NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Technology appraisals

Patient access scheme submission template

Denosumab for the treatment of bone metastases from solid tumours

Date: 15th July 2011

Note: Confidential information is marked, e.g. Commercial in Confidence; Academic in Confidence

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 Clinical 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 Clinical 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' (www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/guidetothemethodsoftechnologyappraisal.jsp)
- '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' (www.nice.org.uk/aboutnice/howwework/devnicetech/technologyappraisalprocessguides/guidetothemethodsoftechnologyappraisal.jsp).

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 technology denosumab will be available as two different medicinal products with different dosing regimens and formulations that reflect their respective therapeutic applications. The medicinal products are XGEVA® and Prolia®. The two medicinal products are subject to two separate European Medicines Agency marketing authorisations, have separate summary of product characteristics and patient information leaflets.

XGEVA® received CHMP positive opinion on 19 May 2011 and is anticipated to receive marketing authorisation in August 2011 for the following indication: for the prevention of skeletal-related events (pathological fractures, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from solid tumours.

XGEVA® is administered as a subcutaneous injection at a dose of 120mg once every four weeks. XGEVA® will only be available as a 120mg vial (proposed list price of £309.86 per 120mg vial).

XGEVA® is currently undergoing a multiple-technology appraisal (MTA) by the Institute for the treatment of bone metastases in patients with solid tumours and multiple myeloma. The MTA process was selected by the Institute as they considered each tumour type (i.e. breast cancer, prostate cancer, other) to represent a separate indication.

Prolia® has been appraised and recommended by the Institute for the treatment of osteoporosis in postmenopausal women at increased risk of fractures [NICE technology appraisal guidance 204; October 2010]. No patient access scheme was proposed by Amgen Limited in conjunction with the appraisal since Prolia® was deemed a cost-effective use of NHS resources by the Institute within a defined patient population.

The simple/straight discount patient access scheme proposal detailed within this document would apply with respect to the medicinal product XGEVA® across all tumour types. Further, the scheme would apply to all current and future indications of XGEVA® (within the duration of the patient access scheme).

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

XGEVA® is currently undergoing a MTA by the Institute for the treatment of bone metastases in patients with solid tumours and multiple myeloma.

The patient access scheme has been developed to facilitate a positive recommendation by the Institute through the health technology appraisal process by deeming XGEVA® a cost-effective use of NHS resources and allow access to XGEVA® for eligible patients.

Denosumab (the technology) has been appraised and recommended by the Institute for the treatment of osteoporosis in postmenopausal women at increased risk of fractures [NICE technology appraisal guidance 204; October 2010] as the medicinal product Prolia®. No patient access scheme was proposed by Amgen Limited in conjunction with the appraisal since Prolia® was deemed a cost-effective use of NHS resources by the Institute within a defined population. The simple/straight discount patient access scheme proposal detailed within this document would apply with respect to the medicinal product XGEVA®.

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

The scheme is a financially based scheme. Our proposal is to offer a [redacted]% confidential discount on the list-price of XGEVA® (list price £309.86/120mg vial). This would result in an NHS acquisition price of £[redacted]/120mg vial (equivalent to £[redacted] discount).

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 proposed license indication for denosumab is for the prevention of skeletal-related events in adults with bone metastases from solid tumours. This patient

access scheme applies to the whole population for which XGEVA® is anticipated to be licensed.

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 scheme we are proposing is a financially based scheme in the form of a [redacted]% confidential discount for the medicinal product XGEVA®. The scheme is not dependent on any specific criteria, e.g. patient level criteria.

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

This patient access scheme applies to the whole population for which XGEVA® is licensed.

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

The scheme we are proposing is a financially based scheme in the form of a [redacted]% confidential discount for the medicinal product XGEVA®. The scheme is not dependent on any specific criteria, e.g. patient level criteria. This discount would be given to the NHS at the point of order, eliminating any potential burden on the NHS to have to retrospectively request a rebate.

There will be no wholesaler involvement in distributing XGEVA® to the NHS (distribution will be direct from manufacturer). Amgen will be responsible for administering the [redacted]% confidential discount at the point of order for XGEVA®. This distribution route will ensure the appropriate application of the scheme to the relevant medicinal product (XGEVA®).

