NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

GUIDANCE EXECUTIVE (GE)

Review of TA272; Vinflunine for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract.

This guidance was issued in January 2013.

The review date for this guidance is November 2015.

1. Recommendation

The guidance should be transferred to the 'static guidance list'. That we consult on this proposal.

2. Original remit(s)

To appraise the clinical and cost effectiveness of vinflunine monotherapy for the second line treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of prior platinum-containing chemotherapy.

3. Current guidance

1.1 Vinflunine is not recommended within its marketing authorisation for the treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract that has progressed after treatment with platinum-based chemotherapy.

1.2 People currently receiving vinflunine that is not recommended according to 1.1 should be able to continue treatment until they and their clinician consider it appropriate to stop.

4. Rationale[1]

This review did not identify new evidence for vinflunine that could be considered more robust, or relevant to UK clinical practice, than the evidence considered in TA272. Neither the marketing authorisation nor the list price of vinflunine has changed.

[redacted]

5. Implications for other guidance producing programmes

The Centre for Clinical Practice has no comments to make on this proposal.

[1] A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper

6. New evidence

The search strategy from the original manufacturer's report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from May 2010 onwards were reviewed. Additional searches of clinical trials registries and other sources were also carried out. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies.

7. Summary of evidence and implications for review

At the time of TA272, vinflunine had a marketing authorisation as monotherapy for treating adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen. This indication has not changed.

[redacted]. Such new indications would normally be considered separately through the topic selection function at NICE.

The Committee concluded that the extent of clinical effectiveness of vinflunine compared with best supportive care had not been conclusively demonstrated because of the uncertainty of the overall survival results. Furthermore, it was not persuaded that the evidence for the effectiveness of vinflunine would be generalisable to the whole population who might receive vinflunine in UK clinical practice compared with best supportive care. This review did not identify new evidence for vinflunine that could be considered more robust, or relevant to UK clinical practice, than the evidence previously considered. The company indicated that new evidence exists for the current licensed indication and could be submitted by the beginning of 2016. However, no details were provided on the nature of this evidence in relation to the uncertainties in the original evidence base to enable the full consideration of the value of an STA-review.

The Committee noted the need for research on second-line treatments for transitional cell carcinoma of the urothelial tract, but did not make research recommendations specific to vinflunine.

Vinflunine was appraised based on a list price of £212.50 for a 50-mg vial and £1062.50 for a 250-mg vial. The list price of vinflunine has not changed since TA272. In view of the above information, and without sufficient information about the new evidence for vinflunine from the company, it is recommended that TA272 is moved to the static list.

8. Implementation

No submission was received from Implementation.

9. Equality issues

No equality issues were raised during the scoping exercise or through the course of this appraisal.

GE paper sign off: Helen Knight, Associate Director – 14 October 2015

Contributors to this paper:

Information Specialist:	Toni Price
Technical Lead:	Ahmed Elsada
Project Manager:	Andrew Kenyon
CCP input:	Katie Perryman Ford

Appendix 1 – explanation of options

When considering whether to review one of its Technology Appraisals NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
A review of the guidance should be planned into the appraisal work programme. The review will be conducted through the [specify STA or MTA] process.	A review of the appraisal will be planned into the NICE's work programme.	No
The decision to review the guidance should be deferred to [specify date or trial].	NICE will reconsider whether a review is necessary at the specified date.	No
A review of the guidance should be combined with a review of a related technology appraisal. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the specified related technology.	No
A review of the guidance should be combined with a new technology appraisal that has recently been referred to NICE. The review will be conducted through the MTA process.	A review of the appraisal(s) will be planned into NICE's work programme as a Multiple Technology Appraisal, alongside the newly referred technology.	No
The guidance should be incorporated into an on-going clinical guideline.	The on-going guideline will include the recommendations of the technology appraisal. The technology appraisal will remain extant alongside the guideline. Normally it will also be recommended that the technology appraisal guidance is moved to the static list until such time as the clinical guideline is considered for review. This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal.	No

Options	Consequence	Selected – 'Yes/No'
The guidance should be updated in an on-going clinical guideline.	Responsibility for the updating the technology appraisal passes to the NICE Clinical Guidelines programme. Once the guideline is published the technology appraisal will be withdrawn. Note that this option does not preserve the funding direction associated with a positive recommendation in a NICE Technology Appraisal. However, if the recommendations are unchanged from the technology appraisal, the technology appraisal can be left in place (effectively the same as incorporation).	No
The guidance should be transferred to the 'static guidance list'.	The guidance will remain in place, in its current form, unless NICE becomes aware of substantive information which would make it reconsider. Literature searches are carried out every 5 years to check whether any of the Appraisals on the static list should be flagged for review.	Yes

NICE would typically consider updating a technology appraisal in an ongoing guideline if the following criteria were met:

i. The technology falls within the scope of a clinical guideline (or public health guidance)

ii. There is no proposed change to an existing Patient Access Scheme or Flexible Pricing arrangement for the technology, or no new proposal(s) for such a scheme or arrangement

iii. There is no new evidence that is likely to lead to a significant change in the clinical and cost effectiveness of a treatment

iv. The treatment is well established and embedded in the NHS. Evidence that a treatment is not well established or embedded may include;

- Spending on a treatment for the indication which was the subject of the appraisal continues to rise
- There is evidence of unjustified variation across the country in access to a treatment
- There is plausible and verifiable information to suggest that the availability of the treatment is likely to suffer if the funding direction were removed

- The treatment is excluded from the Payment by Results tariff

v. Stakeholder opinion, expressed in response to review consultation, is broadly supportive of the proposal.

