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NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Technology appraisals

Patient access scheme submission template

October 2009

1 Introduction

The 2009 Pharmaceutical Price Regulation Scheme (PPRS) (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS) is a non-contractual scheme between the Department of Health and the Association of the British Pharmaceutical Industry. The purpose of the 2009 PPRS is to ensure that safe and cost-effective medicines are available on reasonable terms to the NHS in England and Wales. One of the features of the 2009 PPRS is to improve patients' access to medicines at prices that better reflect their value through patient access schemes.

Patient access schemes are arrangements which may be used on an exceptional basis for the acquisition of medicines for the NHS in England and Wales. Patient access schemes propose either a discount or rebate that may be linked to the number, type or response of patients, or a change in the list price of a medicine linked to the collection of new evidence (outcomes). These schemes help to improve the cost effectiveness of a medicine and therefore allow the National Institute for Health and Care Excellence (NICE) to recommend treatments which it would otherwise not have found to be cost effective. More information on the framework for patient access schemes is provided in the 2009 PPRS (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS.

Patient access schemes are proposed by a pharmaceutical company and agreed with the Department of Health, with input from the Patient Access Schemes Liaison Unit (PASLU) within the Centre for Health Technology Evaluation at NICE.

2 Instructions for manufacturers and sponsors

This document is the patient access scheme submission template for technology appraisals. If manufacturers and sponsors want the National Institute for Health and Care Excellence (NICE) to consider a patient access scheme as part of a technology appraisal, they should use this template. NICE can only consider a patient access scheme after formal referral from the Department of Health.

The template contains the information NICE requires to assess the impact of a patient access scheme on the clinical and cost effectiveness of a technology, in the context of a technology appraisal, and explains the way in which background information (evidence) should be presented. If you are unable to follow this format, you must state your reasons clearly. You should insert 'N/A' against sections that you do not consider relevant, and give a reason for this response.

Please refer to the following documents when completing the template:

- 'Guide to the methods of technology appraisal' (http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9)
- 'Specification for manufacturer/sponsor submission of evidence' (http://www.nice.org.uk/aboutnice/howwework/devnicetech/singletechnologyappraisalsubmissiontemplates.jsp) and
- Pharmaceutical Price Regulation Scheme 2009 (www.dh.gov.uk/en/Healthcare/Medicinespharmacyandindustry/Pharmaceuticalpriceregulationscheme/2009PPRS).

For further details on the technology appraisal process, please see NICE's 'Guide to the single technology appraisal (STA) process' and 'Guide to the multiple technology appraisal (MTA) process' (http://www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/technology_appraisal_process_guides.jsp). The

‘Specification for manufacturer/sponsor submission of evidence’ provides details on disclosure of information and equality issues.

Make the submission as brief and informative as possible. Only mark information as confidential when absolutely necessary. Sufficient information must be publicly available for stakeholders to comment on the full content of the technology appraisal, including details of the proposed patient access scheme. Send submissions electronically to NICE in Word or a compatible format, not as a PDF file.

Appendices may be used to include additional information that is considered relevant to the submission. Do not include information in the appendices that has been requested in the template. Appendices should be clearly referenced in the main submission.

When making a patient access scheme submission, include:

- an updated version of the checklist of confidential information, if necessary
- an economic model with the patient access scheme incorporated, in accordance with the ‘Guide to the methods of technology appraisal’ (http://publications.nice.org.uk/guide-to-the-methods-of-technology-appraisal-2013-pmg9).

If you are submitting the patient access scheme at the end of the appraisal process, you should update the economic model to reflect the assumptions that the Appraisal Committee considered to be most plausible. No other changes should be made to the model.

3 Details of the patient access scheme

3.1 Please give the name of the technology and the disease area to which the patient access scheme applies.

The name of the technology is tolvaptan (brand name Jinarc).

The patient access scheme applies to the proposed indication for tolvaptan to slow the progression of cyst development and renal insufficiency of autosomal dominant polycystic kidney disease (ADPKD) in patients with CKD stage 1 to 3 at initiation of treatment and evidence of rapidly progressing disease. Jinarc is indicated in adults (Otsuka Pharmaceutical Europe Ltd, 2014).

3.2 Please outline the rationale for developing the patient access scheme.

The patient access scheme is a mechanism through which the NHS will be able to procure tolvaptan for ADPKD at a price lower than list price. The rationale for developing this scheme is to provide a cost-effective therapy to the NHS, thereby facilitating access for patients with ADPKD.

3.3 Please describe the type of patient access scheme, as defined by the PPRS.

The proposed patient access scheme is a fixed price discount scheme.

3.4 Please provide specific details of the patient population to which the patient access scheme applies. Does the scheme apply to the whole licensed population or only to a specific subgroup (for example, type of tumour, location of tumour)? If so:

- How is the subgroup defined?
- If certain criteria have been used to select patients, why have these have been chosen?
- How are the criteria measured and why have the measures been chosen?

The patient access scheme applies to the whole population for which tolvaptan is expected to be indicated, as presented in Section 3.1 of this template.

