National Institute for Health and Care Excellence

Health Technology Evaluation

Erdafitinib for treating metastatic or unresectable FGFR-altered urothelial cancer ID1333

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Janssen-Cilag Ltd	The evaluation and proposed evaluation route are appropriate.	Comment noted, no action required.
	British Uro Oncology Group	This represents a novel technology and the first treatment for a urothelial cancer subset with a selection biomarker. It represents a new treatment option in this group of patients with limited options and poor prognosis, and an overall survival advantage has been shown compared to chemotherapy. STA seems appropriate.	Comment noted, no action required.
	Action Bladder Cancer UK	This topic is appropriate for evaluation for an Appraisal. Treatment options for bladder cancer are very limited; current treatment options for this patient group can also adversely affect quality of life. It is of particular appropriateness given trial results for Erdafitinib therapy demonstrates longer overall survival than chemotherapy (current most common treatment) among patients with metastatic urothelial carcinoma and	Comment noted, no action required.

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		FGFR alterations after previous anti-PD-1 or anti-PD-L1 treatment.	
	Royal College of Physicians	Yes, the evaluation of this technology is appropriate and timely. This is a novel technology and will be the first biomarker selected targeted therapy in metastatic urothelial cancer. This will be an important addition to treatment options within a group of patients with poor prognosis.	Comment noted, no action required.
	Fight Bladder Cancer	We urge NICE to assess its impact and characteristics carefully to select the most appropriate evaluation route for timely assessment.	Comment noted, no action required.
Wording	Janssen-Cilag Ltd	Yes, the wording of the remit reflect the issues of clinical and cost-effectiveness about this technology.	Comment noted, no action required.
	British Uro Oncology Group	Yes, other than I would change the word 'positive' which is not really correct to altered.	The title has been changed to use the word 'altered' rather than positive.
	Action Bladder Cancer UK	There is an unmet need for treatment for this patient group following chemotherapy or where chemotherapy has proved unsuitable. There is little other treatment choice available. Note: the list of related NICE appraisals of immunotherapies given below, currently includes some which have received negative decisions regarding availability, giving an impression of wider clinician and patient choice regarding possible treatments available within the NHS for this patient group than that which currently exists.	Comment noted. TA530 and TA692 have been removed from this section due to the negative recommendation.
	Royal College of Physicians	I agree with the wording	Comment noted, no action required.
	Fight Bladder Cancer	Yes	Comment noted, no

Section	Stakeholder	Comments [sic]	Action
			action required.
Timing issues	Janssen-Cilag Ltd	There are no licensed medications in this fibroblast growth factor receptor (FGFR)-positive disease setting, and outcomes with current treatment options are generally poor. In addition, there is a high attrition rate in patients with locally advanced unresectable or metastatic urothelial carcinoma, with many people receiving no active treatment and/or best supportive care. There is, therefore, an urgent need for a treatment option that offers better clinical outcomes than current available treatments (chemotherapy and best supportive care) for FGFR-positive patients.	Comment noted, no action required.
	British Uro Oncology Group	This drug has been tested in phase 3 trials and licensed in US and is becoming available elsewhere. There is a survival benefit established. Given the limited options and poor prognosis in this patient group it should be considered for NHS use as soon as possible ideally.	Comment noted. NICE aims to publish final guidance for all new technologies within 90 days of receiving marketing authorisation.
	Action Bladder Cancer UK	The availability of effective treatment options for this patient group is of pressing need, thus has an urgency for the NHS.	Comment noted. NICE aims to publish final guidance for all new technologies within 90 days of receiving marketing authorisation.
	Royal College of Physicians	There is phase II and phase III clinical trial data and evidence to support the use of this technology. Patients will benefit from the availability of Erdafitinib after disease progression on platinum-based chemotherapy and immune check point inhibitor.	Comment noted, no action required.
	Fight Bladder Cancer	Urothelial carcinoma, particularly in its advanced or metastatic stages, represents a condition with significant morbidity and mortality. Evidence suggests that erdafitinib can significantly improve outcomes such as	Comment noted. NICE aims to publish final