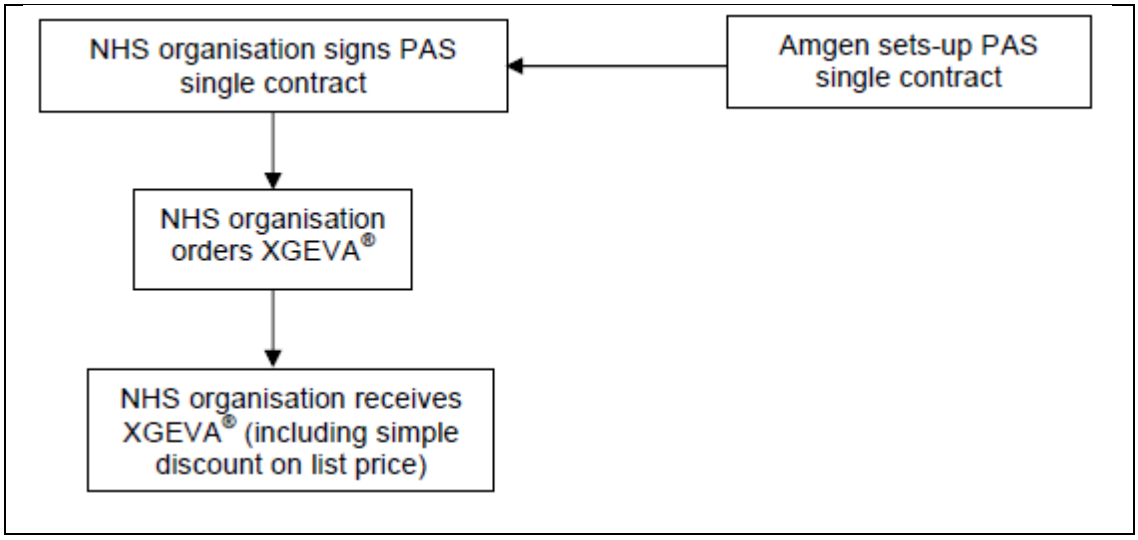
The proposed scheme is identical in operation and administration (confidential discount) as that currently provided by Amgen Limited for romiplostim (Nplate®) for the treatment of chronic immune (idiopathic) thrombocytopenic purpura [NICE technology appraisal guidance 221; April 2011].

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.

[redacted]

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

There will be no wholesaler involvement in distributing XGEVA® to the NHS (distribution will be direct from manufacturer). Amgen will be responsible for administering the [redacted]% confidential discount at the point of order and distributing stock to the NHS. This distribution route will ensure the appropriate application of the scheme to the relevant medicinal product (XGEVA®).



3.10 Please provide details of the duration of the scheme.

The proposed patient access scheme will remain in place until the proposed review date of any resulting NICE guidance.

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?

There are no equity or equality issues relating to the scheme.

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.

The patient access scheme does not require any additional forms, registration or other administrative process to claim the confidential discount for XGEVA®. The scheme requires a single contract to be set-up between the manufacturer and NHS organisation.

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 patient access scheme applies to the entire licensed population.

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 patient access scheme is incorporated into the economic through an effective change in the acquisition price. The list-price of XGEVA® is £309.86/120mg vial. The [redacted]% confidential discount results in an NHS acquisition price of £[redacted]/120mg vial.

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.

The clinical effectiveness data does not change in the presence or absence of the patient access scheme as this scheme is a financially based scheme.

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'.

There will be no costs associated with the implementation and operation of the proposed patient access scheme as this scheme is financially based. The patient access scheme does not require any additional forms, registration or other administrative process to claim the confidential discount for XGEVA®. The scheme requires a single contract to be set-up between the manufacturer and NHS organisation.

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.

There will be no additional treatment related costs incurred by implementing the patient access scheme as this scheme is a financially based scheme.

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.*

Denosumab is anticipated to be an appropriate option for the prevention of SREs for patients with bone metastases from solid tumours. The cost-effectiveness of denosumab is considered individually by primary tumour type. Zoledronic has been deemed the primary bisphosphonate comparator in all tumours. Supplementary comparisons with disodium pamidronate are made in breast cancer and other solid tumours, whilst ibandronic acid is additionally considered in breast cancer. In prostate cancer and other solid tumour patients who would not be treated with bisphosphonates as they are free of pain and/or have not experienced a prior SRE, best supportive care (defined as no active treatment for the purposes of this appraisal) has been identified as the primary comparator. The analyses detailed in Table 1 are presented with and without the patient access scheme.

