# NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

# GUIDANCE EXECUTIVE (GE)

## Review of TA184: Topotecan for the treatment of relapsed small-cell lung cancer

This guidance was issued in November 2009.

The review date for this guidance is November 2012.

### 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 topotecan within its licensed indication for the second-line treatment of small cell lung cancer.

### 3. Current guidance

1.1. Oral topotecan is recommended as an option only for people with relapsed small-cell lung cancer for whom:

- re-treatment with the first-line regimen is not considered appropriate **and**
- the combination of cyclophosphamide, doxorubicin and vincristine (CAV) is contraindicated (for details of the contraindications to CAV see the summary of product characteristics for each of the component drugs).

1.2. Intravenous topotecan is not recommended for people with relapsed small-cell lung cancer.

1.3. People with relapsed small-cell lung cancer currently receiving oral topotecan who do not meet the criteria specified in 1.1, or who are receiving intravenous topotecan should have the option to continue their treatment until they and their clinicians consider it appropriate to stop.

### 4. Rationale[1]

Since the publication of TA84, no significant new evidence has become available that would impact on the current guidance. The patent for intravenous topotecan has

[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

expired, with generic formulations now available; however this is not likely to impact on the current recommendation for intravenous topotecan. It is therefore appropriate for the guidance to be to be transferred to the 'static guidance list'.

## 5. Implications for other guidance producing programmes

This TA overlaps with the Lung cancer clinical guideline CG121. CCP supports the proposal to transfer to the static list.

## 6. New evidence

The search strategy from the original assessment report was re-run on the Cochrane Library, Medline, Medline In-Process and Embase. References from February 2009 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

TA184 compared the use of topotecan (oral and intravenous) with best supportive care or other chemotherapy regimens for the treatment of relapsed small-cell lung cancer. The Committee noted that intravenous topotecan had no clinical advantages over oral topotecan, and that intravenous topotecan required patients to attend hospital for 5 consecutive days each cycle which was inconvenient for patients and costly. As a result, intravenous topotecan was not recommended for people with relapsed small-cell lung cancer. However oral topotecan was recommended as a cost effective option for people with relapsed small-cell lung cancer for whom re-treatment with the first-line regimen is not appropriate, and the combination of cyclophosphamide, doxorubicin and vincristine (CAV) is contraindicated.

During the appraisal of TA184, the Committee consulted clinical specialists and concluded that there are limited data available on the clinical effectiveness of amrubicin for small-cell lung cancer, and that this was due to amrubicin not holding a marketing authorisation for use in the UK and not being routinely used in UK clinical practice. The Committee concluded that amrubicin was not to be considered a comparator for topotecan. However it noted that an ongoing clinical trial comparing intravenous amrubicin with intravenous topotecan could provide evidence when published. Since the guidance was published, results of the trial have been reported in two conference papers. The first conference paper from 2011 (Hudgens, King, and Khan), reported that amrubicin was associated with better symptom control and quality of life improvements compared with topotecan. The second conference paper from 2012 (O'Brien, Hudgens, and King et al), reported meaningful reductions (improvements) associated with amrubicin compared with topotecan on the Lung Cancer Symptom Scale. It also reported that people receiving amrubicin experienced fewer symptom deterioration during treatment compared with people receiving topotecan. However, amrubicin does not hold a marketing authorisation for use in the UK and is not routinely used in UK clinical practice, therefore would not be considered a comparator for topotecan.

The list prices of branded formulations of topotecan have not changed since TA184 was published. Generic formulations of intravenous topotecan are now available; however the non-proprietary list price is only marginally cheaper than the branded formulation (see Appendix 2). Even taking into consideration the average price that the NHS may pay for generic intravenous topotecan, given the administration costs to attend hospital for 5 consecutive days each cycle, it would not be considered cost-effective compared with oral topotecan. This is therefore not likely to impact on the current recommendations for intravenous topotecan. Since publication of TA184, the price of comparator drugs has not changed, nor are there any technologies that have received a marketing authorisation in this indication, or that are routinely used in UK clinical practice.