3.5 Please provide details of when the scheme will apply to the population specified in 3.4. Is the scheme dependent on certain criteria, for example, degree of response, response by a certain time point, number of injections? If so:

- Why have the criteria been chosen?
- How are the criteria measured and why have the measures been chosen.

The proposed fixed price discount scheme will be applied to all strengths and all pack sizes of tolvaptan. The scheme will not be dependent on certain criteria.

3.6 What proportion of the patient population (specified in 3.4) is expected to meet the scheme criteria (specified in 3.5)?

100% of the patient population specified in Section 3.4 is expected to meet the proposed patient access scheme criteria.

3.7 Please explain in detail the financial aspects of the scheme. How will any rebates be calculated and paid?

The fixed price will be applied to all original invoices for tolvaptan in AKPKD.

All tolvaptan packs commercially available across all dose ranges containing 28 days' supply will be flat priced.

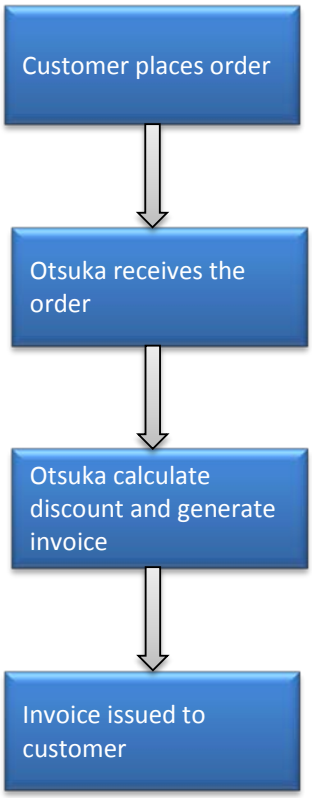
3.8 Please provide details of how the scheme will be administered. Please specify whether any additional information will need to be collected, explaining when this will be done and by whom.

There is no additional administrative burden (except a simple confidentiality agreement) to take advantage of the discount offered in this scheme.

3.9 Please provide a flow diagram that clearly shows how the scheme will operate. Any funding flows must be clearly demonstrated.

The patient access scheme flow diagram is presented in Figure 1.

Figure 1. Patient Access Scheme Flow Diagram



3.10 Please provide details of the duration of the scheme.

The scheme will be effective until NICE reviews the guidance for tolvaptan in ADPKD and any future indications, subject to agreement with the Department of Health. Otsuka does not currently consider there to be any circumstances under which it would terminate the proposed scheme.

3.11 Are there any equity or equalities issues relating to the scheme, taking into account current legislation and, if applicable, any concerns identified during the course of the appraisal? If so, how have these been addressed?

Not applicable. The proposed fixed price discount scheme will be applied to all tolvaptan packs commercially available across all dose ranges containing 28 days' supply.

3.12 If available, please list any scheme agreement forms, patient registration forms, pharmacy claim forms/rebate forms, guides for pharmacists and physicians and patient information documents. Please include copies in the appendices.

Confidentiality agreement

3.13 In the exceptional case that you are submitting an outcome-based scheme, as defined by the PPRS, please also refer to appendix B.

Not applicable.

4 Cost effectiveness

4.1 If the population to whom the scheme applies (as described in sections 3.4 and 3.5) has not been presented in the main manufacturer/sponsor submission of evidence for the technology appraisal (for example, the population is different as there has been a change in clinical outcomes or a new continuation rule), please (re-)submit the relevant sections from the 'Specification for manufacturer/sponsor submission of evidence' (particularly sections 5.5, 6.7 and 6.9). You should complete those sections both with and without the patient access scheme. You must also complete the rest of this template.

The proposed patient access scheme population is consistent with the population presented in the main manufacturer/sponsor submission of evidence for the technology appraisal, i.e., the proposed indication presented in Section 3.1 of this template.

4.2 If you are submitting the patient access scheme at the end of the technology appraisal process, you should update the economic model to reflect the assumptions that the Appraisal Committee considered to be most plausible. No other changes should be made to the model.

Not applicable.

4.3 Please provide details of how the patient access scheme has been incorporated into the economic model. If applicable, please also provide details of any changes made to the model to reflect the assumptions that the Appraisal Committee considered most plausible.

The proposed patient access scheme has been incorporated into the economic model by applying a discount to the annual drug cost.

4.4 Please provide the clinical effectiveness data resulting from the evidence synthesis and used in the economic model which includes the patient access scheme.

No clinical effectiveness data are used in the context of the proposed patient access scheme. It has been incorporated into the economic model by applying a discount to the annual drug cost.

4.5 Please list any costs associated with the implementation and operation of the patient access scheme (for example, additional pharmacy time for stock management or rebate calculations). A suggested format is presented in table 1. Please give the reference source of these costs. Please refer to section 6.5 of the 'Specification for manufacturer/sponsor submission of evidence'.

The proposed patient access scheme is a fixed price discount scheme. There are no costs associated with its implementation or operation.

