will send the ESR to the company (marketing authorisation holder) and to clinicians in Wales for comment. Clinicians, company representatives and patient organisation representatives will be invited to attend the meeting of the One Wales Medicines Assessment Group (OWMAG) to consider the ESR. The OWMAG constitution is available online.

3.	Evidence and background information considered. For example: • population data • staff and service users' data, as applicable • needs assessment • engagement and involvement findings • research • good practice guidelines • participant knowledge • list of stakeholders and how stakeholders have engaged in the development stages • comments from those involved in the designing and development stages Population pyramids are available from Public Health Wales Observatory.	Low-grade serous ovarian cancer (LGSOC) is rare and accounts for about 5% of all epithelial ovarian cancers, which make up 90% of all ovarian cancers. In 2021, there were 330 diagnoses of ovarian cancer in Wales (WCISU): around 14 cases of LGSOC per year. LGSOC tends to grow slowly but is more resistant to chemotherapy and has different driver mutations. Nearly all cases show oestrogen or progesterone positivity and around 60% of cases have mutations in the ERK/MAPK pathway. Affected people are often younger at presentation and in most cases the disease extends beyond the ovaries at diagnosis, with over 70% of people with LGSOC experiencing disease recurrence (Gershenson et al, 2022). People with LGSOC often survive for longer than people with other types of ovarian cancer. Median overall survival (OS) for LGSOC has been reported to be 90.8 months, compared to 40.7 months for high-grade ovarian cancer (Gockley et al, 2017). During the COVID 19 pandemic, trametinib was available to use as a treatment for LGSOC as an oral alternative to intravenous chemotherapy and to reduce the risk of immunosuppression. This formed part of the NHS England interim treatment options during the COVID-19 pandemic (NG161), guidance which also applied to Wales. After the withdrawal of NG161 in September 2023, trametinib is no longer routinely available for use in Wales. It has since been commissioned in England (2023) and Scotland (2024). Access in Wales is through IPFR or local commissioning arrangements. Two cancer centres in Wales have formally requested trametinib treatment through the One Wales medicines process. We estimate that 3 patients a year would be eligible for treatment with trametinib in one health board, which equates to around 10 patients per year across Wales. This might be higher than predicted using the WISCU data, and assumes trametinib would not be suitable for all of the estimated 70% of patients who would have a recurrence.

		Trametinib inhibits MEK1 and MEK2, which are part of the ERK/MAPK signalling pathway. The recommended dose to treat LGSOC is 2 mg once daily given orally, which is the licensed dose (SmPC). This use of trametinib is off label. Trametinib is licensed only for the treatment of melanoma and non-small cell lung cancer. NHS England approved trametinib use in NHS England in November 2023: Clinical panel report: Trametinib in recurrent or progressive low grade serous ovarian cancer (adults). The National Cancer Medicines Advisory Group (NCMAG) supported its use in Scotland in October 2024: NCMAG118 Trametinib advice document: October 2024 – Healthcare Improvement Scotland. The European Society for Medical Oncology (ESMO), and the National Comprehensive Cancer Network (NCCN) support the use of trametinib for recurrent disease in recurrent low grade serous ovarian carcinoma. Current standard treatment for LGSOC is surgery that aims to remove all of the tumour deposits and obtain complete remission. After surgery, adjuvant platinum-based chemotherapy and paclitaxel can be offered, although the benefit of this is uncertain. Individuals who have recurrent LGSOC with operable disease after treatment will be considered for further surgery. However, some people will present with, or go on to develop, disease that is either not amenable to surgical resection due to its widespread nature, or disease which may potentially be operable but where surgery has been declined or is unable to be performed due to other factors (such as other health problems). These patients will receive first-line treatment with a platinum-based chemotherapy and paclitaxel. Hormonal therapies can be given after surgery or after chemotherapy. Letrozole (an aromatase inhibitor) and tamoxifen (a selective oestrogen receptor modulator) are most commonly used. Endocrine therapy is generally continued until disease progression or unacceptable toxicity. Most people with LGSOC do not respond to platinum-based chemotherapy, and most will

