Colistimethate sodium powder and tobramycin powder for inhalation for the treatment of chronic *Pseudomonas aeruginosa* lung infection in cystic fibrosis

Addendum (1) to Assessment Report: Economic analysis of a proposed Patient Access Scheme for tobramycin DPI

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A1.1 Introduction

The Novartis submission to NICE[1] did not present any incremental cost-effectiveness results for tobramycin DPI versus any other comparator. In addition, whilst patient-level data FEV_1 were requested by the Assessment Group these were not provided by the manufacturer during the assessment period. Novartis submitted a proposed patient access scheme (PAS) in May 2012.[2] This proposed PAS assumed a simple price reduction resulting in a net price of [redacted] per 28 day pack (224 capsules plus 5 Podhaler devices) or [redacted] per 7 day pack (56 capsules plus 1 Podhaler device). These prices exclude VAT. The proposed PAS application from Novartis did not include an economic analysis. The Assessment Group was concerned about the basis for this proposed PAS as the proposal application did not provide sufficient information with which to assess the relative costs and outcomes of tobramycin DPI against any other comparator(s), nor did it state which comparator(s) was relevant. As a consequence, the Assessment Group re-requested individual patient-level FEV_1 data together with aggregated data on exacerbations from the EAGER trial[4] in order to allow for a full economic evaluation of tobramycin DPI. This obviates the need for assumptions of equivalence between treatment comparators and means that tobramycin DPI is subjected to the same economic framework used to assess the incremental costs and health effects of colistimethate sodium DPI (see Chapter 6 of the Assessment Report[3]). Novartis provided the requested data in August 2012. This addendum reports the methods and results of the analysis of the proposed PAS for tobramycin DPI.

A1.2 Methods

A1.2.1 Methods used in the economic analysis and changes to data sources and assumptions

The general methods and assumptions used in the Assessment Group's analysis of the proposed PAS are the same as those used for the economic evaluation of colistimethate sodium DPI versus nebulised tobramycin, as detailed in Chapter 6 of the Assessment Report.[3] Owing to the absence of sufficient evidence relating to any other comparator, the economic analysis for tobramycin DPI is restricted solely to a direct economic comparison against nebulised tobramycin. In line with licensed indications, both the intervention and comparator are assumed to be used for a period of 28 days (8 capsules per day) followed by 28 days without use of the drug.

The analysis of the proposed PAS required additional data/assumptions relating to four factors: (i) data relating to FEV_1 change for each treatment group; (ii) probabilities of exacerbation for each treatment group; (iii) amended age estimates to reflect the slightly older population recruited into the EAGER trial[4] and; (iv) amended prices for tobramycin DPI to reflect the impact of the proposed PAS.

(i) FEV_1 data

Novartis made available patient-level data from the EAGER trial relating to change in FEV_1 before and after administration of the intervention/comparator at study baseline (week 0), before and after administration of the intervention/comparator at week 20, and a final measurement at week 24. The latter timepoint relates to an "off-cycle" and therefore is most similar to a pre-dose measurement. Three groups of analyses were undertaken by the Assessment Group:

1. Pre-dose FEV_1 at week 0 to FEV_1 at week 24;
2. Pre-dose FEV_1 at week 0 to pre-dose FEV_1 at week 20;
3. Post-dose FEV_1 at week 0 to post-dose FEV_1 at week 20.

There is uncertainty with respect to which of these analyses should be considered the most reliable due to the effect of tobramycin on FEV_1 immediately after administration. The Assessment Group is of the view that the analysis "Pre-dose FEV_1 at week 0 to FEV_1 at week 24" is most appropriate and should be treated as a base case for the economic analysis. However, separate analyses are presented for all three scenarios to explore whether this issue impacts upon the results of the economic analysis. The analysis of the patient-level FEV_1 data resulted in the following transition data across the three health states.