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		progression-free survival and overall survival in a targeted population. The lack of effective alternatives for people with FGFR-positive cancer increases the urgency of evaluating and potentially integrating erdafitinib into NHS treatment pathways, to ensure the healthcare system can rapidly integrate and utilise essential medical advancements for bladder cancer care.	guidance for all new technologies within 90 days of receiving marketing authorisation.
Additional comments on the draft remit	Janssen-Cilag Ltd	No additional comments to make.	Comment noted, no action required.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Janssen-Cilag Ltd	The background states that "In 2021, 9,401 new bladder cancers were diagnosed in England." Cancer Data reported a higher number of 16,547 in England (https://www.cancerdata.nhs.uk/getdataout/bladder). As Fight Bladder Cancer mention, the Cancer Research UK statistics only consider bladder cancer classified as C67 (malignant neoplasm of bladder) (https://www.fightbladdercancer.co.uk/get-help/what-bladder-cancer). Janssen suggests that the text should be edited to reflect the correct classification of the reported numbers. In the paragraph starting with "For locally advanced or metastatic cancer, NICE guideline NG2…" after the sentence "Following treatment with platinum-containing chemotherapy (cisplatin or carboplatin), or where chemotherapy is not suitable, people may be offered immunotherapy".	Comment noted. The incidence figure has been updated based on the broader classification of bladder cancer (ICD-10 codes C67, D09.0 and D41.4). Comments noted. This section has been updated to add more detail to the clinical

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		NG2 does not reflect the recommended technology appraisals and current standard practice. Some details on first line and second-line treatments are missing, following recent approved technology appraisals. Janssen suggest updating the text to reflect the recommended technology appraisals and current clinical practice by adding the following: "Untreated people who are eligible may be offered immunotherapy (NICE technology appraisal 739). Stable patients on first line chemotherapy may be offered maintenance Avelumab (NICE technology appraisal 778)". Under the paragraph starting with "Currently, related NICE guidance includes", the second bullet point you state that: "NICE technology appraisal 530, which recommends nivolumab for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy". However, nivolumab is not recommended for treating locally advanced unresectable or metastatic urothelial cancer after platinum-containing chemotherapy (https://www.nice.org.uk/guidance/ta530/chapter/1-Recommendations).	pathway. Comment noted. TA530 has been removed from this section due to the negative recommendation.
	British Uro Oncology Group	Largely. The figure quoted of 20% with FGFR alterations may be on the high side in terms of who would actually be treated. One of the THOR trial manuscripts states 16.6% had an FGFR alteration (1212/7293 with a 'validated' test result) but 8733 were molecularly screened which would reduce this down to 13.8% of those where the test was attempted. And they then randomised 617 of these patients across both cohorts (that were only partly co-recruited temporally). So the denominator matters and we will probably not treat 20% of those with advanced UC.	Comment noted. The proportion of people with FGFR alterations has been updated the reflect the lower estimates. The background section

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		The background does not describe other options following platinum based chemotherapy and immunotherapy. In the UK these would be single agent chemotherapy with paclitaxel or docetaxel (which you then list as comparators) or enfortumab vedotin (licensed and the standard of care approach if available but not NICE appraised in this indication)	has been updated to reflect that people may be offered further lines of chemotherapy following platinum based chemotherapy. Enfortumab vedotin has not been included as a comparator as it has not been recommended in NICE guidance and is not established practice in the NHS.
	Action Bladder Cancer UK	We would question the background information given regarding the incidence of bladder cancer, particularly when citing Cancer Research UK statistics. These statistics do not include the early stage bladder cancer as defined in histology by Ta/CIS which gives an annual total of over 20,300 pa (total from cancer data codes C67, D090 and D414, rather than just C67). There is no reference to the high level of recurrence in bladder cancer, with accompanying risk of progression. There is no reference to the quality of life for patients with existing recommended common treatment (chemotherapy), or the percentage of	Comment noted. The incidence figure has been updated based on the broader classification of bladder cancer (ICD-10 codes C67, D09.0 and D41.4). The high recurrence rates for bladder cancer has been added. Adverse effects of