Since the publication of TA184 NICE Clinical Guidance 121 'The diagnosis and treatment of lung cancer' (CG121) was published (April 2011). The guidance recommends treatment with an anthracycline-containing regimen or further treatment with a platinum-based regimen to a maximum of six cycles for people who have relapsed small-cell lung cancer and who are suitable for chemotherapy. It also recommends radiotherapy for palliation of local symptoms to people with relapsed small-cell lung cancer relapsed. The recommendations in CG121 do not impact on the guidance for topotecan; TA184 is incorporated into the guideline.

Based on the above information, it is proposed that TA184 be moved to the 'static' list.

## 8. Implementation

A submission from Implementation is included in Appendix 3.

The cost and volume of oral and intravenous topotecan prescribed and dispensed in hospitals has increased considerably since TA184 was published in 2009. However because guidance TA183 was also published in 2009, it is unclear what the impact of TA184 has been on prescription and dispensing of oral and intravenous topotecan.

## 9. Equality issues

No equality issues were raised when the scope for this appraisal was developed, or during the course of the appraisal.

**GE paper sign off:** Helen Knight, 19/10/12

**Contributors to this paper:**

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CCP input: Claire Turner

# 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. | A review of the appraisal will be planned into the NICE's work programme. | No |
| The decision to review the guidance should be deferred. | 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. | 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. | 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.<br>This option has the effect of preserving the funding direction associated with a positive recommendation in a NICE technology appraisal. | 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.<br>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 |

| Options | Consequence | Selected – 'Yes/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*

Lung cancer: the diagnosis and treatment of lung cancer. Clinical Guideline CG121, issued: April 2011. Review date: 2014.

Lung cancer for adults. Quality Standard QS17, issued: March 2012.

## Details of changes to the indications of the technology

| Indication considered in original appraisal | Proposed indication (for this appraisal) |
|---|---|
| Monotherapy for patients with relapsed small-cell lung cancer for whom re-treatment with the first-line regimen is not considered appropriate.<br>The acquisition cost for intravenous topotecan was £97.65 for a 1-mg vial or £290.62 for a 4-mg vial at the time of TA184. For oral topotecan the price was £30 per 1 mg capsule (excluding VAT). | No change.<br>The list price of branded formulations of topotecan remain the same as at the time of the original appraisal. Generic intravenous formulations are available.<br>BNF October 2012: Topotecan (Non-proprietary) – Concentrate for intravenous infusion, topotecan (as hydrochloride) 1 mg/mL, net price 1-mL vial = £87.88, 4-mL vial = £261.55; Intravenous infusion, powder for reconstitution, topotecan (as hydrochloride), net price 1-mg vial = £97.00, 4-mg vial = £290.00 |

## Details of new products

| Drug (manufacturer) | Details (phase of development, expected launch date, ) |
|---|---|
| Amrubicin (Celgene) | Phase III for relapsed small-cell lung cancer. Anticipated launch date unknown. |
| Picoplatin (Poniard Pharmaceuticals) | Phase III for relapsed small-cell lung cancer. Anticipated launch date unknown. |

## Registered and unpublished trials

| Trial name and registration number | Details |
|---|---|
| A Randomized, Open-Label, Multinational Phase 3 Trial Comparing Amrubicin Versus Topotecan in Patients With Extensive or Limited and Sensitive or Refractory Small Cell Lung Cancer After Failure of First-Line Chemotherapy<br>NCT00547651; EudraCT 2007-003989-18; AMR PH GL 2007 CL 001. | Completed ~May 2011<br>n = 637<br>Primary outcome measure: overall survival |

## References


Hartwell D, Jones J, Loveman E et al. (2011) Topotecan for relapsed small cell lung cancer: A systematic review and economic evaluation. *Cancer Treatment Reviews.* 37 (3) pp. 242-249.