Table 1 Costs associated with the implementation and operation of the patient access scheme (PAS)

	Calculation of cost	Reference source
Stock management		
Administration of claim forms		
Staff training		
Other costs…		
…		
…		
Total implementation/ operation costs		

4.6 Please provide details of any additional treatment-related costs incurred by implementing the patient access scheme. A suggested format is presented in table 2. The costs should be provided for the intervention both with and without the patient access scheme. Please give the reference source of these costs.

The proposed patient access scheme is a fixed price discount scheme. There are no costs associated with its implementation or operation

Table 2 Additional treatment-related costs for the intervention both with and without the patient access scheme (PAS)

	Intervention without PAS		Intervention with PAS		Reference source
	Unit cost (£)	**Total cost e.g. per cycle, per patient (£)**	**Unit cost (£)**	**Total cost e.g. per cycle, per patient (£)**	
Interventions					
Monitoring tests					
Diagnostic tests					
Appointments					
Other costs…					
…					
…					
Total treatment-related costs					

Summary results

Base-case analysis

4.7 Please present in separate tables the cost-effectiveness results as follows.[1]

- the results for the intervention without the patient access scheme
- the results for the intervention with the patient access scheme.

The probabilistic mean base-case results are shown in Table 3 without the patient access scheme and in Table 4 with the patient access scheme.

[1] For outcome-based schemes, please see section 5.2.8 in appendix B.

Table 3 Base-case cost-effectiveness results without the patient access scheme

	Tolvaptan	No Active Treatment
Intervention cost (£)	£[redacted]	£0.00
Other costs (£)	£[redacted]	£[redacted]
Total costs (£)	£[redacted]	£[redacted]
Difference in total costs (£)	N/A	£132,127
LYG	17.58	16.76
LYG difference	N/A	0.82
QALYs	13.54	12.63
QALY difference	N/A	0.91
ICER (£)	N/A	£[redacted]

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio; NA = not applicable.

Table 4 Base-case cost-effectiveness results with the patient access scheme

	Tolvaptan	No Active Treatment
Intervention cost (£)	£[redacted]	£0.00
Other costs (£)	£[redacted]	£[redacted]
Total costs (£)	£[redacted]	£[redacted]
Difference in total costs (£)	N/A	£31,583
LYG	17.58	16.76
LYG difference	N/A	0.82
QALYs	13.54	12.63
QALY difference	N/A	0.91
ICER (£)	N/A	£34,769

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio; NA = not applicable.

4.8 Please present in separate tables the incremental results as follows. [2]

- the results for the intervention without the patient access scheme
- the results for the intervention with the patient access scheme.

[2] For outcome-based schemes, please see section 5.2.9 in appendix B.

The base case probabilistic mean results are presented in Table 5 without the patient access scheme and in Table 6 with the patient access scheme.

Table 5 Base-case results (discounted probabilistic mean total expected lifetime estimates, per patient) without the patient access scheme

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) incremental (QALYs)
No active treatment	£[redacted]	16.76	12.63	-	-	-	-
Tolvaptan	£[redacted]	17.58	13.54	£132,127	0.82	0.91	£[redacted]

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Table 6 Base-case results (discounted probabilistic mean total expected lifetime estimates, per patient) with the patient access scheme

Technologies	Total costs (£)	Total LYG	Total QALYs	Incremental costs (£)	Incremental LYG	Incremental QALYs	ICER (£) incremental (QALYs)
No active treatment	£[redacted]	16.76	12.63	-	-	-	-
Tolvaptan	£[redacted]	17.58	13.54	£31,583	0.82	0.91	£34,769

LYG: life-year gained; QALY: quality-adjusted life-year; ICER: incremental cost-effectiveness ratio.

Sensitivity analyses

4.9 Please present deterministic sensitivity analysis results as described for the main manufacturer/sponsor submission of evidence for the technology appraisal. Consider using tornado diagrams.

The stochastic individual patient simulation (with sampling of baseline characteristics) and probabilistic sensitivity analysis were programmed to run simultaneously; therefore conventional deterministic sensitivity analyses (in which alternative fixed estimates of the mean values of model parameters are explored) were not performed. However, structural sensitivity analyses were performed and scenario analyses were performed in which alternative sources for individual parameters and assumptions were explored. The results of these analyses are presented in section 4.11.