Table 1 Summary of the presented cost-effectiveness analyses

Analysis	Primary Tumour	Population	Primary Comparator	Supplementary Comparators
1	Breast cancer	All patients	Zoledronic acid	Disodium pamidronate and ibandronic acid
2	Prostate cancer	Pain and prior SRE	Zoledronic acid	None
3		No pain or pain with no prior SRE	BSC (no active treatment)	None
4	Other Solid Tumours	Pain and prior SRE	Zoledronic acid	Disodium pamidronate
5		No pain or pain with no prior SRE	BSC (no active treatment)	None

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

Analysis 1 - Breast cancer

Table 2. Breakdown of total costs and total benefits per patient [without PAS]

	Denosumab	ZOL	PAM	IBA
Total LYs	3.165	3.165	3.165	3.165
QALYs				
QALYs related to "No SRE history" health state	0.725	0.687	0.665	0.696
QALYs related to "SRE history" health state	1.225	1.261	1.281	1.253
QALYs related to SREs	-0.038	-0.042	-0.044	-0.041
QALYs related to AEs	-0.0004	-0.001	-0.0036	-0.0005
Total QALYs	1.912	1.904	1.898	1.907
Costs (£)				
SRE costs	2,932	3,241	3,435	3,199
AE costs	93	137	317	37
Technology costs	[redacted]	[redacted]	[redacted]	[redacted]
Death costs	4,356	4,356	4,356	4,356
Total costs	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; IBA, ibandronic acid; LYs, life-years; QALYs, quality-adjusted life years

Table 3. Breakdown of total costs and total benefits per patient [with PAS]

	Denosumab	ZOL	PAM	IBA
Total LYs	3.165	3.165	3.165	3.165
QALYs				
QALYs related to "No SRE history" health state	0.725	0.687	0.665	0.696
QALYs related to "SRE history" health state	1.225	1.261	1.281	1.253
QALYs related to SREs	-0.038	-0.042	-0.044	-0.041
QALYs related to AEs	-0.0004	-0.001	-0.0036	-0.0005
Total QALYs	1.912	1.904	1.898	1.907
Costs (£)				
SRE costs	2,932	3,241	3,435	3,199
AE costs	93	137	317	37
Technology costs	[redacted]	[redacted]	[redacted]	[redacted]
Death costs	4,356	4,356	4,356	4,356
Total costs	[redacted]	[redacted]	[redacted]	[redacted]

Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; IBA, ibandronic acid; LYs, life-years; QALYs, quality-adjusted life years

Analysis 2: Prostate cancer, pain and history of a prior SRE

Table 4. Breakdown of total costs and total benefits per patient [without PAS]

	Denosumab	ZOL
Total LYs	2.044	2.044
QALYs		
QALYs related to ”No SRE history” health state	0.000	0.000
QALYs related to “SRE history” health state	1.179	1.179
QALYs related to SREs	-0.088	-0.094
QALYs related to AEs	-0.0022	-0.002
Total QALYs	1.089	1.083
Costs (£)		
SRE costs	2,810	3,010
AE costs	165	125
Technology costs	[redacted]	[redacted]
Death costs	4,625	4,625
Total costs	[redacted]	[redacted]

Abbreviations: ZOL, zoledronic acid; LYs, life-years; QALYs, quality-adjusted life years

Table 5. Breakdown of total costs and total benefits per patient [with PAS]

	Denosumab	ZOL
Total LYs	2.044	2.044
QALYs		
QALYs related to ”No SRE history” health state	0.000	0.000
QALYs related to “SRE history” health state	1.179	1.179
QALYs related to SREs	-0.088	-0.094
QALYs related to AEs	-0.0022	-0.002
Total QALYs	1.089	1.083
Costs (£)		
SRE costs	2,810	3,010
AE costs	165	125
Technology costs	[redacted]	[redacted]
Death costs	4,625	4,625
Total costs	[redacted]	[redacted]

Abbreviations: ZOL, zoledronic acid; LYs, life-years; QALYs, quality-adjusted life years

Analysis 3: Prostate cancer, no pain or pain and no history of a prior SRE

Table 6. Breakdown of total costs and total benefits per patient [without PAS]

	Denosumab	BSC
Total LYs	2.044	2.044
QALYs		
QALYs related to "No SRE history" health state	0.776	0.647
QALYs related to "SRE history" health state	0.494	0.608
QALYs related to SREs	-0.078	-0.105
QALYs related to AEs	-0.0022	0.0000
Total QALYs	1.189	1.150
Costs (£)		
SRE costs	2,184	[redacted]
AE costs	165	0
Technology costs	[redacted]	0
Death costs	4,625	4,625
Total costs	[redacted]	[redacted]

Abbreviations: BSC, best supportive care; LYs, life-years; QALYs, quality-adjusted life years

Table 7. Breakdown of total costs and total benefits per patient [with PAS]