		eventually experience disease progression or recurrence. Progressive disease is defined as disease that has not responded to platinum-based chemotherapy. Recurrent disease is defined as disease that at first responds to treatment with platinum-based chemotherapy with/without surgery, but which subsequently recurs. Once disease progression or recurrence occurs other treatment options can be offered including hormonal therapy (if not previously given) or further chemotherapy. Further chemotherapy options include paclitaxel alone, or pegylated liposomal doxorubicin hydrochloride (PLDH) (NICE TA389). However, due to the chemotherapy-resistant nature of LGSOC, the effectiveness of these treatments in preventing further disease progression is often limited. People with LGSOC are first treated by gynaecology oncology specialists and oncologists who specialise in treating ovarian cancer. Once progression or recurrence occurs, most people will need support from palliative care specialists and community teams. The most frequent complications of recurrent LGSOC are those that arise from widespread peritoneal disease and include bowel obstruction, hydronephrosis, fistulation and general organ failure (NHSE 2023). The GOG 281/LOGS study was a phase II/III randomised, open-label, multicentre trial which compared trametinib with study standard of care (SOC) (physician choice of either paclitaxel, pegylated liposomal doxorubicin, topotecan, letrozole and tamoxifen) in 260 patients with recurrent LGSOC who had received at least one prior line of platinum chemotherapy. At the primary analysis, there were 217 progression-free survival events (101 [78%] in the trametinib group and 116 [89%] in the standard-of-care group). Median progression-free survival in the trametinib group was 13·0 months (95% CI 9·9-15·0) compared with 7·2 months (5·6-9·9) in the standard-of-care group (hazard ratio 0·48 [95% CI 0·36-0·64]; p<0·0001). Overall survival improvements were numerically in favour of trametinib, although a high proportion of patients in the SOC arm crossed over to trametinib, confounding

		and potentially underestimating the survival benefit. No clinically significant differences in QoL measurements were found between treatments. In the GOG 281/LOGS study, the most frequent grade 3 or 4 adverse events in the trametinib group were skin rash (17 [13%] of 128), anaemia (16 [13%]), hypertension (15 [12%]), diarrhoea (13 [10%]), nausea (12 [9%]), and fatigue (ten [8%]). The most frequent grade 3 or 4 adverse events in the standard-of-care group were abdominal pain (22 [17%]), nausea (14 [11%]), anaemia (12 [10%]), and vomiting (ten [8%]). There were no treatment-related deaths. A total of 46 (36%) of 128 patients discontinued trametinib due to toxicity compared with 38 (30%) of 127 patients who discontinued SOC therapy due to toxicity.
4.	Who will this project affect?	People in Wales with recurrent low-grade serous ovarian carcinoma (LGSOC) that has progressed after at least one platinum-based regimen, and their families and carers.

5. EQIA - How will the project impact on people?

Questions in this section relate to the impact on people based on the 'protected characteristics' of the Equality Act 2010, and other factors.

How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
5.1 Age For most purposes, the main categories are people aged: • under 18 years; • between 18 and 65 years; • over 65 years.	We do not expect a potential negative, or unequal, impact on people based on their age. [Note: For prescription medicines we expect the prescriber to have prescribed or advised their use within the terms of their UK marketing authorisations. Healthcare professionals should take note of the contraindications, warnings, safety recommendations and any monitoring needs for the medicine. These are explained in the Summary of Product Characteristics (SmPC) for the medicine or the British National Formulary.	N/A	N/A