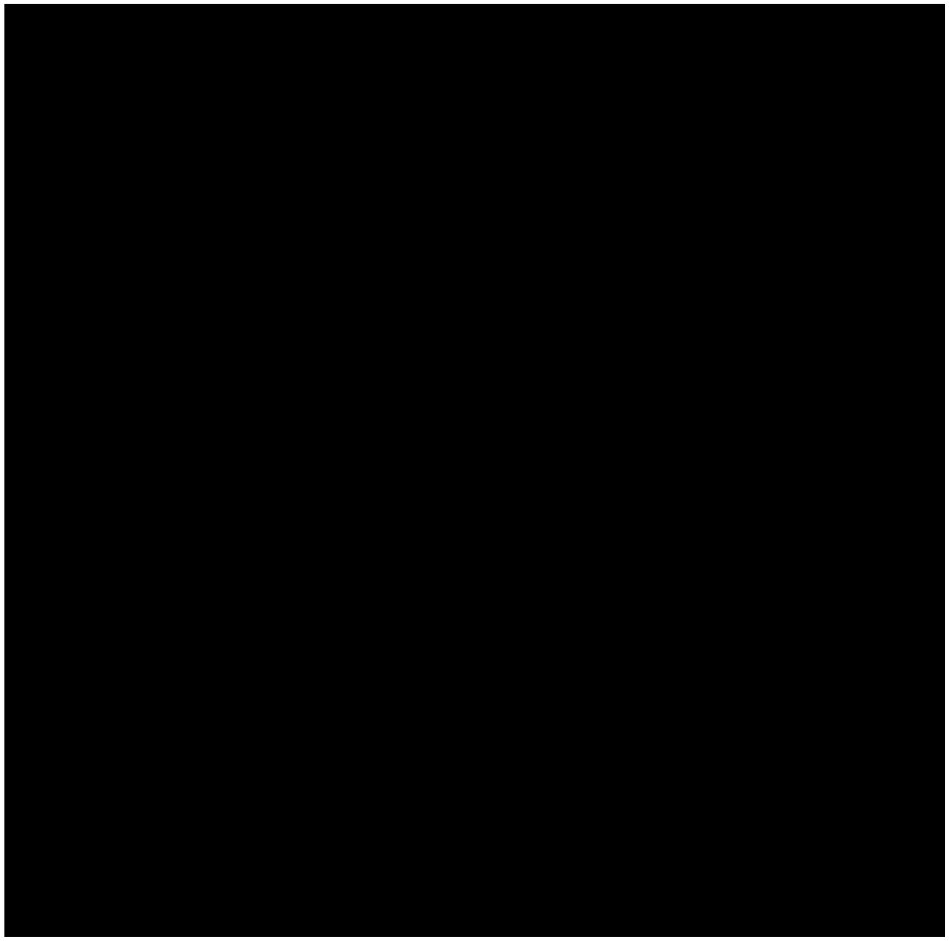
4.10 Please present any probabilistic sensitivity analysis results, and include scatter plots and cost-effectiveness acceptability curves.

The results of 1,000 probabilistic simulations (each including 500 patients with identical characteristics) are presented on the cost-effectiveness plane in Figure 1 and Figure 2 for without the patient access scheme and with the patient access scheme, respectively. The cost-effectiveness acceptability curve is presented in Figure 3 and Figure 4 for without the patient access scheme and with the patient access scheme, respectively.

Without the patient access scheme, the probability of cost-effectiveness was [redacted]% at a willingness-to-pay threshold at £30,000, £35,000 and £40,000 per QALY.

With the patient access scheme, the probability of cost-effectiveness at a willingness-to-pay threshold of £30,000, £35,000 and £40,000 per QALY was [redacted]%, [redacted]% and [redacted]%, respectively.

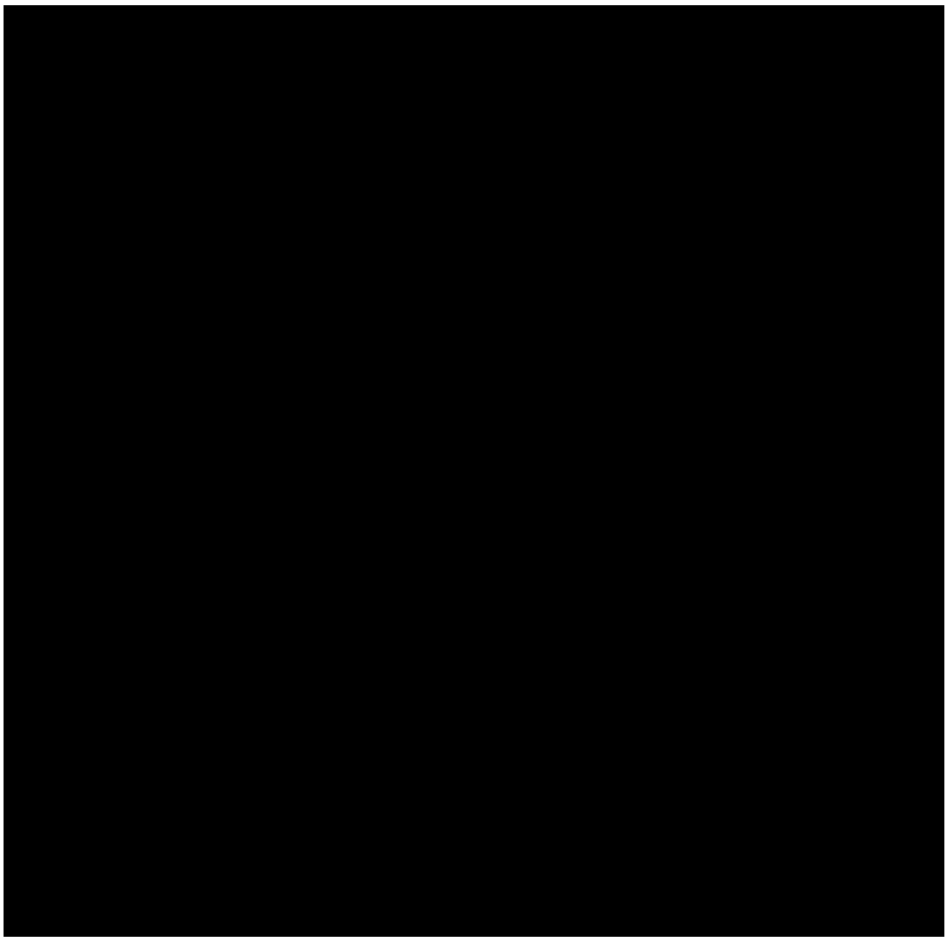
Figure 1. Probabilistic ICER estimates presented on the cost-effectiveness plane without the patient access scheme