	Denosumab	BSC
Total LYs	2.044	2.044
QALYs		
QALYs related to "No SRE history" health state	0.776	0.647
QALYs related to "SRE history" health state	0.494	0.608
QALYs related to SREs	-0.078	-0.105
QALYs related to AEs	-0.0022	0.0000
Total QALYs	1.189	1.150
Costs (£)		
SRE costs	2,184	[redacted]
AE costs	165	0
Technology costs	[redacted]	0
Death costs	4,625	4,625
Total costs	[redacted]	[redacted]

Abbreviations: BSC, best supportive care; LYs, life-years; QALYs, quality-adjusted life years

Analysis 4: Other solid tumours, pain and history of a prior SRE

Table 8. Breakdown of total costs and total benefits per patient [without PAS]

	Denosumab	ZOL	PAM
Total LYs	1.640	1.640	1.640
QALYs			
QALYs related to ”No SRE history” health state	0.000	0.000	0.000
QALYs related to “SRE history” health state	0.823	0.823	0.823
QALYs related to SREs	-0.058	-0.061	-0.062
QALYs related to AEs	-0.0007	-0.001	-0.0021
Total QALYs	0.765	0.761	0.759
Costs (£)			
SRE costs	2,556	2,714	2,754
AE costs	57	57	183
Technology costs	[redacted]	[redacted]	[redacted]
Death costs	4,612	4,612	4,612
Total costs	[redacted]	[redacted]	[redacted]

Abbreviations: ZOL: zoledronic acid; PAM: disodium pamidronate

Table 9. Breakdown of total costs and total benefits per patient [with PAS]

	Denosumab	ZOL	PAM
Total LYs	1.640	1.640	1.640
QALYs			
QALYs related to ”No SRE history” health state	0.000	0.000	0.000
QALYs related to “SRE history” health state	0.823	0.823	0.823
QALYs related to SREs	-0.058	-0.061	-0.062
QALYs related to AEs	-0.0007	-0.001	-0.0021
Total QALYs	0.765	0.761	0.759
Costs (£)			
SRE costs	2,556	2,714	2,754
AE costs	57	57	183
Technology costs	[redacted]	[redacted]	[redacted]
Death costs	4,612	4,612	4,612
Total costs	[redacted]	[redacted]	[redacted]

Abbreviations: ZOL: zoledronic acid; PAM: disodium pamidronate

Analysis 5: Other solid tumours, no pain or pain and no history of a prior SRE

Table 10. Breakdown of total costs and total benefits per patient [without PAS]

	Denosumab	BSC
Total LYs	1.640	1.640
QALYs		
QALYs related to ”No SRE history” health state	0.472	0.391
QALYs related to “SRE history” health state	0.388	0.463
QALYs related to SREs	-0.058	-0.073
QALYs related to AEs	-0.0007	0.0000
Total QALYs	0.803	0.782
Costs (£)		
SRE costs	2,166	[redacted]
AE costs	57	0
Technology costs	[redacted]	0
Death costs	4,612	4,612
Total costs	[redacted]	[redacted]

Abbreviations: BSC, best supportive care; LYs, life-years; QALYs, quality-adjusted life years

Table 11. Breakdown of total costs and total benefits per patient [with PAS]

	Denosumab	BSC
Total LYs	1.640	1.640
QALYs		
QALYs related to ”No SRE history” health state	0.472	0.391
QALYs related to “SRE history” health state	0.388	0.463
QALYs related to SREs	-0.058	-0.073
QALYs related to AEs	-0.0007	0.0000
Total QALYs	0.803	0.782
Costs (£)		
SRE costs	2,166	[redacted]
AE costs	57	0
Technology costs	[redacted]	0
Death costs	4,612	4,612
Total costs	[redacted]	[redacted]

Abbreviations: BSC, best supportive care; LYs, life-years; QALYs, quality-adjusted life years

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

Analysis 1: Breast cancer

Table 12. Cost-effectiveness of denosumab versus each comparator, breast cancer [without PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			ΔCosts (£)	ΔQALYs	ICER (ΔCost/ΔQALY)
Denosumab	[redacted]	1.912	-	-	-
Primary comparator					
Zoledronic acid	[redacted]	1.904	1,484	0.007	£203,387
Supplementary comparators					
Disodium pamidronate	[redacted]	1.898	-1,486	0.013	Denosumab dominant
Ibandronic acid	[redacted]	1.907	72	0.005	£13,835