Table A1: Scenario 1: Transitions - tobramycin DPI pre-dose FEV_1 week 0 to FEV_1 week 24

	FEV_1>70%	$FEV_1$40-69%	FEV_1<40%	Total
FEV_1>70%	18	12	0	30
$FEV_1$40-69%	18	127	7	152
FEV_1<40%	0	11	28	39

Table A2: Scenario 1: Transitions - nebulised tobramycin pre-dose FEV_1 week 0 to FEV_1 week 24

	FEV_1>70%	$FEV_1$40-69%	FEV_1<40%	Total
FEV_1>70%	18	11	0	29
$FEV_1$40-69%	10	82	10	102
FEV_1<40%	0	5	32	37

Table A3: Scenario 2: Transitions - tobramycin DPI pre-dose FEV_1 week 0 to pre-dose FEV_1 week 20

	FEV_1>70%	$FEV_1$40-69%	FEV_1<40%	Total
FEV_1>70%	19	11	0	30
$FEV_1$40-69%	20	122	13	155
FEV_1<40%	0	17	24	41

Table A4: Scenario 2: Transitions - nebulised tobramycin pre-dose FEV_1 week 0 to pre-dose FEV_1 week 20

	FEV_1>70%	$FEV_1$40-69%	FEV_1<40%	Total
FEV_1>70%	18	11	0	29
$FEV_1$40-69%	11	80	11	102
FEV_1<40%	0	10	29	39

Table A5: Scenario 3: Transitions - tobramycin DPI post-dose FEV_1 week 0 to post-dose FEV_1 week 20

	FEV_1>70%	$FEV_1$40-69%	FEV_1<40%	Total
FEV_1>70%	17	11	0	28
$FEV_1$40-69%	15	107	14	136
FEV_1<40%	0	15	26	41

Table A6: Scenario 3: Transitions - nebulised tobramycin post-dose FEV_1 week 0 to post-dose FEV_1 week 20

	FEV_1>70%	$FEV_1$40-69%	FEV_1<40%	Total
FEV_1>70%	15	8	0	23
$FEV_1$40-69%	10	77	9	96
FEV_1<40%	0	9	24	33

(ii) Exacerbations

Data relating to minor and major exacerbations were not collected within the EAGER trial[4] (see Page 46 of the main Assessment Report[3]). As indicated by Konstan *et al*,[4] lung disorder may represent a reasonable proxy for pulmonary or cystic fibrosis exacerbations, hence these data were used to estimate the probability of any exacerbation (minor or major) in each treatment group. In addition, Novartis undertook additional analyses of the trial data which produced estimates of the number of patients receiving any new antibiotic, total days used, and the number of patients who required both additional antibiotic treatment and hospitalisation in each treatment group. None of these data were ideal in distinguishing between minor and major exacerbations. The estimates of the number of patients who required both additional antibiotic treatment and hospitalisation, combined with the estimated number of exacerbation events from Konstan *et al*,[4] were used to produce a crude estimate of the probability that an exacerbation event was major. This estimate is very similar to that derived from the COLO/DPI/02/06 trial[5] (see Table 41 of the Assessment Report), however its validity remains questionable. These data are summarised in Table A7.

Table A7 Exacerbation parameters used in the proposed PAS analysis

Parameter	Distribution	Alpha	Alpha + Beta	Mean	Source
Probability exacerbation tobramycin DPI	Beta	104	308	0.34	Based on Konstan *et al*[4]
Probability exacerbation tobramycin nebulised	Beta	63	209	0.30	Based on Konstan *et al*[4]
Probability exacerbation is major (pooled across both groups)	Beta	[redacted]	[redacted]	[redacted]	Additional analysis undertaken by Novartis

(iii) Age

In line with the EAGER trial population,[4] the analysis assumes a mean start age of 25.5 years.

(iv) Price of tobramycin DPI

As noted in Section 3.3.5 of the Assessment Report,[3] the BNF list price for tobramycin DPI is £1790.00 per 28 day pack (224 capsules plus 5 Podhaler devices) £447.50 per 7 day pack (56 capsules plus one Podhaler device). This proposed PAS involves a simple price reduction resulting in a net price of [redacted] per 28 day pack or [redacted] per 7 day pack.

[redacted]

In addition to the Reference Case analysis, an additional sensitivity analysis is presented to reflect the lower price of nebulised tobramycin based on estimates from the Commercial Medicines Unit (CMU) Electronic Market Information Tool (E-MIT). In September 2012, this estimated cost to the NHS was £970.12 per pack.

[redacted]

All other data inputs were identical to those detailed in the Assessment Report.[3] All analyses are presented with and without the proposed PAS for the three sets of FEV_1 data. Owing to the absence of a clear proposed price for colistimethate sodium DPI at the time of the assessment and the potential heterogeneities between the populations recruited to the COLO/DPI/02/06 trial[4] and the EAGER trial,[4] a full incremental analysis is not presented here.