ICER: incremental cost-effectiveness ratio

Note: within each probabilistic iteration, 500 patients with identical baseline characteristics were simulated. Between each successive probabilistic iteration, the baseline characteristics of the 500 identical patients were sampled from their distributions (based on the baseline characteristics of the TEMPO 3:4 trial population) and the mean values of all model parameters were sampled from their individual distributions.

Figure 2. Probabilistic ICER estimates presented on the cost-effectiveness plane with the patient access scheme



ICER: incremental cost-effectiveness ratio

Note: within each probabilistic iteration, 500 patients with identical baseline characteristics were simulated. Between each successive probabilistic iteration, the baseline characteristics of the 500 identical patients were sampled from their distributions (based on the baseline characteristics of the TEMPO 3:4 trial population) and the mean values of all model parameters were sampled from their individual distributions.

Figure 3. Cost-effectiveness acceptability curve, without the patient access scheme

[redacted]

Figure 4. Cost-effectiveness acceptability curve, with the patient access scheme

[redacted]

4.11 Please present scenario analysis results as described for the main manufacturer/sponsor submission of evidence for the technology appraisal.

Results of the structural sensitivity analyses and the scenario analyses described in the main submission are presented in Table 7 without the patient

access scheme and in Table 8 with the patient access scheme. The results of the subgroup analyses described in the main submission are presented in Table 9 without the patient access scheme and in Table 10 with the patient access scheme.

Table 7. Results of structural sensitivity and scenario analyses (discounted probabilistic mean total expected lifetime estimates, per patient) without the patient access scheme

Scenario	Total costs (£)		Total LYs		Total QALYs		Incremental costs (£)	Incremental LYs	Incremental QALYs	Cost/ QALY (£)
	Tolvaptan	No active treatment	Tolvaptan	No active treatment	Tolvaptan	No active treatment				
Base-case analysis	£[redacted]	£[redacted]	**17.58**	**16.76**	**13.54**	**12.63**	**£132,127**	**0.82**	**0.91**	£[redacted]
Structural sensitivity analyses										
ESRD therapy eGFR <6	£[redacted]	£[redacted]	17.68	16.87	13.59	12.68	**£131,236**	0.81	0.91	£[redacted]
ESRD therapy eGFR <10	£[redacted]	£[redacted]	17.56	16.70	13.52	12.60	**£131,834**	0.86	0.93	£[redacted]
Severe pain excluded	£[redacted]	£[redacted]	17.56	16.73	13.56	12.64	**£131,962**	0.83	0.91	£[redacted]
Scenario analyses										
Discount rates = 0%	£[redacted]	£[redacted]	27.90	26.36	20.33	18.82	**£173,060**	1.54	1.51	£[redacted]
Discount rates = 1.5%	£[redacted]	£[redacted]	22.49	21.32	16.81	15.59	**£152,673**	1.18	1.22	£[redacted]
Treatment effect CKD-EPI	£[redacted]	£[redacted]	17.44	16.76	13.38	12.63	**£132,599**	0.68	0.75	£[redacted]
Treatment discontinuation year 4+ (0% SE 0%)	£[redacted]	£[redacted]	17.60	16.74	13.56	12.62	**£135,476**	0.86	0.95	£[redacted]
Treatment discontinuation year 4+ (2.0% SE 0.8%)	£[redacted]	£[redacted]	17.51	16.76	13.45	12.63	**£123,604**	0.75	0.83	£[redacted]
Disease progression	£[redacted]	£[redacted]	17.53	16.70	13.48	12.57	**£131,349**	0.83	0.91	£[redacted]
Conservative care (5%)	£[redacted]	£[redacted]	17.79	17.02	13.65	12.78	**£130,450**	0.77	0.88	£[redacted]
Conservative care (15%)	£[redacted]	£[redacted]	17.39	16.50	13.43	12.47	**£134,055**	0.89	0.96	£[redacted]
CKD 3-4 HSUVs (Wu & Yang, 2014)	£[redacted]	£[redacted]	17.58	16.76	13.73	12.83	**£132,127**	0.82	0.90	£[redacted]
ESRD HSUVs decrements (Minimum Values)	£[redacted]	£[redacted]	17.58	16.76	14.19	13.41	**£132,127**	0.82	0.77	£[redacted]
ESRD HSUVs decrements (Maximum Values)	£[redacted]	£[redacted]	17.58	16.76	13.27	12.26	**£132,127**	0.82	1.01	£[redacted]
Disutility with treatment	£[redacted]	£[redacted]	17.58	16.75	13.42	12.62	**£132,229**	0.83	0.79	£[redacted]

