Topotecan, pegylated liposomal doxorubicin hydrochloride, paclitaxel, trabectedin and gemcitabine for advanced recurrent disease only (Review of TA 91 & TA 222)

ADDITIONAL INFORMATION

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BMJ Technology Assessment Group

PLATINUM RESISTANT/REFRACTORY POPULATION

The base case results for the platinum resistant/refractory population were presented in Table 143 in the original report, and the deterministic results are reproduced below in Table A1. The TAG carried out additional scenario analyses to assess the impact of varying the treatment regimen and/or dosage of paclitaxel and PLDH on cost-effectiveness.

Table A1. Results of the Technology Assessment Group base case analysis; platinum resistant/refractory

Treatment	Modelled regimen	Total cost (discounted)	Total QALYs (discounted)	Incremental cost (discounted)	Incremental QALYs (discounted)	Incremental ICER (cost/QALY)	Incremental ICER (cost/QALY) (excluding dominated options)
PLDH	40 mg/m^2 on day 1 of every 28 day cycle	£14,320	1.004	–	–	–	–
Paclitaxel	80mg/m^2 weekly for 18 weeks or until progression	£15,095	0.971	£775	-0.033	Strictly dominated	
Topotecan	1.5 mg/m^2, on days 1-5 of every 21 day cycle	£21,271	1.020	£6,176	0.049	£127,117	£449,553
Abbreviations used in table: AUC, area under the curve; m, metre; mg, milligram; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; PLDH, pegylated liposomal doxorubicin hydrochloride.							

The base case used a low dose of PLDH (40 mg/m^2 on day 1 of every 28 day cycle) as the TAG was informed by its clinical experts that this reflects clinical practice in the UK. However, this was varied so that a higher dose of PLDH was used (50 mg/m^2 on day 1 of every 28 day cycle). The results of this analysis can be found in Table A2. Use of the higher dose increases the overall costs associated with PLDH by £1,122, this results in paclitaxel being the least costly choice of chemotherapy.

Table A2. Results of the Technology Assessment Group scenario analysis using higher dose of PLDH; platinum resistant/refractory

Treatment	Modelled regimen	Total cost (discounted)	Total QALYs (discounted)	Incremental cost (discounted)	Incremental QALYs (discounted)	Incremental ICER (cost/QALY)
Paclitaxel	80mg/m^2 weekly for 18 weeks or until progression	£15,095	0.971	–	–	–
PLDH	50 mg/m^2 on day 1 of every 28 day cycle	£15,442	1.004	£342	0.033	£10,480
Topotecan	1.5 mg/m^2, on days 1-5 of every 21 day cycle	£21,271	1.020	£5,829	0.015	£376,985
Abbreviations used in table: m, metre; mg, milligram; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; PLDH, pegylated liposomal doxorubicin hydrochloride.						

The treatment regimen for paclitaxel was varied to the less frequent treatment regimen of 175 mg/m^2 every three weeks as opposed to 80mg/m^2 weekly which was used in the base case. The dose used in the base case was based on feedback from the TAG's clinical experts on the use of paclitaxel in clinical practice in the UK.

Evidence from Rosenberg *et al.* suggests that efficacy of paclitaxel, based on tumour response rate, may not be affected by the use of weekly rather than three weekly administrations (overall response rate: 37/105 [35.2%] with paclitaxel weekly versus 38/103 [36.9%] paclitaxel every 3 weeks, p = 0.89). The study concluded that paclitaxel administered weekly was better tolerated yet comparably efficacious to paclitaxel administered every 3 weeks. Therefore, the TAG considers it appropriate to use the same trial-based estimates for efficacy for both treatment regimens.

The costs applied in the model based on the two different treatment regimens of paclitaxel are detailed in Table A3. The deterministic results of the scenario analysis using the less frequent treatment regimen of paclitaxel are presented in Table A4. While using the less frequent treatment regimen of paclitaxel increases the cost of chemotherapy per cycle, the reduction in administration leads to an overall reduction in total cost of £3,091, and so it is becomes the least costly treatment regimen.