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		treatment-related adverse events or longer-term tolerability with chemotherapy.	treatment and health-related quality of life are listed in the 'outcomes' section and will therefore be considered for both the intervention and its comparators within the technology appraisal.
		The **NICE Guideline NG2** is referenced - we feel obliged to reference that this Guideline was published in 2015 (9 years ago), has had no substantial update since then and is thus out of date in many key areas particularly regarding treatments or treatment methods, and the care pathway as recommended within this Guideline. We also feel this is a matter which should be considered within any scoping or review of available evidence regarding the treatment of bladder cancer. This necessary update of the Guideline is currently being advocated for strongly by patient organisations and clinical experts with NICE, and a full evidence surveillance review is currently in progress.	Comment noted. We have removed reference to this guideline.
		Background immunotherapy 'related NICE guidance includes' section – requires amendment as below:	
		NICE Appraisal 530: Nivolumab was not recommended by NICE.	
		NICE Appraisal TA692: Pembrolizumab is not recommended by NICE, within its marketing authorisation, for treating locally advanced or metastatic	This has been corrected.

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		urothelial carcinoma in adults who have had platinum-containing chemotherapy (April 2021). NICE Appraisal TA788: Avelumab for maintenance treatment of locally advanced or metastatic urothelial cancer after platinum-based chemotherapy (11 May 2022) is incorrectly listed in Appendix B in one instance as TA778	This has been corrected. This has been corrected.
	Royal College of Physicians	Advanced metastatic bladder cancer remains a life limiting illness. Median survival in platinum eligible patients was previously reported between 14-15 months and for cisplatin ineligible group this was approximately 8-9 months. More recently with the use of immune check point inhibitors and its availability through NICE we are seeing improvements in survival for patients with metastatic bladder cancer. Recent trial (Javelin -100) have reported median survival of 21.4 months in the maintenance avelumab arm compared to 14.3 months for standard of care arm [1]. Survival is measured from the time of randomisation into maintenance Javelin -100 trial. More updated survival data shows survival of 23.8 months in maintenance avelumab arm versus 15 months in standard of care arm with a survival benefit of 8.8 months in the maintenance avelumab arm. Similarly, recently presented EV 302 study that compared EV plus pembrolizumab reported a median survival of 31.5 months in the experimental arm, compared to 16.1 months for standard of care chemotherapy arm [Powles et al; Presented at ESMO annual meeting 2023]. With these improvements in the landscape post chemotherapy NICE technology appraisal has previously recommended the use of maintenance Avelumab in patients who derive response from chemotherapy or at least achieve stable disease. In the event of disease progression 2nd line Atezolizumab is also available for our patients through previous NICE technology appraisal. We are seeing several patients now who are fit for 3rd	Comments noted. No action required.

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		line treatment post platinum-based chemotherapy and immune check point inhibitors and will benefit from the use of erdafitinib for FGFR positive urothelial cancers. Evidence for the use of ERDAFITINIB THOR trial. (BLC3001/NCT03390504) [2] • Phase 3, randomized, open-label, multicenter study. • A total of 629 patients from 345 study locations were screened for the presence of *FGFR* gene alterations and assigned to 2 cohorts based on prior treatment with anti- programmed death ligand 1 (PD-[L]1) agent: ▪ Cohort 1 (n=266): prior chemotherapy with anti-PD-(L)1 treatment in combination or maintenance setting (anti-PD-[L]1 alone in cisplatin-ineligible patients only) ▪ Patients were randomized 1:1 to receive: • Erdafitinib at a starting dose of 8 mg once daily, with uptitration to 9 mg once daily based on day 14 serum phosphate levels (≤9.0 mg/dL and no associated adverse events [AEs]). • Chemotherapy (docetaxel 75 mg/m^2 as a 1-hour intravenous [IV] infusion every 3 weeks [Q3W] or vinflunine 320 mg/m^2 as a 20-minute IV infusion once Q3W).	

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		▪ Cohort 2 (n=351): prior chemotherapy without anti-PD-(L)1 treatment • Patients were randomized 1:1 to receive: • Erdafitinib at a starting dose of 8 mg once daily, with uptitration to 9 mg once daily based on day 14 serum phosphate levels (≤9.0 mg/dL and no associated AEs). • Pembrolizumab 200 mg as a 30-minute IV infusion once Q3W. ***Efficacy: Cohort 1*** • At a median follow-up of 15.9 months, the median OS was 12.1 months for patients receiving erdafitinib vs 7.8 months for patients receiving chemotherapy. Erdafitinib reduced the risk of death by 36% vs chemotherapy. • Hazard ratio (HR), 0.64 (95% confidence interval [CI], 0.47-0.88; *P*=0.005). • Median PFS was 5.6 months for patients receiving erdafitinib vs 2.7 months for patients receiving chemotherapy. • Erdafitinib reduced the risk of progression or death by 42% vs chemotherapy. • HR, 0.58 (95% CI, 0.44-0.78; *P*<0.001). • Patients receiving erdafitinib (n=136) had an ORR of 45.6%, 9 (6.6%) patients had a complete response (CR), and 53 (39%) patients had a partial response (PR). • Patients, receiving chemotherapy (n=130) had an ORR of 11.5%, 1 (0.8%) patient had a CR, and 14 (10.8%) patients had a PR. • Relative risk (RR), 3.94 (95% CI, 2.37-6.57; *P*<0.001).	