Table 13. Cost-effectiveness of denosumab versus each comparator, breast cancer [with PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			ΔCosts (£)	ΔQALYs	ICER (ΔCost/ΔQALY)
Denosumab	[redacted]	1.912	-	-	-
Primary comparator					
Zoledronic acid	[redacted]	1.904	-483	0.007	Denosumab Dominant
Supplementary comparators					
Disodium pamidronate	[redacted]	1.898	-3,453	0.013	Denosumab Dominant
Ibandronic acid	[redacted]	1.907	-1,895	0.005	Denosumab Dominant

Analysis 2: Prostate cancer, pain and history of a prior SRE

Table 14. Cost-effectiveness of denosumab versus each comparator [without PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			ΔCosts (£)	ΔQALYs	ICER (ΔCost/ΔQALY)
Denosumab	[redacted]	1.089	-	-	-
Primary comparator					
Zoledronic acid	[redacted]	1.083	922	0.006	£157,276

Table 15. Cost-effectiveness of denosumab versus each comparator [with PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			ΔCosts (£)	ΔQALYs	ICER (ΔCost/ΔQALY)
Denosumab	[redacted]	1.089	-	-	-
Primary comparator					
Zoledronic acid	[redacted]	1.083	-281	0.006	Denosumab Dominant

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

Analysis 3: Prostate cancer, no pain or pain and no history of a prior SRE

Table 16. Cost-effectiveness of denosumab versus each comparator [without PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			ΔCosts (£)	ΔQALYs	ICER (ΔCost/ΔQALY)
Denosumab	[redacted]	1.189	-	-	-
Primary comparator					
Best supportive care	[redacted]	1.150	3,993	0.039	£102,067

Table 17. Cost-effectiveness of denosumab versus each comparator [with PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			ΔCosts (£)	ΔQALYs	ICER (ΔCost/ΔQALY)
Denosumab	[redacted]	1.189	-	-	-
Primary comparator					
Best supportive care	[redacted]	1.150	2,790	0.039	£71,320

Analysis 4: Other solid tumours, pain and history of a prior SRE

Table 18. Cost-effectiveness of denosumab versus each comparator [without PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			ΔCosts (£)	ΔQALYs	ICER (ΔCost/ΔQALY)
Denosumab	[redacted]	0.765	-	-	-
Primary comparator					
Zoledronic acid	[redacted]	0.761	757	0.004	£205,580
Supplementary comparator(s)					
Disodium pamidronate	[redacted]	0.759	-2,118	0.006	Denosumab dominant

Table 19. Cost-effectiveness of denosumab versus each comparator [with PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			ΔCosts (£)	ΔQALYs	ICER (ΔCost/ΔQALY)
Denosumab	[redacted]	0.765	-	-	-
Primary comparator					
Zoledronic acid	[redacted]	0.761	-43	0.004	Denosumab Dominant
Supplementary comparator					
Disodium pamidronate	[redacted]	0.759	-2,918	0.006	Denosumab Dominant

Analysis 5: Other solid tumours, no pain or pain and no history of a prior SRE

Table 20. Cost-effectiveness of denosumab versus each comparator [without PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			∆Costs (£)	∆QALYs	ICER (∆Cost/∆QALY)
Denosumab	[redacted]	0.803	-	-	-
Primary comparator					
Best supportive care	[redacted]	0.782	2,530	0.021	£122,499

Table 21. Cost-effectiveness of denosumab versus each comparator [with PAS]

Treatment	Costs (£)	QALYs	Denosumab versus comparator		
			∆Costs (£)	∆QALYs	ICER (∆Cost/∆QALY)
Denosumab	[redacted]	0.803	-	-	-
Primary comparator					
Best supportive care	[redacted]	0.782	1,730	0.021	£83,763

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.

Analysis 1 - Breast cancer

Table 22. Scenario analyses: breast cancer [without PAS]