Scenario	Total costs (£)		Total LYs		Total QALYs		Incremental costs (£)	Incremental LYs	Incremental QALYs	Cost/ QALY (£)
	Tolvaptan	No active treatment	Tolvaptan	No active treatment	Tolvaptan	No active treatment				
European population Subgroup	£[redacted]	£[redacted]	17.92	16.89	13.92	12.77	**£134,323**	1.03	1.15	£[redacted]
CKD-EPI= CKD Epidemiology; ESRD = end-stage renal disease; GFR = glomerular filtration rate; HSUV = health state utility value; LY = life-year; QALY = quality-adjusted life-year; SE = standard error										

Table 8. Results of structural sensitivity and scenario analyses (discounted probabilistic mean total expected lifetime estimates, per patient) with the patient access scheme

Scenario	Total costs (£)		Total LYs		Total QALYs		Incremental costs (£)	Incremental LYs	Incremental QALYs	Cost/ QALY (£)
	Tolvaptan	No active treatment	Tolvaptan	No active treatment	Tolvaptan	No active treatment				
Base-case analysis	£[redacted]	£[redacted]	**17.58**	**16.76**	**13.54**	**12.63**	£31,583	**0.82**	**0.91**	£34,769
Structural sensitivity analyses										
ESRD therapy eGFR <6	£[redacted]	£[redacted]	17.68	16.87	13.59	12.68	£30,617	0.81	0.91	£33,627
ESRD therapy eGFR <10	£[redacted]	£[redacted]	17.56	16.70	13.52	12.60	£31,263	0.86	0.93	£33,707
Severe pain excluded	£[redacted]	£[redacted]	17.56	16.73	13.56	12.64	£31,496	0.83	0.91	£34,480
Scenario analyses										
Discount rates = 0%	£[redacted]	£[redacted]	27.90	26.36	20.33	18.82	£41,897	1.54	1.51	£27,668
Discount rates = 1.5%	£[redacted]	£[redacted]	22.49	21.32	16.81	15.59	£36,242	1.18	1.22	£29,791
Treatment effect CKD-EPI	£[redacted]	£[redacted]	17.44	16.76	13.38	12.63	£35,755	0.68	0.75	£47,722
Treatment discontinuation year 4+ (0% SE 0%)	£[redacted]	£[redacted]	17.60	16.74	13.56	12.62	£32,222	0.86	0.95	£34,040
Treatment discontinuation year 4+ (2.0% SE 0.8%)	£[redacted]	£[redacted]	17.51	16.76	13.45	12.63	£30,282	0.75	0.83	£36,651
Disease progression	£[redacted]	£[redacted]	17.53	16.70	13.48	12.57	£31,803	0.83	0.91	£34,909
Conservative care (5%)	£[redacted]	£[redacted]	17.79	17.02	13.65	12.78	£29,855	0.77	0.88	£33,992
Conservative care (15%)	£[redacted]	£[redacted]	17.39	16.50	13.43	12.47	£33,529	0.89	0.96	£35,105

Scenario	Total costs (£)		Total LYs		Total QALYs		Incremental costs (£)	Incremental LYs	Incremental QALYs	Cost/ QALY (£)
	Tolvaptan	No active treatment	Tolvaptan	No active treatment	Tolvaptan	No active treatment				
CKD 3-4 HSUVs (Wu & Yang, 2014)	£[redacted]	£[redacted]	17.58	16.76	13.73	12.83	£31,583	0.82	0.90	£35,211
ESRD HSUVs decrements (Minimum Values)	£[redacted]	£[redacted]	17.58	16.76	14.19	13.41	£31,583	0.82	0.77	£40,819
ESRD HSUVs decrements (Maximum Values)	£[redacted]	£[redacted]	17.58	16.76	13,27	12.26	£31,583	0.82	1.01	£31,208
Disutility with treatment	£[redacted]	£[redacted]	17.58	16.75	13.42	12.62	£31,668	0.83	0.79	£39,959
European population	£[redacted]	£[redacted]	17.92	16.89	13.92	12.77	£26,524	1.03	1.15	£22,993

CKD-EPI= CKD Epidemiology; ESRD = end-stage renal disease; GFR = glomerular filtration rate; HSUV = health state utility value; LY = life-year; QALY = quality-adjusted life-year; SE = standard error

Table 9. Results of the subgroup analyses (discounted probabilistic mean total expected lifetime estimates, per patient) without the patient access scheme