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		BLC2001 Study (NCT02365597) was a phase 2, multicenter, open-label study in adult patients with locally advanced and unresectable or metastatic UC and prespecified *FGFR* genetic alterations (*FGFR3* mutation or *FGFR2/3* fusion) with disease progression during or following ≥1 line of prior systemic chemotherapy or within 12 months of receiving neoadjuvant or adjuvant chemotherapy or were chemotherapy-naïve due to cisplatin ineligibility. Efficacy and safety results are described for patients who received a starting dose of erdafitinib 8 mg orally (PO) once daily (N=99) [Reference 3,4] A total of 99 patients received a median of five cycles of erdafitinib. Of these patients, 43% had received at least two previous courses of treatment, 79% had visceral metastases. Response rate was 40% (3% with a complete response and 37% with a partial response). The median duration of PFS was 5.5 months, and the median duration of OS was 13.8 months. Treatment-related adverse events of grade 3 or higher, which were managed mainly by dose adjustments, were reported in 46% of the patients; 13% of the patients discontinued treatment because of adverse events. There were no treatment-related deaths. The above efficacy and safety data from the phase II and Phase III trials is exciting in this patient population group who have progressed post platinum-based chemotherapy and immune check point inhibitors. 1. Powles, T., et al. (2020). "Avelumab Maintenance Therapy for Advanced or Metastatic Urothelial Carcinoma." New England Journal of Medicine **383**(13): 1218-1230. 2. Loriot Y, Matsubara N, Park SH, et al. Erdafitinib or chemotherapy in advanced or metastatic urothelial carcinoma. *N Engl J Med*. 2023;389:1961-	

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		1971. 3. Loriot Y, Necchi A, Park SH, et al. Erdafitinib in locally advanced or metastatic urothelial carcinoma. *N Engl J Med*. 2019;381(4):338-348. 4. Siefker-Radtke AO, Necchi A, Park SH, et al. Efficacy and safety of erdafitinib in patients with locally advanced or metastatic urothelial carcinoma: long-term follow-up of a phase 2 study. *Lancet Oncol*. 2022;23(2):248-258. In terms of FGFR mutation rate of 20% quoted is likely higher than what we have seen in clinical trials in UK and internationally.	
	Fight Bladder Cancer	The scope says, "In 2021, 9,401 new bladder cancers were diagnosed in England". It should say "In 2020, 16,547 new bladder cancers were diagnosed in England" (https://www.cancerdata.nhs.uk/getdataout/bladder)	The incidence figure has been updated based on the broader classification of bladder cancer (ICD-10 codes C67, D09.0 and D41.4). The data used is from 2021.
Population	Janssen-Cilag Ltd	Yes, the population is defined appropriately	Comment noted, no action required.
	British Uro Oncology Group	Partially. The main phase III clinical trial comprised separately reported randomised comparison cohorts. One randomisation (cohort 1) was in patients who had disease progression after one or two previous systemic treatments that had included immunotherapy and was compared to a chemotherapy choice in the control arm that included docetaxel (or vinflunine	Comment noted, no action required.