Hudgens S, King J, Khan ZM (2011) Quality of life in small cell lung cancer: Results of an open-label phase III clinical trial. *Value in Health.* Conference: ISPOR 14th Annual European Congress. 14 (7) p. A460.

Lung cancer: the diagnosis and treatment of lung cancer. Clinical Guideline CG121, issued: April 2011. Review date: 2014.

O'Brien M, Hudgens S, King J et al. (2012) Evaluating meaningful change on the lung cancer symptom scale in small cell lung cancer: Results from a phase III clinical trial. *Value in Health.* Conference: 17th Annual International Meeting of the International Society for Pharmacoeconomics and Outcomes Research (ISPOR). 15 (4) pp: A227-A228.

## Appendix 3 – Implementation submission

# 1 Routine healthcare activity data

### 1.1 Hospital Pharmacy Audit Index data

This section presents Hospital Pharmacy Audit Index (HPAI) data on the net ingredient cost (NIC) and volume of intraveous topotecan, prescribed and dispensed by hospital pharmacies for use in hospitals in England.

**Figure 1 Net ingredient cost and volume of intravenous Topotecan prescribed and dispensed in hospitals between July 2000 and March 2012 in England**

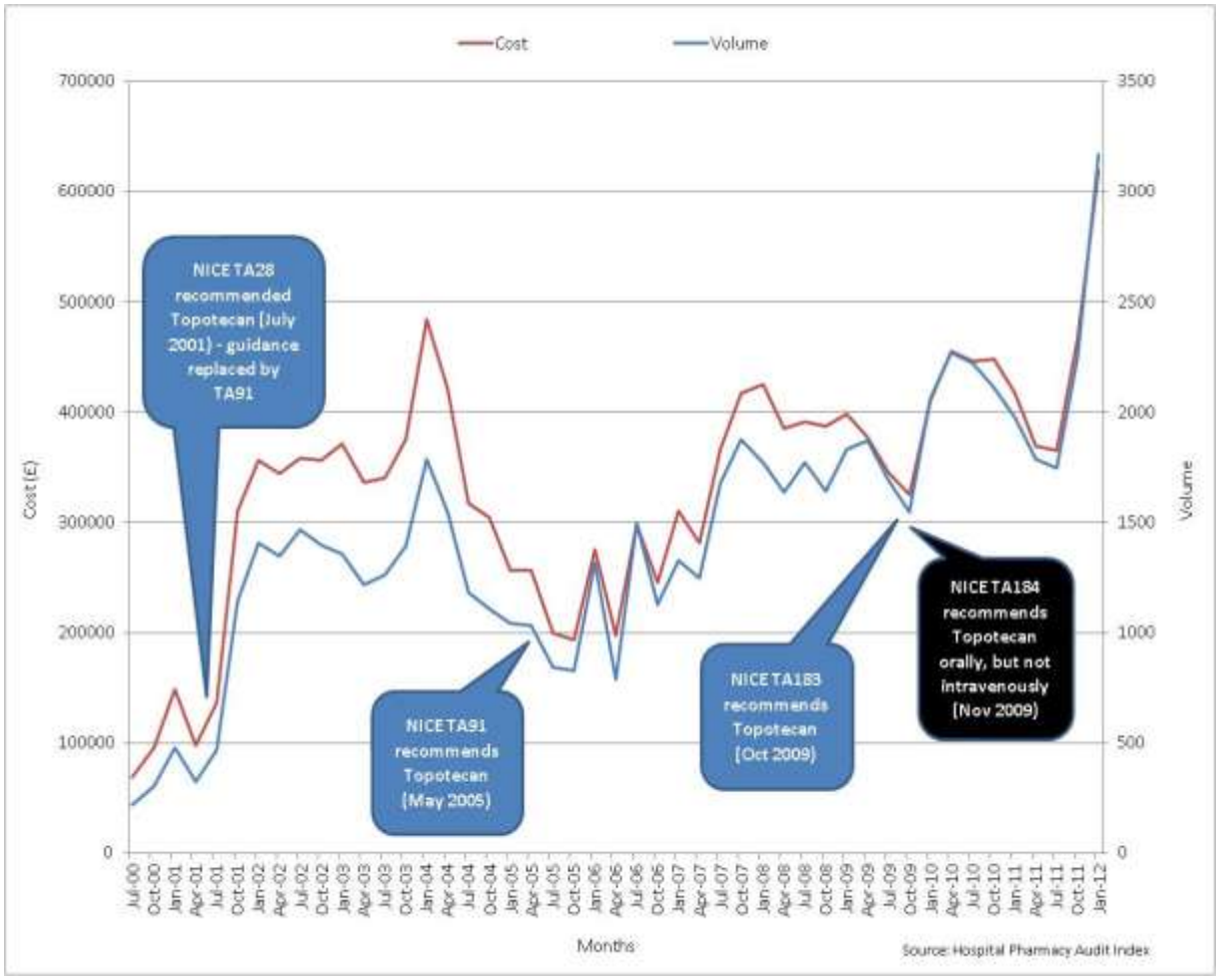
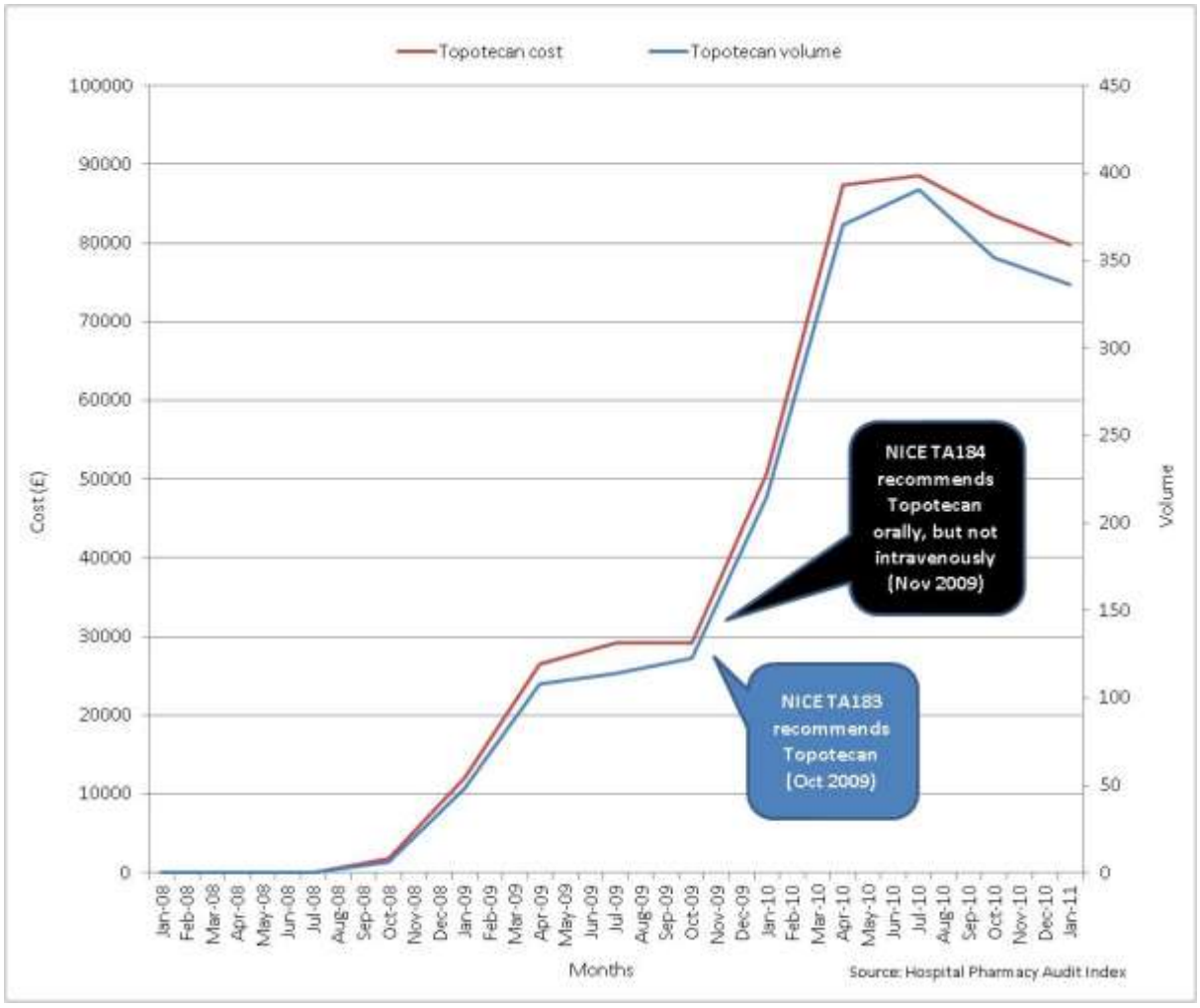