Scenario	Total costs (£)		Total LYs		Total QALYs		Incremental costs (£)	Incremental LYs	Incremental QALYs	Cost/ QALY (£)
	Tolvaptan	No active treatment	Tolvaptan	No active treatment	Tolvaptan	No active treatment				
Base-case analysis	**£[redacted]**	**£[redacted]**	**17.58**	**16.76**	**13.54**	**12.63**	**£132,127**	**0.82**	**0.91**	**£[redacted]**
Subgroup analyses based on TEMPO 3:4 baseline characteristics										
CKD stage 1	£[redacted]	£[redacted]	18.60	17.87	14.81	13.89	£154,030	0.73	0.92	£[redacted]
CKD stage 2	£[redacted]	£[redacted]	17.26	16.44	13.13	12.28	£125,405	0.82	0.86	£[redacted]
CKD stage 3a	£[redacted]	£[redacted]	15.36	14.67	11.01	10.34	£92,881	0.69	0.67	£[redacted]
CKD stage 3b	£[redacted]	£[redacted]	14.93	14.26	10.60	9.96	£83,297	0.68	0.64	£[redacted]
Subgroup analyses based on OVERTURE baseline characteristics										
CKD stage 1	£[redacted]	£[redacted]	20.09	19.34	16.45	15.53	£177,105	0.74	0.92	£[redacted]
CKD stage 2	£[redacted]	£[redacted]	16.03	15.39	11.98	11.17	£124,855	0.64	0.80	£[redacted]

Scenario	Total costs (£)		Total LYs		Total QALYs		Incremental costs (£)	Incremental LYs	Incremental QALYs	Cost/ QALY (£)
	Tolvaptan	No active treatment	Tolvaptan	No active treatment	Tolvaptan	No active treatment				
CKD stage 3a	£[redacted]	£[redacted]	12.87	12.49	8.92	8.39	£80,058	0.38	0.53	£[redacted]
CKD stage 3b	£[redacted]	£[redacted]	11.58	11.25	7.57	7.14	£55,486	0.33	0.43	£[redacted]

Table 10. Results of the subgroup analyses (discounted probabilistic mean total expected lifetime estimates, per patient) with the patient access scheme

Scenario	Total costs (£)		Total LYs		Total QALYs		Incremental costs (£)	Incremental LYs	Incremental QALYs	Cost/ QALY (£)
	Tolvaptan	No active treatment	Tolvaptan	No active treatment	Tolvaptan	No active treatment				
Base-case analysis	£[redacted]	£[redacted]	**17.58**	**16.76**	**13.54**	**12.63**	**£31,583**	**0.82**	**0.91**	**£34,769**
Subgroup analyses based on TEMPO 3:4 baseline characteristics										
CKD stage 1	£[redacted]	£[redacted]	18.60	17.87	14.81	13.89	£33,824	0.73	0.92	£36,888
CKD stage 2	£[redacted]	£[redacted]	17.26	16.44	13.13	12.28	£32,150	0.82	0.86	£37,542
CKD stage 3a	£[redacted]	£[redacted]	15.36	14.67	11.01	10.34	£24,625	0.69	0.67	£36,916
CKD stage 3b	£[redacted]	£[redacted]	14.93	14.26	10.60	9.96	£22,473	0.68	0.64	£35,040
Subgroup analyses based on OVERTURE baseline characteristics										
CKD stage 1	£[redacted]	£[redacted]	20.09	19.34	16.45	15.53	£44,256	0.74	0.92	£48,239
CKD stage 2	£[redacted]	£[redacted]	16.03	15.39	11.98	11.17	£24,539	0.64	0.80	£30,496
CKD stage 3a	£[redacted]	£[redacted]	12.87	12.49	8.92	8.39	£11,670	0.38	0.53	£22,129
CKD stage 3b	£[redacted]	£[redacted]	11.58	11.25	7.57	7.14	£7,967	0.33	0.43	£18,579

4.12 If any of the criteria on which the patient access scheme depends are clinical variable (for example, choice of response measure, level of response, duration of treatment), sensitivity analyses around the individual criteria should be provided, so that the Appraisal Committee can determine which criteria are the most appropriate to use.

Not applicable. The patient access scheme does not depend on any criteria.

Impact of patient access scheme on ICERs

4.13 For financially based schemes, please present the results showing the impact of the patient access scheme on the ICERs for the base-case and any scenario analyses. A suggested format is shown below (see table 11). If you are submitting the patient access scheme at the end of the appraisal process, you must include the scenario with the assumptions that the Appraisal Committee considered to be most plausible.