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		which you have rejected in this disease). The other randomisation (cohort 2) was in patients who had disease progression after one previous systemic treatment (but who had not received immunotherapy) and was compared to pembrolizumab immunotherapy.	
	Action Bladder Cancer UK	Yes, for this appraisal	Comment noted, no action required.
	Royal College of Physicians	Yes, these trials have been done in biomarker selected patients. The phase III clinical trial discussed here was in patients who had at least 1 line of treatment, platinum based hemotherapy or Immune check point inhibitors or both.	Comment noted, no action required.
	Fight Bladder Cancer	It's important to also consider who may not have received standard prior therapies due to specific contraindications. This includes people who cannot undergo chemotherapy because of issues like poor kidney function or hearing loss, and those who cannot receive immunotherapy due to the risk of adverse reactions or pre-existing autoimmune diseases. By not accounting for these people' unique circumstances in eligibility criteria, there's a risk of unfairly disadvantaging them in access to new treatments.	Comment noted. The remit of NICE is to assess the clinical- and cost-effectiveness of the technology within its marketing authorisation. No action required.
Subgroups	Janssen-Cilag Ltd	There are no sub-groups that should be considered separately. The two proposed sub-groups make up the target population, i.e., patients with FGFR-positive alterations with disease progression during or following at least one line of therapy containing a programmed death receptor-1 (PD-1) or programmed death-ligand 1 (PD-(L)1) inhibitor.	Comment noted. The subgroups are kept inclusive at this stage. If there is insufficient evidence for them to be considered, or if they are not relevant, the company is invited to

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			justify this in its submission.
	British Uro Oncology Group	The frequency of FGFR alterations may be higher in upper urinary tract tumours (compared to bladder cancers) but all patients will have an alteration to be suitable for this treatment. Consider patients who have contraindications to either chemotherapy (e.g. poor renal function, hearing impairment) or immunotherapy (autoimmune disease) who may not be able to have some of the relevant prior therapy but would be expected to benefit from erdafitinib. The subgroup suggested for 'previous anti-PD-(L) 1 treatment' (immunotherapy) simply determines which THOR randomisation cohort is relevant. So it's not really a subgroup in the sense that THOR did a fully powered randomisation for this group of patients. The data on FGFR alteration type has been presented but not (fully) published. It gets us into small subsets that are exploratory and under powered. These data are all consistent with the overall effect size for the relevant trial cohort and I don't believe there is any justification for choosing one alteration type over another for treatment selection.	Comment noted. Upper tract urothelial cancer has been added as a subgroup. Comment noted. The remit of NICE is to assess the clinical- and cost-effectiveness of the technology within its marketing authorisation. No action required. The subgroups are kept inclusive at this stage. If there is insufficient evidence for them to be considered, or if they are not relevant, the company is invited to justify this in its submission.
	Action Bladder	Sub-groups are appropriate.	Comment noted, no

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	Cancer UK		action required.
	Royal College of Physicians	Benefit of Erdafitinib was seen across the subgroups. Higher mutation rates may be seen in upper tract urothelial cancers.	Comment noted. Upper tract urothelial cancer has been added as a subgroup.
	Fight Bladder Cancer	Upper tract urothelial cancer (UTUC) is a variant of urothelial cancer located in the ureter or the renal pelvis, which connects the kidney to the ureter. This type of cancer shares many characteristics with bladder cancer but occurs less frequently and is often diagnosed at a more advanced stage due to less apparent symptoms. Given the higher rate of FGFR alterations in UTUC compared to bladder cancer, the impact of FGFR targeting agents like erdafitinib is anticipated to be potentially greater in people with UTUC.	Comment noted. Upper tract urothelial cancer has been added as a subgroup.
Comparators	Janssen-Cilag Ltd	Janssen believe that the comparators list should be: **Chemotherapy** (including but not limited to paclitaxel and docetaxel). Janssen also proposes to include: **Best Supportive Care** Janssen believe that PD-(L)1 inhibitors are not appropriate to be comparators for erdafitinib as erdafitinib is indicated for patients with prior exposure to PD-(L)1 inhibitor(s). Retreating with PD-(L)1 inhibitors is not considered standard of care in England and there is no clinical rationale or consensus to re-challenge with a PD-1 or PD-(L)1 inhibitor.	Comments noted. Best supportive care has been added as a comparator. The comparators are kept inclusive at this stage. The company is invited to justify if/why any comparators are not relevant in its submission.