**Figure 2 Net ingredient cost and volume of oral Topotecan prescribed and dispensed in hospitals between January 2008 and January 2011 in England**




# 2 Implementation studies from published literature

Information is taken from the uptake database (ERNIE) website.

## 2.1 All Wales Medicines Strategy Group (2011) **Monitoring of AWMSG recommendations**

This paper covers medicines that have been recommended by the All Wales Medicines Strategy Group (AWMSG) for use in NHS Wales. Five of these medicines, Adalimumab, Teriparatide, Topotecan Hydrochloride, Bortezomib and Docetaxel are also covered by a NICE Technology Appraisal. The report includes hospital and

homecare usage data for three of these drugs, Adalimumab, Teriparatide, Topotecan Hydrochloride.

**2.2** Richards, M (2010) **Extent and causes of international variation in drug usage: A report for the Secretary of State for Health by Professor Sir Mike Richards CBE**

This report looks at medicines usage between countries, using IMS Health data. The WHO defined daily dose or the maximum or prescribed daily dose was used to measure usage. Results rank the UK relative to other countries usage and present calculations showing how close or otherwise the UK is to the average use across groups of other countries. It should be noted that countries other than the UK would not be expected to adhere to NICE guidance making comparisons between countries not possible.

# 3 Qualitative input from the field team

***The implementation field team have recorded the following feedback in relation to this guidance:***

Nothing to add at this time.

## Appendix A: Healthcare activity data definitions

*IMS HEALTH Hospital Pharmacy Audit Index (IMS HPAI)*

IMS HEALTH collects information from pharmacies in hospital trusts in the UK. The section of this database relating to England is available for monitoring the overall usage in drugs appraised by NICE. The IMS HPAI database is based on issues of medicines recorded on hospital pharmacy systems. Issues refer to all medicines supplied from hospital pharmacies: to wards; departments; clinics; theatres; satellite sites and to patients in outpatient clinics and on discharge.

***Measures of prescribing***

Volume: The HPAI database measures volume in packs and a drug may be available in different pack sizes and pack sizes can vary between medicines.

Cost: Estimated costs are also calculated by IMS using the drug tariff and other standard price lists. Many hospitals receive discounts from suppliers and this is not reflected in the estimated cost.

Costs based on the drug tariff provide a degree of standardization allowing comparisons of prescribing data from different sources to be made. The costs stated in this report do not represent the true price paid by the NHS on medicines. The estimated costs are used as a proxy for utilization and are not suitable for financial planning.

***Data limitations***

IMS HPAI data do not link to demographic or to diagnosis information on patients. Therefore, it cannot be used to provide prescribing information on age and sex or for prescribing of specific conditions where the same drug is licensed for more than one indication.