Table 11. Results showing the impact of patient access scheme on ICERs

	ICER for Tolvaptan versus No Active Treatment	
	Without PAS	**With PAS**
Base-Case	£[redacted]	£34,769
Structural sensitivity analyses		
ESRD therapy eGFR <6	£[redacted]	£33,627
ESRD therapy eGFR <10	£[redacted]	£33,707
Severe pain excluded	£[redacted]	£34,480
Scenario analyses		
Discount rates = 0%	£[redacted]	£27,668
Discount rates = 1.5%	£[redacted]	£29,791
Treatment effect CKD-EPI	£[redacted]	£47,722
Treatment discontinuation year 4+ (0% SE 0%)	£[redacted]	£34,040
Treatment discontinuation year 4+ (2.0% SE 0.8%)	£[redacted]	£36,651
Disease progression	£[redacted]	£34,909
Conservative care (5%)	£[redacted]	£33,992
Conservative care (15%)	£[redacted]	£35,105
CKD 3-4 HSUVs (Wu & Yang, 2014)	£[redacted]	£35,211
ESRD HSUVs (Minimum Values)	£[redacted]	£40,819
ESRD HSUVs (Maximum Values)	£[redacted]	£31,208
Disutility with treatment	£[redacted]	£39,959
European population	£[redacted]	£22,993

Subgroup analyses based on TEMPO 3:4 baseline characteristics		
CKD stage 1	£[redacted]	£36,888
CKD stage 2	£[redacted]	£37,542
CKD stage 3a	£[redacted]	£36,916
CKD stage 3b	£[redacted]	£35,040
Subgroup analyses based on OVERTURE baseline characteristics		
CKD stage 1	£[redacted]	£48,239
CKD stage 2	£[redacted]	£30,496
CKD stage 3a	£[redacted]	£22,129
CKD stage 3b	£[redacted]	£18,579

CKD-EPI= CKD Epidemiology; ESRD = end-stage renal disease; GFR = glomerular filtration rate; HSUV = health state utility value; LY = life-year; QALY = quality-adjusted life-year; SE = standard error

5 Appendices

5.1 Appendix A: Additional documents

5.1.1 If available, please include copies of patient access scheme agreement forms, patient registration forms, pharmacy claim forms/rebate forms, guides for pharmacists and physicians, patient information documents.

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5.2 Appendix B: Details of outcome-based schemes

The proposed patient access scheme is not an outcome-based scheme

5.2.1 If you are submitting a proven value: price increase scheme, as defined in the PPRS, please provide the following information:

- the current price of the intervention
- the proposed higher price of the intervention, which will be supported by the collection of new evidence
- a suggested date for when NICE should consider the additional evidence.

NA

5.2.2 If you are submitting an expected value: rebate scheme, as defined in the PPRS, please provide the following details:

- the current price of the intervention (the price that will be supported by the collection of new evidence)
- the planned lower price of the intervention in the event that the additional evidence does not support the current price
- a suggested date for when NICE should consider the additional evidence.

NA

5.2.3 If you are submitting a risk-sharing scheme, as defined in the PPRS, please provide the following details:

- the current price of the intervention (the price that will be supported by the collection of new evidence)
- the proposed relationship between future price changes and the evidence to be collected.

NA

5.2.4 For outcome-based schemes, as defined in the PPRS, please provide the full details of the new information (evidence) planned to be collected, who will collect it and who will carry the cost associated with this planned data collection. Details of the new information (evidence) may include:

- design of the new study
- patient population of the new study
- outcomes of the new study
- expected duration of data collection
- planned statistical analysis, definition of study groups and reporting (including uncertainty)
- expected results of the new study
- planned evidence synthesis/pooling of data (if applicable)
- expected results of the evidence synthesis/pooling of data (if applicable).

NA

5.2.5 If you are submitting a risk-sharing scheme, please specify the period between the time points when the additional evidence will be considered.

NA

5.2.6 Please provide the clinical effectiveness data resulting from the evidence synthesis and used in the economic modelling of the patient access scheme at the different time points when the additional evidence is to be considered.

NA

5.2.7 Please provide the other data used in the economic modelling of the patient access scheme at the different time points when the additional evidence is to be considered. These data could include cost/resource use, health-related quality of life and utilities.

NA

5.2.8 Please present the cost-effectiveness results as follows.

- For proven value: price increase schemes, please summarise in separate tables:
  - the results based on current evidence and current price
  - the anticipated results based on the expected new evidence and the proposed higher price.
- For expected value: rebate schemes, please summarise in separate tables:
  - the results based on the expected new evidence and the current price (which will be supported by the additional evidence collection)
  - the results based on the current evidence and the lower price (if the new evidence is not forthcoming).
- For risk-sharing schemes, please summarise in separate tables:
  - the results based on current evidence and current price
  - the results based on the expected new evidence and the current price (which will be supported by the additional evidence collection)
  - the results based on the current evidence and the lower price (if the new evidence is not forthcoming)
  - the anticipated results based on the expected new evidence and the proposed higher price.

A suggested format is shown in table 3, section 4.7.

5.2.9 Please present in separate tables the incremental results for the different scenarios as described above in section 5.2.8 for the type of outcome-based scheme being submitted.

List the interventions and comparator(s) from least to most expensive. Present the incremental cost-effectiveness ratios (ICERs) in comparison with baseline (usually standard care), and the incremental analysis ranking technologies in terms of dominance and extended dominance. A suggested format is presented in table 4, section 4.8.

NA