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	British Uro Oncology Group	Licensed treatment enfortumab vedotin is not considered (accepting not currently available in the NHS). Otherwise yes.	Comment noted. Enfortumab vedotin has not been included as a comparator as it has not been recommended in NICE guidance and is not established practice in the NHS.
	Action Bladder Cancer UK	Where comparators list immunotherapies: see comments above regarding negative NICE decisions relating to Nivolumab and also Pembrolizumab availability for NHS use.	Comment noted. These corrections have been made.
	Royal College of Physicians	In NHS weekly paclitaxel is used in patients with disease progression post platinum-based chemotherapy and immune check point inhibitors. 4 weekly cycle with 3 weeks on and 1 week off regimen is used that requires visit to the hospital at weekly intervals. We routinely do scans after 3 cycles. A maximum of 6 cycles is given over 6 months. Median survival is approximately 4-5 months, hence the availability of ERDAFITNIB through NICE positive appraisal will be an excellent news for patients and GU clinicians treating these patients.	Comment noted, no action required.
	Fight Bladder Cancer	In some cases, the treatment might involve combinations of, or sequential use of, chemotherapy with immunotherapy. The scope currently overlooks third-line treatments such as paclitaxel and docetaxel, which are chemotherapies used for advanced cancer, and	Comment noted. This would be included within ‘established clinical management’. Paclitaxel and docetaxel are included

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		enfortumab vedotin, a newer, licensed therapy targeting cancer cells specifically.	as comparators. Enfortumab vedotin has not been included as a comparator as it has not been recommended in NICE guidance and is not established practice in the NHS.
Outcomes	Janssen-Cilag Ltd	Janssen propose one additional outcome measure (in bold) to fully capture the most important health benefits of erdafitinib. • overall survival • progression-free survival • response rates • **duration of response** • adverse effects of treatment • health-related quality of life.	Comment noted. The draft scope has been updated to specify that 'response rates' includes both type and duration of response.
	British Uro Oncology Group	These seem appropriate. Overall survival and HRQOL are the most important.	Comment noted, no action required.
	Action Bladder Cancer UK	As always, we would advocate that adverse effects of comparator treatments and the benefits of health-related quality of life for this patient group, as well as improved survival, are given sufficient and equal weight within any scoping and appraisal.	Comment noted, no action required.
	Royal College of Physicians	Yes	Comment noted, no

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			action required.
	Fight Bladder Cancer	For people who respond to treatment, the **duration of response** could be important for understanding the long-term benefits and planning subsequent treatments.	Comment noted. The draft scope has been updated to specify that 'response rates' includes both type and duration of response.
Equality	Janssen-Cilag Ltd	Janssen does not believe that there are any issues with regards to equality in the proposed remit and scope.	Comment noted, no action required.
	British Uro Oncology Group	No obvious discrimination risk evident.	Comment noted, no action required.
	Royal College of Physicians	No evident discrimination seen. A positive technology appraisal will provide further treatment options in a biomarker selected patient population within this elderly patient population group.	Comment noted, no action required.
	Fight Bladder Cancer	People in remote or rural areas might face challenges accessing treatment centres offering testing and treatment. The scope should consider the availability of the treatment across different healthcare settings to ensure equitable access. We are aware of the disturbing disparities in bladder cancer outcomes between men and women, with research consistently showing that women with this disease experience higher mortality rates and worse outcomes	Thank you for your comment. The committee will consider these potential equality issues.

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		compared to their male counterparts. Evaluations of this treatment must analyse and report data disaggregated by gender. This approach will enable a clear understanding of the efficacy and safety of this treatment in women compared to men, potentially illuminating pathways to mitigate the observed disparities. Fight Bladder Cancer acknowledges the National Institute for Health and Care Excellence's (NICE) recent methodological updates for health technology evaluations, notably the shift from end-of-life criteria to introducing a severity modifier. This change, intended to refine the assessment of the cost-effectiveness of new medications, is a critical development with implications for older people with bladder cancer. This raises concerns about the potential for older people to face indirect disadvantages under the new system. Bladder cancer, predominantly affecting this demographic, could see treatments undervalued if the severity of the condition and the Quality-Adjusted Life Year (QALY) shortfall are not adequately recognised.	Committee will conduct the evaluation in accordance with the current methods manual. The manual states that the committee will consider the severity of the condition, defined as the future health lost by people living with the condition. They will consider both the absolute and proportional QALY shortfall.
Other considerations	Janssen-Cilag Ltd	To prescribe erdafitinib, diagnostic testing is required to confirm FGFR mutations. Genetic tests for the FGFR mutation are already included in the National Genomic Test Directory (https://www.england.nhs.uk/genomics/the-national-genomic-test-directory) and would be needed for patients with	Comment noted. The text has been updated to specify that costs for diagnostic tests should