Description		Incremental costs for denosumab with comparator (£)			Incremental QALYs for denosumab with comparator			ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)		
		ZOL	**PAM**	**IBA**	**ZOL**	**PAM**	**IBA**	**ZOL**	**PAM**	**IBA**
Base-case		1,484	-1,486	72	0.007	0.013	0.005	203,387	Dmab Domt	13,835
Time horizon	Time horizon = 2 years	1,133	-548	633	0.004	0.009	0.004	254,527	Dmab Domt	149,460
	Time horizon = 5 years	1,453	-1,278	257	0.007	0.013	0.005	212,975	Dmab Domt	48,494
21-day window	Without 21 day-window	1,394	-1,633	-7	0.009	0.016	0.006	161,545	Dmab Domt	Dmab Domt
Asymptomatic events	Include costs for trial-defined asymptomatic events	1,437	-1,562	32	0.007	0.013	0.005	196,979	Dmab Domt	6,115
SRE costs	Based on NHS reference costs	1,519	-1,428	103	0.007	0.013	0.005	208,292	Dmab Domt	19,782
SRE utilities	Based on TTO	1,484	-1,486	72	0.009	0.017	0.007	159,317	Dmab Domt	10,163
	Based on Weinfurt 2005	1,484	-1,486	72	0.006	0.011	0.004	255,628	Dmab Domt	16,985
AE utilities	Normal model	1,484	-1,486	72	0.008	0.014	0.005	197,267	Dmab Domt	13,705
Starting age	Starting age = 50	1,487	-1,495	67	0.007	0.013	0.005	203,089	Dmab Domt	12,844
	Starting age = 65	1,474	-1,463	85	0.007	0.013	0.005	204,158	Dmab Domt	16,384
IV dosing frequency	Based on UK treatment patterns of Q3-4W dosing	1,180	-1,928	-314	0.007	0.013	0.005	161,827	Dmab Domt	Dmab Domt
Ibandronic acid	Ibandronic acid administered orally	1,484	-1,486	2,015	0.007	0.013	0.005	203,387	Dmab Domt	387,403
Denosumab setting	Community (district nurse)	1,270	-1,700	-141	0.007	0.013	0.005	174,161	Dmab Domt	Dmab Domt
Discontinuation	Zero for all treatments	2,756	93	2,566	0.013	0.027	0.016	218,070	3,49	163,595
	0.025 per cycle for all treatments	1,498	-54	1,409	0.007	0.015	0.009	204,073	Dmab Domt	157,566
Discounting	0% for costs and benefits	1,581	-1,650	-13	0.008	0.014	0.005	199,800	Dmab Domt	Dmab Domt
	0% for costs and 6% benefits	1,581	-1,650	-13	0.007	0.013	0.005	225,328	Dmab Domt	Dmab Domt

Note: Dmab Domt, denosumab dominant. Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; IBA, ibandronic acid; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Table 23. Scenario analyses: breast cancer [with PAS]

Description		Incremental costs for denosumab with comparator (£)			Incremental QALYs for denosumab with comparator			ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)		
		ZOL	**PAM**	**IBA**	**ZOL**	**PAM**	**IBA**	**ZOL**	**PAM**	**IBA**
Base-case		-483	-3,453	-1,895	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt
Time horizon	Time horizon = 2 years	-320	-2,001	-820	0.004	0.009	0.004	Dmab Domt	Dmab Domt	Dmab Domt
	Time horizon = 5 years	-460	-3,192	-1,656	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt
21-day window	Without 21 day-window	-573	-3,600	-1,974	0.009	0.016	0.006	Dmab Domt	Dmab Domt	Dmab Domt
Asymptomatic events	Include costs for trial-defined asymptomatic events	-530	-3,529	-1,935	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt
SRE costs	Based on NHS reference costs	-447	-3,395	-1,864	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt
SRE utilities	Based on TTO	-483	-3,453	-1,895	0.009	0.017	0.007	Dmab Domt	Dmab Domt	Dmab Domt
	Based on Weinfurt 2005	-483	-3,453	-1,895	0.006	0.011	0.004	Dmab Domt	Dmab Domt	Dmab Domt
AE utilities	Normal model	-483	-3,453	-1,895	0.008	0.014	0.005	Dmab Domt	Dmab Domt	Dmab Domt
Starting age	Starting age = 50	-485	-3,468	-1,905	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt
	Starting age = 65	-479	-3,416	-1,868	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt
IV dosing frequency	Based on UK treatment patterns of Q3-4W dosing	-786	-3,895	-2,281	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt
Ibandronic acid	Ibandronic acid administered orally	-483	-3,453	49	0.007	0.013	0.005	Dmab Domt	Dmab Domt	9,354
Denosumab setting	Community (district nurse)	-696	-3,666	-2,108	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt
Discontinuation	Zero for all treatments	-851	-3,514	-1,041	0.013	0.027	0.016	Dmab Domt	Dmab Domt	Dmab Domt
	0.025 per cycle for all treatments	-467	-2,019	-556	0.007	0.015	0.009	Dmab Domt	Dmab Domt	Dmab Domt
Discounting	0% for costs and benefits	-515	-3,724	-2,087	0.008	0.014	0.005	Dmab Domt	Dmab Domt	Dmab Domt
	0% for costs and 6% benefits	-515	-3,724	-2,087	0.007	0.013	0.005	Dmab Domt	Dmab Domt	Dmab Domt