Table A3. Estimated chemotherapy and administration costs based on alternative treatment regimens for paclitaxel

Regimen description	Chemotherapy cost per cycle	Pharmacy preparation cost per cycle	First cycle delivery cost	Subsequent cycle delivery costs
Paclitaxel 80 mg/m^2 weekly for 18 weeks or until progression	£306	£16	£200	£270
Paclitaxel 175 mg/m^2 day 1 every 21 day cycle (maximum of six cycles)	£638	£16	£331	£270

Table A4. Results of the Technology Assessment Group scenario analysis; platinum resistant/refractory

Treatment	Modelled regimen	Total cost (discounted)	Total QALYs (discounted)	Incremental cost (discounted)	Incremental QALYs (discounted)	Incremental ICER (cost/QALY)
Paclitaxel	175 mg/m^2 every three weeks (maximum of six cycles)	£12,004	0.971	–	–	–
PLDH	40 mg/m^2 on day 1 of every 28 day cycle	£14,320	1.004	£2,316	0.033	£69,935
Topotecan	1.5 mg/m^2, on days 1-5 of every 21 day cycle	£21,271	1.020	£6,951	0.015	£449,553
Abbreviations used in table: m, metre; mg, milligram; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; PLDH, pegylated liposomal doxorubicin hydrochloride.						

The scenario analysis in Table A4 was also varied to include the higher dose of PLDH (50 mg/m^2 on day 1 of every 28 day cycle). The results of this analysis can be found in Table A5.

Table A5. Results of the Technology Assessment Group scenario analysis using higher dose of PLDH; platinum resistant/refractory

Treatment	Modelled regimen	Total cost (discounted)	Total QALYs (discounted)	Incremental cost (discounted)	Incremental QALYs (discounted)	Incremental ICER (cost/QALY)
Paclitaxel	175 mg/m^2 every three weeks (maximum of six cycles)	£12,004	0.971	–	–	–
PLDH	50 mg/m^2 on day 1 of every 28 day cycle	£15,442	1.004	£3,438	0.033	£103,810
Topotecan	1.5 mg/m^2, on days 1-5 of every 21 day cycle	£21,271	1.020	£5,829	0.015	£376,985
Abbreviations used in table: m, metre; mg, milligram; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; PLDH, pegylated liposomal doxorubicin hydrochloride.						

As a final scenario analysis, the TAG explored the effect of using paclitaxel 80 mg/m^2 each week for 3 weeks with a one week break, every 4 weeks, for 18 weeks or until progression. The results with the lower and higher doses of PLDH are presented in Tables A6 and A7, respectively, and also show paclitaxel to be the least costly chemotherapy option.

Table A6. Results of the Technology Assessment Group using paclitaxel for 3 weeks every 4 weeks; platinum resistant/refractory

Treatment	Modelled regimen	Total cost (discounted)	Total QALYs (discounted)	Incremental cost (discounted)	Incremental QALYs (discounted)	Incremental ICER (cost/QALY)
Paclitaxel	80mg/m^2 weekly for 3 weeks every 4 weeks for 18 weeks or until progression	£13,305	0.971	–	–	–
PLDH	40 mg/m^2 on day 1 of every 28 day cycle	£14,320	1.004	£1,016	0.033	£30,660
Topotecan	1.5 mg/m^2, on days 1-5 of every 21 day cycle	£21,271	1.020	£6,951	0.015	£449,553
Abbreviations used in table: m, metre; mg, milligram; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; PLDH, pegylated liposomal doxorubicin hydrochloride.						

Table A7. Results of the Technology Assessment Group scenario analysis using paclitaxel for 3 weeks every 4 weeks and using higher dose of PLDH; platinum resistant/refractory

Treatment	Modelled regimen	Total cost (discounted)	Total QALYs (discounted)	Incremental cost (discounted)	Incremental QALYs (discounted)	Incremental ICER (cost/QALY)
Paclitaxel	80mg/m^2 weekly for 3 weeks every 4 weeks for 18 weeks or until progression	£13,305	0.971	–	–	–
PLDH	50 mg/m^2 on day 1 of every 28 day cycle	£15,442	1.004	£2,138	0.033	£64,535
Topotecan	1.5 mg/m^2, on days 1-5 of every 21 day cycle	£21,271	1.020	£5,829	0.015	£376,985
Abbreviations used in table: m, metre; mg, milligram; ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; PLDH, pegylated liposomal doxorubicin hydrochloride.						

REFERENCES

Rosenberg P, Andersson H, Boman K, Ridderheim M, Sorbe B, Puistola U, *et al*. Randomized trial of single agent paclitaxel given weekly versus every three weeks and with peroral versus intravenous steroid premedication to patients with ovarian cancer previously treated with platinum. *Acta Oncologica* 2002; **41**(5):418–24.