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		metastatic urothelial cancer (mUC) after PD-1 or PD-(L)1 inhibitor therapy.	only be included 'if applicable'.
	British Uro Oncology Group	The technology has some toxicities e.g. eye, skin and cardiac toxicities that could impact on other support specialities. Ophthalmology for screening and treatment of ocular toxicity is probably the main example that would be novel in this patient group and would need to be available.	Comment noted. All relevant NHS costs that change because of an intervention should be included in the company's evidence submission for consideration by committee.
		There is a need to consider availability and access to FGFR alteration screening in archival tumour samples. There is a risk in discrimination against people where the treatment team were unable to access this. It is on the national test directory and so is theoretically 'available' but there is national heterogeneity relating to capacity to test (that is slowly improving through other indications in other cancers driving change).	Comment noted. Committee will consider potential inequality in access to diagnostic tests.
	Fight Bladder Cancer	Erdafitinib may cause certain toxicities, including issues affecting the eyes, skin, and heart. Erdafitinib can also cause changes to the fingernails, which may include discolouration, nail bed inflammation, or even nail loss. When starting people on erdafitinib, nurses should focus on educating people about potential side effects. They should also monitor for adverse reactions, particularly skin and nail changes, and provide guidance on managing these	Comment noted. All relevant NHS costs that change because of an intervention should be included in the company's evidence

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		effects. Regularly assessing patient response and tolerability to the medication and maintaining open communication for any concerns or symptoms experienced are essential. There is also the need for collaborative care from specialised services like ophthalmology for both monitoring and addressing complications. The variability in the availability of genetic mutation screening could limit treatment access, potentially disadvantaging people in regions where such diagnostic services are inconsistent or scarce.	submission for consideration by committee. Committee will consider potential inequality in access to diagnostic tests.
Questions for consultation	Janssen-Cilag Ltd	**Where do you consider erdafitinib will fit into the existing care pathway for metastatic or unresectable FGFR-positive urothelial cancer?** Erdafitinib will fit in the NICE pathway for managing locally advanced unresectable or metastatic urothelial cancer patients harbouring FGFR mutations that have been or are currently being treated with at least one line of therapy containing a PD-1 or PD-(L)1 inhibitor. **What is established clinical management for people with metastatic or unresectable FGFR-positive urothelial cancer following chemotherapy and/or immunotherapy?** There is no specific treatment for people with metastatic or locally advanced unresectable FGFR-positive urothelial cancer following chemotherapy and/or immunotherapy. These people receive the same treatment as those with wild-type FGFR alterations, as erdafitinib is the first FGFR inhibitor in metastatic	Comment noted, no action required. Comment noted, no action required.

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		urothelial cancer. According to the anticipated label, Janssen suggests to only focus on metastatic or unresectable FGFR-positive urothelial cancer following at least one line of therapy containing a PD-1 or PD-(L)1 inhibitor **Would erdafitinib be a candidate for managed access?** Janssen consider that mature evidence is available, and any evidence gaps are unlikely to result in significant uncertainty for decision making. Erdafitinib would therefore not be a candidate for managed access. **Do you consider that the use of erdafitinib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** There are potentially uncaptured benefits such as hope in an otherwise hopeless end of life situation, carer burden and the value of innovation to bridge current and future patients to being eligible for future innovation. Supporting evidence is in development and may include: • Literature, • Reports from in-depth patient interviews and patient surveys conducted by Janssen	Comment noted, no action required. Comment noted. The company is invited to include this data in its submission document, for consideration by the committee.