Note: Dmab Domt, denosumab dominant. Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; IBA, ibandronic acid; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Analysis 2 - Prostate cancer, pain and history of a prior SRE

Table 24. Scenario analyses: Prostate cancer, pain and history of a prior SRE [without PAS]

Description		Incremental costs for denosumab with comparator (£)	Incremental QALYs for denosumab with comparator	ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)
		ZOL	ZOL	ZOL
Base-case		922	0.006	157,276
Time horizon	Time = 2 years	838	0.005	160,254
	Time = 5 years	919	0.006	157,349
21-day window	Without 21 day-window	853	0.010	89,267
Asymptomatic events	Include costs for trial-defined asymptomatic events	896	0.006	152,865
SRE costs	Based on NHS reference costs	988	0.006	168,541
SRE utilities	SRE utilities based on TTO	922	0.006	148,550
	SRE utilities based on Weinfurt 2005	922	0.002	383,878
AE utilities	Normal model	922	0.006	157,972
Starting age	Starting age = 50	938	0.006	156,644
	Starting age = 80	891	0.006	158,492
IV dosing frequency	Based on UK treatment patterns of Q3-4W dosing	734	0.006	125,258
Denosumab setting	Community (district nurse)	791	0.006	135,024
Discontinuation	Zero for all treatments	1,727	0.011	150,928
	0.025 per cycle for all treatments	1,137	0.007	154,736
Discounting	0% for costs and benefits	950	0.006	156,587
	0% for costs and 6% benefits	950	0.006	166,132

Abbreviations: ZOL, zoledronic acid; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Table 25. Scenario analyses: Prostate cancer, pain and history of a prior SRE [with PAS]

Description		Incremental costs for denosumab with comparator (£)	Incremental QALYs for denosumab with comparator	ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)
		ZOL	ZOL	ZOL
Base-case		-281	0.006	Dmab Domt
Time horizon	Time = 2 years	-240	0.005	Dmab Domt
	Time = 5 years	-279	0.006	Dmab Domt
21-day window	Without 21 day-window	-350	0.010	Dmab Domt
Asymptomatic events	Include costs for trial-defined asymptomatic events	-307	0.006	Dmab Domt
SRE costs	Based on NHS reference costs	-215	0.006	Dmab Domt
SRE utilities	SRE utilities based on TTO	-281	0.006	Dmab Domt
	SRE utilities based on Weinfurt 2005	-281	0.002	Dmab Domt
AE utilities	Normal model	-281	0.006	Dmab Domt
Starting age	Starting age = 50	-288	0.006	Dmab Domt
	Starting age = 80	-269	0.006	Dmab Domt
IV dosing frequency	Based on UK treatment patterns of Q3-4W dosing	-469	0.006	Dmab Domt
Denosumab setting	Community (district nurse)	-412	0.006	Dmab Domt
Discontinuation	Zero for all treatments	-561	0.011	Dmab Domt
	0.025 per cycle for all treatments	-334	0.007	Dmab Domt
Discounting	0% for costs and benefits	-292	0.006	Dmab Domt
	0% for costs and 6% benefits	-292	0.006	Dmab Domt

Abbreviations: ZOL, zoledronic acid; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Analysis 3 - Prostate cancer, no pain or pain and no history of a prior SRE

Table 26. Scenario analyses: Prostate cancer, no pain or pain and no history of a prior SRE [without PAS]

Description		Incremental costs for denosumab with comparator (£)	Incremental QALYs for denosumab with comparator	ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)
		BSC	**BSC**	**BSC**
Base-case		3,993	0.039	102,067
Time horizon	Time = 2 years	3,640	0.030	119,441
	Time = 5 years	3,987	0.038	103,669
21-day window	Without 21 day-window	3,787	0.051	74,963
Asymptomatic events	Include costs for trial-defined asymptomatic events	3,895	0.039	99,573
SRE costs	Based on NHS reference costs	4,246	0.039	108,543
SRE utilities	Based on TTO	3,993	0.023	172,109
	Based on Weinfurt 2005	3,993	0.008	508,331
AE utilities	Normal model	3,993	0.039	102,202
Starting age	Starting age = 50	4,065	0.040	100,580
	Starting age = 80	3,863	0.037	104,835
Denosumab setting	Community (district nurse)	3,863	0.039	98,735
Discontinuation	Zero for all treatments	7,584	0.069	109,945
	0.025 per cycle for all treatments	4,879	0.047	103,898
Discounting	0% for costs and benefits	4,116	0.041	100,039
	0% for costs and 6% benefits	4,116	0.038	108,866