A1.3 Cost-effectiveness results

A1.3.1 Reference Case analysis

Table A8 presents the central estimates of cost-effectiveness for tobramycin DPI versus nebulised tobramycin based on the probabilistic Reference Case model. The model suggests that irrespective of which FEV_1 efficacy data are used, tobramycin DPI is consistently expected to produce additional QALY gains compared to nebulised tobramycin. Much of this incremental benefit is driven by the small gains observed within the trial period which are inflated considerably by extrapolating over the patient's remaining lifetime. Over the patient's lifetime this incremental gain is expected to range from 0.04 QALYs (post-dose 0-20 weeks) to 0.34 QALYs (pre-dose 0-24 weeks). Based on its current list price, the incremental cost-effectiveness of tobramycin DPI is expected to range from around £124,000 to in excess of £1million per QALY gained. The introduction of the proposed PAS results in a situation whereby tobramycin DPI is expected to dominate nebulised tobramycin under all scenarios. The short-term model results (Table A9) suggest a similar situation when the extrapolation is excluded from the analysis. Based on its current list price, tobramycin DPI is expected to range from around £376,000 to over £2.8million per QALY gained. The introduction of the proposed PAS

again is expected to result in a situation whereby tobramycin DPI consistently dominates nebulised tobramycin irrespective of which FEV_1 data are used.

Table A8 Probabilistic cost-effectiveness results – Reference Case analysis

Scenario	QALYs			Costs			ICER
	Tobi DPI	Tobi neb	Inc.	Tobi DPI	Tobi neb	Inc.	
Without PAS							
Pre-dose wk0-24	8.73	8.38	**0.34**	£136,965.02	£94,511.82	**£42,453.20**	**£123,563**
Pre-dose wk0-20	8.72	8.52	**0.19**	£136,912.19	£94,761.35	**£42,150.84**	**£218,158**
Post-dose wk0-20	8.62	8.58	**0.04**	£136,695.90	£94,852.38	**£41,843.53**	**£1,005,476**
With PAS							
Pre-dose wk0-24	8.73	8.38	**0.34**	£75,237.19	£94,511.82	**-£19,274.63**	**Dominating**
Pre-dose wk0-20	8.72	8.52	**0.19**	£75,208.17	£94,761.35	**-£19,553.18**	**Dominating**
Post-dose wk0-20	8.62	8.58	**0.04**	£75,089.36	£94,852.38	**-£19,763.01**	**Dominating**

Table A9 Probabilistic cost-effectiveness results – short-term "within trial" analysis

Scenario	QALYs			Costs			ICER
	Tobi DPI	Tobi neb	Inc.	Tobi DPI	Tobi neb	Inc.	
Without PAS							
Pre-dose wk0-24	0.36	0.35	**0.00**	£5,696.47	£3,956.13	**£1,740.35**	**£375,998**
Pre-dose wk0-20	0.36	0.35	**0.00**	£5,696.43	£3,956.22	**£1,740.22**	**£481,987**
Post-dose wk0-20	0.36	0.35	**0.00**	£5,696.15	£3,956.28	**£1,739.87**	**£2,800,138**
With PAS							
Pre-dose wk0-24	0.36	0.35	**0.00**	£3,129.22	£3,956.13	**-£826.91**	**Dominating**
Pre-dose wk0-20	0.36	0.35	**0.00**	£3,129.20	£3,956.22	**-£827.02**	**Dominating**
Post-dose wk0-20	0.36	0.35	**0.00**	£3,129.04	£3,956.28	**-£827.24**	**Dominating**

Table A10 shows a summary of the cost-effectiveness acceptability curves with and without the proposed PAS. For the sake of brevity, full curves are not shown here. The CEACs suggest that without the PAS, the probability that tobramycin DPI produces more net benefit than nebulised tobramycin is approximately zero. When the proposed PAS is introduced, the probability that tobramycin DPI produces more net benefit than nebulised tobramycin is approximately 1.0.