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		NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope: • **could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which erdafitinib will be licensed;** • **could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;** • **could have any adverse impact on people with a particular disability or disabilities.** **Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.** No issues have been identified in relation to the exclusion of any people protected by the equality legislation who fall within the patient population or recommendations that have a different impact or adverse impact on people	Comment noted, no action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		with particular disabilities.	
	Action Bladder Cancer UK	**Do you consider that the use of erdafitnib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Clinical trial results have shown that erdafitnib can give a significantly improved survival rate, with a lower rate adverse treatment events for this patient group. The patient benefits of QoL, benefits to physical and mental well-being, less adverse effects, as well as improved survival should be given adequate weight for a patient group with very limited available treatment options.	Comment noted, no action required.
	Royal College of Physicians	Availability and access of mutation screening must be made available to improve the access of the drug for our patients nationally. The technology reports some new toxicities, and it will be important to work closely with allied specialities like ophthalmology for the safe delivery of the treatment.	Committee will consider potential inequality in access to diagnostic tests. Comment noted, no action required.
	Fight Bladder Cancer	**Where do you consider erdafitinib will fit into the existing care pathway for metastatic** **or unresectable FGFR-positive urothelial cancer?** Erdafitinib's placement within the existing care pathway for metastatic or unresectable FGFR-positive urothelial cancer is likely to be as a targeted therapy option for people who have progressed following first-line chemotherapy and/or immunotherapy, for those with confirmed FGFR gene alterations. It may also includes people with FGFR mutations who cannot undergo chemotherapy because of issues like poor kidney function or hearing	Comment noted, no action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		loss, and those who cannot receive immunotherapy due to the risk of adverse reactions or pre-existing autoimmune diseases. **What is established clinical management for people with metastatic or unresectable** **FGFR-positive urothelial cancer following chemotherapy and/or immunotherapy?** The established clinical management for people with metastatic or unresectable FGFR-positive urothelial cancer following chemotherapy and/or immunotherapy currently includes further chemotherapy options, additional rounds of immunotherapy, or participation in clinical trials. The choice of subsequent treatment typically depends on the person's overall health, prior treatment response, and the specific characteristics of their cancer. Erdafitinib could offer a novel mechanism of action for people with FGFR alterations. **Would erdafitinib be a candidate for managed access?** Erdafitinib presents a compelling case for inclusion in managed access schemes within England's healthcare framework, such as the Cancer Drugs Fund, which could facilitate its use while enabling the collection of vital real-world evidence. Erdafitinib, with its potential for significant clinical benefit in a subset of people with urothelial cancer, could also be a prime candidate for the Early Access to Medicines Scheme (EAMS). **Do you consider that the use of erdafitinib can result in any potential substantial** **health-related benefits that are unlikely to be included in the QALY**	Comment noted, no action required. Comment noted, no action required.

Section	Consultee/ Commentator	Comments [sic]	Action
		calculation? These could include improvements in patient-reported outcomes such as reduced symptom burden, better management of treatment-related side effects, and improvements in mental health and well-being. The specific targeting of FGFR mutations may lead to better disease control with fewer side effects compared to more general chemotherapy or immunotherapy, contributing to improved quality of life. These aspects, while challenging to quantify, are crucial for understanding the holistic value of new treatments like erdafitinib. The burden faced by carers and family members in managing urothelial cancer deserves recognition. By adopting more effective treatments, some of this pressure could be lessened, allowing carers the opportunity to return to their professional activities and contributions to society.	Comment noted. The company is invited to include evidence on any health-related benefits that are unlikely to be included in the QALY calculation in its submission.
Additional comments on the draft scope	Janssen-Cilag Ltd	No additional comments to make.	Comment noted, no action required.
	Action Bladder Cancer UK	In related technology recommendations on pgs 3 & 4 – please refer to below: NICE TA674: Pembrolizumab for untreated PD-L1-positive, locally advanced or metastatic urothelial cancer when cisplatin is unsuitable (terminated appraisal) (Replaces TA522) (Negative Decision date - March 2021) NICE TA692: Pembrolizumab for treating locally advanced or metastatic urothelial carcinoma after platinum containing chemotherapy (Negative Decision date – April 2021) NICE TA530: Nivolumab (Opdivo) is not recommended for treating locally advanced unresectable or metastatic urothelial carcinoma in adults who have had platinum-containing therapy (Negative Decision date - July 2018)	This section has been updated to indicate the negative decisions and terminated appraisals.

Section	Consultee/ Commentator	Comments [sic]	Action
		Related NICE Guidelines: Nice Guideline NG2 2015 – please refer to earlier comments that this guideline is now seriously out of date and is currently in process of a full evidence surveillance review. This has potentially serious impact on treatment guidelines and recommendations available.	

The following stakeholders indicated that they had no comments on the draft remit and/or the draft scope

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