# Pixantrone monotherapy for the treatment of relapsed or refractory aggressive non-Hodgkin's lymphoma
ERRATUM

This report was commissioned by the NIHR HTA Programme as project number 10/59

BMJ Technology Assessment Group

This document contains errata in respect of the ERG report in response to the manufacturer's factual inaccuracy check.

The table below lists the page to be replaced in the original document and the nature of the change:

| Page No. | Change |
|---|---|
| 8 | Explanation of ICER confidence interval calculations added |
| 15 | The text around direction of model bias has been amended to include the word "potentially". |
| 109 | The duration associated with the cost of hospice care has been corrected from "annual" to "28 days" |

| | |
|---|---|
| NICE | National Institute for Health and Clinical Excellence |
| NMA | Network meta-analysis |
| ORR | Overall response rate |
| OS | Overall survival |
| OWSA | One-way sensitivity analysis |
| PET | Positron emission tomography |
| PFS | Progression-free survival |
| PSA | Probabilistic sensitivity analysis |
| QALY | Quality adjusted life year |
| R-CHOP | Rituximab added to cyclophosphamide, vincristine, doxorubicin and prednisolone |
| RCT | Randomised controlled trial |
| SD | Standard deviation |
| SE | Standard error |
| SmPC | Summary of Product Characteristics |
| STA | Single Technology Appraisal |
| TPC | Treatment of physician's choice |
| TTP | Time to progression |
| UK | United Kingdom |
| USA | United States of America |
| vs | versus |
| WHO | World Health Organization |
| WTP | Willingness-to-pay threshold |

## Glossary

| Term | Explanation |
|---|---|
| Methodology used to calculate 95% confidence intervals (CIs) around probabilistic incremental cost-effectiveness (ICER) estimates | All probabilistic estimates were taken from the manufacturer's model. To calculate the 95% CI around each probabilistic ICER estimate, the ERG first set ICERs indicating that pixantrone is dominant over treatment of physician's choice (TPC) to an extreme negative value and ICERs indicating that pixantrone is dominated by TPC to an extreme positive value. The ICERs were then ordered smallest to largest and the 2.5% and 97.5% percentiles selected; that is, the 125$^{th}$ and 4,875$^{th}$ ICERs in the list. |

0.54 to 2.81). The ERG's clinical expert indicated that the Western Europe subgroup could potentially have more severe disease than a patient who would typically be eligible for treatment with pixantrone in the UK. That is, compared with the Western Europe subgroup, patients in clinical practice in the UK might have received fewer lines of treatment before being considered eligible for treatment with pixantrone, with pixantrone potentially being given as a third-line treatment rather than fourth or fifth line treatment.

Comparative clinical effectiveness results for most subgroups presented (e.g., histologically confirmed aggressive B-cell NHL, prior treatment with rituximab, and geographic region) are based on *post hoc* subgroup analyses. Moreover, as subgroups, the power to detect a difference is reduced further, the number of patients in the analysis is generally small, and there is increased uncertainty around the robustness of the result. In the case of subgroups based on retrospective histological confirmation of disease and prior rituximab treatment, because randomisation was not stratified by these factors, there is the potential for unbalanced groups. For these reasons, the ERG considers that results of the subgroup analyses should be interpreted with caution.

*Economic*

The uncertainty associated with the limited clinical data available to inform the manufacturer's economic evaluation is propagated throughout the economic model, resulting in wide CIs around the probabilistic ICERs. In particular, ICERs associated with *post hoc* subgroup analyses.

When compared with the clinical trial result, both the manufacturer's base case analysis and the analysis carried out in the histologically confirmed aggressive B-cell patient population (i.e., the patient population most relevant to the decision problem) were potentially biased towards pixantrone as a result of overestimation of the relative PFS benefit of pixantrone versus TPC.

The absence of relevant HRQoL data from clinical trials resulted in a variety of sources being used to inform the utility and disutility values used in the manufacturer's economic evaluation. The ERG identified several values that may not have been appropriate for use in the patient population that is the focus of this STA.

### 1.1.1 Areas of uncertainty

The ERG considers that the key area of uncertainty relevant to the decision problem relates to the clinical benefit of pixantrone in patients who have previously been treated with rituximab. No statistically significant differences were found between pixantrone and TPC in response (CR/CRu), OS, or PFS in patients who had received prior rituximab.

In the Western Europe subgroup, results for median PFS and OS favour TPC. Based on differences in baseline severity of disease between the Western Europe subgroup and the Rest of World subgroup,

The constitution of each health state, with respect to the elements of patient care outlined above, were estimated from a survey of three key opinion leaders, commissioned by the manufacturer. The unit costs of each element of patient care were sourced from NHS reference costs 2010–2011, the Unit Costs of Health and Social Care 2011 or National Audit Office, End of Life Care.[69;70] Overall, the manufacturer estimated the per cycle cost of patient care to be £383.33, £202.67 and £798.00 for patients in the "PFS, on 3rd (or 4th) line treatment", "PFS, discontinued 3rd (or 4th) line treatment" and "PD", respectively. Tables 37 to 40 summarise the unit costs and resource use assumed in the calculation of each component of health state costs.

Table 37. Resource use and costs associated with professional and social services used in the manufacturer's model

| Resource | Resource use (days)[a] | | | Unit costs of resource (£) | Duration | Source |
|---|---|---|---|---|---|---|
| | PFS on 3rd (or 4th) line treatment | PFS, discontinued 3rd (or 4th) line treatment | PD | | | |
| Residential care | 2.99 | 0.75 | – | 71.00 | 28 days | Unit costs of health and social care[69] |
| Day care | 1.12 | 0.28 | 1.87 | 36.00 | 28 days | |
| Home care | 4.67 | 1.17 | 9.33 | 28.89 | 28 days | National Audit Office, End of Life Care.[70] |
| Hospice | 0.65 | 0.16 | 12.13 | 136.57 | 28 days | |
| Total per cycle costs (£)[b] | **119.10** | **29.78** | **498.47** | – | | |

[a] Estimated from expert clinical opinion.

[b] Calculated as a weighted average of unit costs per week (i.e., unit cost/duration*7 days); weighted by resource use.

Abbreviations used in table: PD, progressive disease; PFS, progression-free survival.

Table 38. Resource use and costs associated with health care professionals, used in the manufacturer's model

| Resource | Resource use (number of visits)[a] | | | Unit costs (per 28 days) of resources (£) | Source |
|---|---|---|---|---|---|
| | PFS on 3rd (or 4th) line treatment | PFS, discontinued 3rd (or 4th) line treatment | PD | | |
| ***Hospital-based health care*** | | | | | |
| Oncologist | 1.67 | 0.42 | 0.33 | 119.99 | National Schedule of Reference Costs Year: 2010–2011. NHS Trusts and PCTs combined[50] |
| Haematologist | 0.78 | 0.19 | 1.00 | 148.00 | |
| Radiologist | 1.33 | 0.33 | 0.00 | 17.00 | |
| Nurse | 4.00 | 1.00 | 0.00 | 50.00 | Unit costs of health and social care[69] |