Table A10 Probability that tobramycin DPI produces the greatest net benefit

Scenario	Probability tobramycin DPI produces greatest net benefit at threshold λ (Reference Case model)	
	λ=£20,000/QALY gained	λ=£30,000/QALY gained
Without PAS		
Pre-dose wk0-24	0.00	0.00
Pre-dose wk0-20	0.00	0.00
Post-dose wk0-20	0.00	0.00
With PAS		
Pre-dose wk0-24	1.00	1.00
Pre-dose wk0-20	1.00	1.00

Post-dose wk0-20	1.00	1.00

A1.3.2 Additional sensitivity analysis using E-MIT price

Table A11 presents the results of the analysis based on the E-MIT price for nebulised tobramycin. Without the proposed PAS, the incremental cost-effectiveness of tobramycin DPI versus nebulised tobramycin is estimated to be in the range £168,347 per QALY gained to £1,376,550 per QALY gained. When the proposed PAS is incorporated into the analysis, tobramycin DPI is expected to dominate nebulised tobramycin.

Table A11 Cost-effectiveness results for tobramycin DPI versus nebulised tobramycin using E-MIT price for nebulised tobramycin

Scenario	QALYs			Costs			ICER
	Tobi DPI	Tobi neb	Inc.	Tobi DPI	Tobi neb	Inc.	
Without PAS							
Pre-dose wk0-24	8.73	8.38	**0.34**	£136,947.89	£79,107.74	**£57,840.15**	**£168,347**
Pre-dose wk0-20	8.72	8.52	**0.19**	£136,895.07	£79,316.60	**£57,578.47**	**£298,007**
Post-dose wk0-20	8.62	8.58	**0.04**	£136,678.81	£79,392.79	**£57,286.02**	**£1,376,550**
With PAS							
Pre-dose wk0-24	8.73	8.38	**0.34**	£75,245.75	£79,107.74	**-£3,861.99**	**dominating**
Pre-dose wk0-20	8.72	8.52	**0.19**	£75,216.73	£79,316.60	**-£4,099.87**	**dominating**
Post-dose wk0-20	8.62	8.58	**0.04**	£75,097.91	£79,392.79	**-£4,294.88**	**dominating**

A1.3.3 Other simple sensitivity analysis

Table A12 presents the results of the other simple sensitivity analysis, based on the scenarios used in the main Assessment Report. For the vast majority of the analyses based on the list prices for the intervention and comparator, the incremental cost-effectiveness of tobramycin DPI versus nebulised tobramycin is above £110,000 per QALY gained. When the proposed PAS is included in the analysis, tobramycin DPI dominates nebulised tobramycin in most scenarios.

Table A12 Simple sensitivity analysis results

	QALYs			**Costs**			
Scenario	**Tobi DPI**	**Tobi neb**	**Inc.**	**Tobi DPI**	**Tobi neb**	**Inc.**	**ICER**
1. Deterministic point estimates for parameters							
Without PAS							
Pre-dose wk0-24	8.69	8.35	0.34	£136,416.60	£94,179.93	£42,236.66	**£124,090**
Pre-dose wk0-20	8.68	8.49	0.19	£136,358.45	£94,413.35	£41,945.10	**£217,351**
Post-dose wk0-20	8.59	8.54	0.04	£136,151.15	£94,502.02	£41,649.13	**£953,264**
With PAS							
Pre-dose wk0-24	8.69	8.35	0.34	£74,955.85	£94,179.93	-£19,224.08	**dominating**
Pre-dose wk0-20	8.68	8.49	0.19	£74,923.90	£94,413.35	-£19,489.45	**dominating**
Post-dose wk0-20	8.59	8.54	0.04	£74,810.00	£94,502.02	-£19,692.02	**dominating**
2. Time trade off utility values from Yi et al[6]							
Without PAS							