How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
	Healthcare professionals should follow relevant professional guidance and take full responsibility for the decision when prescribing or advising the use of off-label or unlicensed medicines. This includes considering the contraindications, warnings, monitoring requirements and other safety recommendations for the medicine (MHRA guidance on off-label or unlicensed use of medicines)]		
5.2 Persons with a disability as defined in the Equality Act 2010 Those with physical impairments, learning disability, sensory loss or impairment, mental health conditions, long-term medical conditions such as diabetes.	We do not expect a potential negative, or unequal, impact on people with a disability.	All related documents published on the AWTTC website will meet accessibility requirements. Any patient-facing materials will be also be produced as easy read booklets in Welsh and English.	N/A

How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
5.3 People of different genders: Consider men, women, people undergoing gender reassignment. **N.B.** Gender-reassignment is anyone who proposes to, starts, is going through or who has completed a process to change his or her gender with or without going through any medical procedures. Sometimes referred to as Trans or Transgender.	We do not expect a potential negative, or unequal, impact on people based on their gender, or on people undergoing gender reassignment. Ovarian cancer can affect anyone with an ovary; we might expect a positive impact on people with this type of ovarian cancer (LGSOC) if the criteria for treatment are met.	N/A	N/A
5.4 People who are married or who have a civil partner.	We do not expect a potential negative, or unequal, impact on people based on their marital status or being in a civil partnership.	N/A	N/A
5.5 Women who are expecting a baby, who are on a break from work after having a baby, or who are breastfeeding. They are protected for 26 weeks after having a baby whether or not they are on maternity leave.	We do not expect a potential negative, or unequal, impact on women who are expecting a baby, are breastfeeding, or are on a break from work after having a baby.	Prescribers should take account of the SmPC when prescribing any medicines for women who are pregnant, or who are breastfeeding.	The SmPC criteria specify which people are excluded from treatment due to the associated risks of treatment. This will be identified for consideration of any change to the advice at the next review if there is a change to the current

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	Trametinib should not be administered during pregnancy, and should not be given to women who are breastfeeding. Please refer to the SmPC. The SmPC states that a decision should be made whether to stop breastfeeding or discontinue trametinib, taking into account the benefit of breastfeeding for the child and the benefit of therapy for the mother. The SmPC states that female patients of reproductive potential must be advised to use effective methods of contraception during treatment with trametinib and for 16 weeks after stopping treatment.		advice for pregnant and breastfeeding women.
5.6 People of a different race, nationality, colour, culture or ethnic origin including non-English speakers, gypsies and travellers, migrant workers.	We do not expect a potential negative, or unequal, impact on people of a different race,	N/A	N/A

How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
The Runnymede Trust	nationality, colour, culture or ethnic origin. People of different race and ethnicities can have varying responses to medicines.		
5.7 People with a religion or belief or with no religion or belief. The term 'religion' includes a religious or philosophical belief. Implications of religious beliefs on selection of medicines (BMJ) In practice: guidance on religion, personal values and beliefs (General Pharmaceutical Council)	We do not expect a potential negative, or unequal, impact on people who have a religion or belief, or people with no religion of belief. Some medicines are made from certain animal products and people might not want to take them because of religion or belief.	N/A	N/A
5.8 People who are attracted to other people of: • the opposite sex (heterosexual); • the same sex (lesbian or gay); • both sexes (bisexual). Stonewall	We do not expect a potential negative, or unequal, impact on people based on who they are attracted to.	N/A	N/A

How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
5.9 People who communicate using the Welsh language in terms of correspondence, information leaflets, or service plans and design.	We do not expect a potential negative, or unequal, impact on people who communicate using the Welsh language. Any patient-facing materials will be produced in Welsh and English, in line with the Welsh language standards, including easy read booklets.	Any patient-facing materials will be produced in Welsh and English, in line with the Welsh language standards, including easy read booklets	N/A
5.10 People according to their income related group. *Consider people on low income, economically inactive, unemployed/workless, people who are unable to work due to ill-health.*	We do not expect a potential negative, or unequal, impact on people based on their income-related group. In Wales, all prescription medicines are free-of-charge for patients; positive recommendations through this project will not affect people depending on their income-related group.	N/A	N/A
5.11 People according to where they live.	We do not expect a potential negative, or unequal, impact on people based on where they live.	N/A	N/A