Appendix 2 – supporting information

Relevant Institute work

Published

Bladder cancer: diagnosis and management of bladder cancer (2015) NICE guideline 2.

Improving outcomes in urological cancers (2002) NICE guidelines CSGUC.

Suspected cancer: recognition and referral (2015) NICE guideline 12.

Details of changes to the indications of the technology

Indication and price considered in original appraisal	Proposed indication (for this appraisal) and current price
Vinflunine has a marketing authorisation for use as 'monotherapy for the treatment of adult patients with advanced or metastatic transitional cell carcinoma of the urothelial tract after failure of a prior platinum-containing regimen'. The summary of product characteristics (SPC) notes that vinflunine has not been studied in patients with a performance status of 2 or more. The SPC states that the recommended dosage of vinflunine is 320 mg/m^2 as a 20-minute intravenous infusion every 3 weeks. The SPC also states that in patients with a World Health Organization (WHO)/Eastern Cooperative Oncology Group (ECOG) performance status of 1 or of 0 who have had pelvic irradiation, treatment should be started at a dose of 280 mg/m^2; in the absence of any haematological toxicity during the first cycle causing treatment delay or dose reduction, the dosage can be increased to 320 mg/m^2 every 3 weeks for the subsequent cycles. The SPC states that monitoring of complete blood counts should be conducted before each treatment cycle, and that oral hydration and laxatives should be given during each cycle. Vinflunine is available in 50 mg and 250 mg vials, costing £212.50 and £1062.50 respectively (excluding VAT; 'British National Formulary' edition 64). The acquisition cost of vinflunine for an entire course of treatment is £9817.50, assuming an average of 4.2 cycles, a dose of 287 mg/m^2 and a body surface area of 1.85 m^2 (see section 3.10).	Indication in the SPC (last updated July 2014) is the same, including performance status. The price is the same.

Details of new products

Drug (company)	Details (phase of development, expected launch date)	In topic selection
Atezolizumab for locally advanced or metastatic urothelial bladder cancer; second or subsequent line (Roche)	Phase III, with phase II results just announced July 15. [redacted]	TS 7903 A listed – proceed to scoping (7 May 15)
Pembrolizumab for metastatic or locally advanced/unresectable urothelial cancer that has recurred or progressed following platinum-based chemotherapy (Merck Sharp & Dohme)	Phase III in progress. [redacted]	TS 8097, status: CCPHA checking (1 July 15)

Registered and unpublished trials

Trial name and registration number	Details
A Randomised Phase II/III Study of Cabazitaxel Versus Vinflunine in Metastatic or Locally Advanced Transitional Cell Carcinoma of the Urothelium Secavin-12 NCT01830231	Phase II/III, currently recruiting. Estimated enrolment: 372. Estimated primary completion date: November 2016. Primary Outcome Measures: • Phase II main objective: to assess the efficacy of cabazitaxel compared to vinflunine in terms of improved objective response rate (ORR) of subjects with metastatic or locally advanced previously treated TCCU. [Time Frame: From date of randomization to disease progression or until 18 months from enrolment] • Efficacy of cabazitaxel compared to vinflunine on terms of improved objective response rate (ORR) • Phase III main objective: To assess the efficacy of cabazitaxel compared to vinflunine in terms of improved overall survival (OS) of subjects with metastatic or locally advanced, previously treated TCCU. [Time Frame: From date of randomization to death from any cause or until 18 months from enrolment]

Trial name and registration number	Details
A Phase III Randomized Clinical Trial of Pembrolizumab (MK-3475) Versus Paclitaxel, Docetaxel or Vinflunine in Subjects With Recurrent or Progressive Metastatic Urothelial Cancer. NCT02256436 Other IDs: 3475-045, 2014-002009-40, 152903	Phase III, currently recruiting. Estimated enrolment: 470. Estimated primary completion date: January 2017. Primary Outcome Measures: • Overall survival (OS) [Time Frame: Up to 27 months] • Progression-free survival (PFS) per Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST 1.1) [Time Frame: Up to 27 months]
A phase III, open-label, multicenter, randomized study to investigate the efficacy and safety of MPDL3280A (anti-PD-L1 antibody) compared with chemotherapy in patients with locally advanced or metastatic urothelial bladder cancer after failure with platinum-containing chemotherapy. *Comparator: 'vinflunine, paclitaxel, or docetaxel per the investigator's choice and administered according to local label.'* NCT02302807 Other IDs: GO29294, 2014-003231-19	Phase III, currently recruiting. Estimated enrolment: 767. Estimated primary completion date: January 2017. Primary Outcome Measures: Overall survival [Time Frame: Between randomization and death due to any cause, up to approximately 23 months after first patient enrolled]

Relevant services covered by NHS England specialised commissioning

A resubmission of a June 2013 application for vinflunine to be added to the Cancer Drugs Fund list for this indication was rejected (document undated but appears to be September 2013, using the url).

There are specialised urology services that cover urological cancers.