Scenario	QALYs			Costs			ICER
	Tobi DPI	Tobi neb	Inc.	Tobi DPI	Tobi neb	Inc.	
Pre-dose wk0-24	10.52	10.41	0.11	£136,350.12	£94,194.34	£42,155.78	**£373,679**
Pre-dose wk0-20	10.51	10.45	0.06	£136,312.55	£94,479.26	£41,833.29	**£676,461**
Post-dose wk0-20	10.48	10.47	0.02	£136,127.11	£94,501.12	£41,625.98	**£2,638,863**
With PAS							
Pre-dose wk0-24	10.52	10.41	0.11	£74,919.33	£94,194.34	-£19,275.01	**dominating**
Pre-dose wk0-20	10.51	10.45	0.06	£74,898.68	£94,479.26	-£19,580.58	**dominating**
Post-dose wk0-20	10.48	10.47	0.02	£74,796.79	£94,501.12	-£19,704.34	**dominating**
3. Standard gamble utility values from Yi et al[6]							
Without PAS							
Pre-dose wk0-24	10.17	9.91	0.27	£136,350.12	£94,194.34	£42,155.78	**£158,471**
Pre-dose wk0-20	10.16	10.02	0.14	£136,312.55	£94,479.26	£41,833.29	**£307,188**
Post-dose wk0-20	10.09	10.04	0.05	£136,127.11	£94,501.12	£41,625.98	**£875,357**
With PAS							
Pre-dose wk0-24	10.17	9.91	0.27	£74,919.33	£94,194.34	-£19,275.01	**dominating**
Pre-dose wk0-20	10.16	10.02	0.14	£74,898.68	£94,479.26	-£19,580.58	**dominating**
Post-dose wk0-20	10.09	10.04	0.05	£74,796.79	£94,501.12	-£19,704.34	**dominating**
4. HUI-2 utility values from Yi et al[6]							
Without PAS							
Pre-dose wk0-24	9.06	9.00	0.06	£136,350.12	£94,194.34	£42,155.78	**£693,184**
Pre-dose wk0-20	9.06	9.04	0.03	£136,312.55	£94,479.26	£41,833.29	**£1,648,334**
Post-dose wk0-20	9.05	9.03	0.02	£136,127.11	£94,501.12	£41,625.98	**£2,257,700**
With PAS							
Pre-dose wk0-24	9.06	9.00	0.06	£74,919.33	£94,194.34	-£19,275.01	**dominating**
Pre-dose wk0-20	9.06	9.04	0.03	£74,898.68	£94,479.26	-£19,580.58	**dominating**
Post-dose wk0-20	9.05	9.03	0.02	£74,796.79	£94,501.12	-£19,704.34	**dominating**
5. EQ-5D values from Stahl et al[7] (GOLD criteria)							
Without PAS							
Pre-dose wk0-24	7.76	7.38	0.38	£136,350.12	£94,194.34	£42,155.78	**£109,991**
Pre-dose wk0-20	7.75	7.65	0.09	£136,312.55	£94,479.26	£41,833.29	**£442,825**
Post-dose wk0-20	7.66	7.64	0.02	£136,127.11	£94,501.12	£41,625.98	**£2,307,399**
With PAS							
Pre-dose wk0-24	7.76	7.38	0.38	£74,919.33	£94,194.34	-£19,275.01	**dominating**
Pre-dose wk0-20	7.75	7.65	0.09	£74,898.68	£94,479.26	-£19,580.58	**dominating**
Post-dose wk0-20	7.66	7.64	0.02	£74,796.79	£94,501.12	-£19,704.34	**dominating**
6. EQ-5D values from Stahl et al[7] (BTS criteria)							
Without PAS							
Pre-dose wk0-24	7.87	7.68	0.19	£136,350.12	£94,194.34	£42,155.78	**£222,250**
Pre-dose wk0-20	7.88	7.89	-0.01	£136,312.55	£94,479.26	£41,833.29	**dominated**
Post-dose wk0-20	7.84	7.84	0.00	£136,127.11	£94,501.12	£41,625.98	**dominated**
With PAS							
Pre-dose wk0-24	7.87	7.68	0.19	£74,919.33	£94,194.34	-£19,275.01	**dominating**
Pre-dose wk0-20	7.88	7.89	-0.01	£74,898.68	£94,479.26	-£19,580.58	**£2,604,059**
Post-dose wk0-20	7.84	7.84	0.00	£74,796.79	£94,501.12	-£19,704.34	**£9,171,576**
7. Transition probabilities for nebulised tobramycin set equal to those for tobramycin DPI							
Without PAS							
Pre-dose wk0-24	8.70	8.70	0.00	£136,424.40	£94,783.61	£41,640.79	**dominated**
Pre-dose wk0-20	8.69	8.69	0.00	£136,362.57	£94,740.66	£41,621.91	**dominated**
Post-dose wk0-20	8.59	8.59	0.00	£136,152.66	£94,594.82	£41,557.84	**dominated**
With PAS							
Pre-dose wk0-24	8.70	8.70	0.00	£74,960.14	£94,783.61	-£19,823.48	**£9,943,642**
Pre-dose wk0-20	8.69	8.69	0.00	£74,926.16	£94,740.66	-£19,814.49	**£9,943,642**
Post-dose wk0-20	8.59	8.59	0.00	£74,810.83	£94,594.82	-£19,783.99	**£9,943,642**
8. Utility decrement for exacerbations doubled							
Without PAS							
Pre-dose wk0-24	8.66	8.32	0.34	£136,416.60	£94,179.93	£42,236.66	**£124,901**