How will the project impact on, or affect:	Potential positive and/or negative impacts	Recommendations for improvement/ mitigation	Actions taken (and who by).
5.12 Consider others who face health inequalities, such as: • Looked after and accommodated children and young people • Carers: paid/unpaid, family members • People who are homeless or those who experience homelessness: people on the street; those staying temporarily with friends/family; those in hostels/B&Bs • People involved in the criminal justice system: offenders in prison or on probation, ex-offenders • People with addictions and substance misuse problems • People who have poor literacy • People living in remote, rural and island locations	We do not expect a potential negative, or unequal, impact on people who face health inequalities.	N/A	N/A
5.13 Consider any other groups and risk factors relevant to this project.	N/A	N/A	N/A

6. HIA - How will the project impact on the health and wellbeing of people in Wales and help address inequalities in health?

Questions in this section relate to the impact on the overall health of individual people, and the impact on the population in Wales.

How will the project impact on, or affect:	Potential positive and/or negative impacts and any particular groups affected	Recommendations for improvement/ mitigation	Actions taken (and who by) *Refer to where the mitigation is included in the document, as appropriate.*
6.1 People being able to access the service offered.	We do not expect a potential negative, or unequal, impact on people's ability to access the service offered.	N/A	N/A
6.2 People being able to improve or maintain healthy lifestyles.	We do not expect a potential negative, or unequal, impact on people's ability to improve or maintain healthy lifestyles.	N/A	N/A
6.3 People in terms of their income and employment status.	We do not expect a potential negative, or unequal, impact on people in terms of their income and employment status.	N/A	N/A
6.4 People in terms of their use of the physical environment.	We do not expect a potential negative, or unequal, impact on people's use of the physical environment.	N/A	N/A
6.5 People in terms of social and community influences on their health.	We do not expect a potential negative, or unequal, impact on people in terms of social and community influences on their health.	N/A	N/A

How will the project impact on, or affect:	Potential positive and/or negative impacts and any particular groups affected	Recommendations for improvement/ mitigation	Actions taken (and who by) *Refer to where the mitigation is included in the document, as appropriate.*
6.6 People in terms of macro-economic, environmental and sustainability factors.	We do not expect a potential negative, or unequal, impact on people in terms of macroeconomic, environmental and sustainability factors.	N/A	N/A

7. **Please fill in section 7.1 after completing the EqHIA, and fill in the action plan.**

7.1 Please summarize the potential positive and/or negative impacts of the project.	No potential negative impacts identified. We might expect a potential positive impact on people with this type of ovarian cancer, LGSOC, and their families and carers.

Action plan for mitigation or improvement and implementation

	Action	**Lead(s)**	**Timescale**	**Actions taken** *(state who by)*
7.2 What are the key actions identified as a result of completing the EqHIA?	• Consult with clinical experts in Wales, patient organisations, patients and carers in Wales (or the UK) and invite comments through the AWTTC website. • AWTTC to prepare an Evidence Summary Report (ESR) • One Wales Medicines Assessment Group (OWMAG) meet to consider and agree a recommendation. • AWMSG meet to ratify OWMAG's recommendation about the use of trametinib to treat LGSOC in Wales.	AWTTC	Feb-Mar 2025 Mar 2025 May 2025 Jun 2025	

	Action	Lead(s)	Timescale	Actions taken *(state who by)*
7.3 Is a more comprehensive Equalities Impact Assessment or Health Impact Assessment needed?	No			
7.4 What are the next steps?	AWTTC to write an evidence summary report for consideration by the One Wales Medicines Assessment Group (OWMAG).	AWTTC	Mar 2025	AWTTC
7.5 Review of project and EqHIA		AWTTC	[TBC]	

AWTTC's EqHIA template is adapted from the Cardiff & Vale University Health Board EHIA template.