Scenario	QALYs			Costs			ICER
	Tobi DPI	Tobi neb	Inc.	Tobi DPI	Tobi neb	Inc.	
Pre-dose wk0-20	8.65	8.46	0.19	£136,358.45	£94,413.35	£41,945.10	**£219,754**
Post-dose wk0-20	8.55	8.51	0.04	£136,151.15	£94,502.02	£41,649.13	**£999,542**
With PAS							
Pre-dose wk0-24	8.66	8.32	0.34	£74,955.85	£94,179.93	-£19,224.08	**dominating**
Pre-dose wk0-20	8.65	8.46	0.19	£74,923.90	£94,413.35	-£19,489.45	**dominating**
Post-dose wk0-20	8.55	8.51	0.04	£74,810.00	£94,502.02	-£19,692.02	**dominating**
9. Cost of hospitalisation doubled							
Without PAS							
Pre-dose wk0-24	8.69	8.35	0.34	£144,509.98	£101,359.39	£43,150.59	**£126,775**
Pre-dose wk0-20	8.68	8.49	0.19	£144,448.38	£101,610.60	£42,837.78	**£221,976**
Post-dose wk0-20	8.59	8.54	0.04	£144,228.78	£101,706.03	£42,522.75	**£973,259**
With PAS							
Pre-dose wk0-24	8.69	8.35	0.34	£83,049.23	£101,359.39	-£18,310.16	**dominating**
Pre-dose wk0-20	8.68	8.49	0.19	£83,013.83	£101,610.60	-£18,596.77	**dominating**
Post-dose wk0-20	8.59	8.54	0.04	£82,887.63	£101,706.03	-£18,818.40	**dominating**

A1.4 Discussion

The Reference Case analysis presented within this addendum suggests that tobramycin DPI is expected to produce more QALYs than nebulised tobramycin under the base case scenario. When based on current list prices for these products, tobramycin DPI is expected to have an incremental cost-effectiveness ratio in excess of £123,000 per QALY gained when compared against nebulised tobramycin. When the proposed PAS is incorporated into the analysis, tobramycin DPI is expected to dominate nebulised tobramycin.

The analysis presented here is based on exactly the same model used to evaluate colistimethate sodium DPI (see Chapter 6 of the Assessment Report report[3]), albeit using different prices for the intervention, new FEV_1 and exacerbation data from the EAGER trial[4] and an assumption of a slightly older patient population. As such, the model is subject to the same data limitations as described in the main report, most notably, the uncertainty surrounding the extrapolation of short-term FEV_1 transitions without the inclusion of other likely correlated factors. However, the analyses presented here indicate that the conclusions of the analysis hold even when the unobserved extrapolation period is removed from the analysis. Two additional limitations should also be noted here. Firstly, the EAGER trial did not include the collection of exacerbation data hence the use of lung disorder as a proxy is subject to uncertainty. Whilst clearly this is an important characteristic of the disease, its impact within the model is secondary to changes in lung health characterised by FEV_1. Secondly, across the three sets of FEV_1 data, there is a notable amount of missing data with somewhat higher rates of attrition in the tobramycin DPI arm (27%-33% in the tobramycin DPI group versus 19%-27% in the nebulised tobramycin group). In order for patients to be included in the analysis they needed to have FEV_1 measurements at both week 0 and week 20/24 – therefore the transition data may reflect a "best-case scenario" whereby only responders are captured in either group. Given the apparent

imbalance in missing data across the two treatment groups, the true cost-effectiveness of tobramycin DPI could be less favourable than the estimates presented here.

A1.5 Conclusions

Despite uncertainties in the evidence available for the economic evaluation of tobramycin DPI, the economic analysis suggests that the introduction of the proposed PAS is likely to result in a situation whereby tobramycin DPI dominates nebulised tobramycin. The cost-effectiveness of tobramycin DPI versus any other comparator is unknown.

A1.6 References

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