Abbreviations: BSC, best supportive care; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Table 27. Scenario analyses: Prostate cancer, no pain or pain and no history of a prior SRE [with PAS]

Description		Incremental costs for denosumab with comparator (£)	Incremental QALYs for denosumab with comparator	ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)
		BSC	**BSC**	**BSC**
Base-case		2,790	0.039	71,320
Time horizon	Time = 2 years	2,562	0.030	84,079
	Time = 5 years	2,788	0.038	72,496
21-day window	Without 21 day-window	2,584	0.051	51,153
Asymptomatic events	Include costs for trial-defined asymptomatic events	2,693	0.039	68,826
SRE costs	Based on NHS reference costs	3,044	0.039	77,796
SRE utilities	Based on TTO	2,790	0.023	120,262
	Based on Weinfurt 2005	2,790	0.008	355,201
AE utilities	Normal model	2,790	0.039	71,415
Starting age	Starting age = 50	2,838	0.040	70,233
	Starting age = 80	2,702	0.037	73,343
Denosumab setting	Community (district nurse)	2,660	0.039	67,988
Discontinuation	Zero for all treatments	5,296	0.069	76,777
	0.025 per cycle for all treatments	3,408	0.047	72,572
Discounting	0% for costs and benefits	2,874	0.041	69,835
	0% for costs and 6% benefits	2,874	0.038	75,997

Abbreviations: BSC, best supportive care; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Analysis 4 - Other solid tumours, pain and history of a prior SRE

Table 28. Scenario analyses: Other solid tumours, pain and history of a prior SRE [without PAS]

Description		Incremental costs for denosumab with comparator (£)		Incremental QALYs for denosumab with comparator		ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)	
		ZOL	**PAM**	**ZOL**	**PAM**	**ZOL**	**PAM**
Base-case		757	-2,118	0.004	0.006	205,580	Dmab Domt
Time horizon	Time = 2 years	700	-1,239	0.003	0.006	207,642	Dmab Domt
	Time = 5 years	755	-1,927	0.004	0.006	205,610	Dmab Domt
21-day window	Without 21 day-window	722	-2,162	0.005	0.007	143,728	Dmab Domt
Asymptomatic events	Include costs for trial-defined asymptomatic events	744	-2,134	0.004	0.006	202,151	Dmab Domt
SRE costs	Based on NHS reference costs	792	-2,074	0.004	0.006	215,057	Dmab Domt
SRE utilities	Based on TTO	757	-2,118	0.004	0.006	189,826	Dmab Domt
	Based on Weinfurt 2005	757	-2,118	0.002	0.003	419,642	Dmab Domt
AE utilities	Normal model	757	-2,118	0.004	0.006	210,615	Dmab Domt
Starting age	Starting age = 50	759	-2,134	0.004	0.006	205,492	Dmab Domt
	Starting age = 70	752	-2,068	0.004	0.006	205,864	Dmab Domt
IV dosing frequency	Based on UK treatment patterns of Q3-4W dosing	643	-2,377	0.004	0.006	175,542	Dmab Domt
Denosumab setting	Community (district nurse)	670	-2,205	0.004	0.006	182,034	Dmab Domt
Disodium pamidronate efficacy	No efficacy (placebo treatment effect)	670	-2,468	0.004	0.011	205,580	Dmab Domt
Discontinuation	Zero for all treatments	1,192	-613	0.008	0.018	150,841	Dmab Domt
	0.025 per cycle for all treatments	758	-345	0.005	0.011	157,303	Dmab Domt
Discounting	0% for costs and benefits	690	-2,382	0.004	0.006	204,751	Dmab Domt
	0% for costs and 6% benefits	690	-2,382	0.004	0.006	216,033	Dmab Domt

Note: Dmab Domt, denosumab dominant. Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Table 29. Scenario analyses: Other solid tumours, pain and history of a prior SRE [with PAS]

Description		Incremental costs for denosumab with comparator (£)		Incremental QALYs for denosumab with comparator		ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)	
		ZOL	**PAM**	**ZOL**	**PAM**	**ZOL**	**PAM**
Base-case		-43	-2,918	0.004	0.006	Dmab Domt	Dmab Domt
Time horizon	Time = 2 years	-63	-2,002	0.003	0.006	Dmab Domt	Dmab Domt
	Time = 5 years	-44	-2,726	0.004	0.006	Dmab Domt	Dmab Domt
21-day window	Without 21 day-window	-78	-2,961	0.005	0.007	Dmab Domt	Dmab Domt
Asymptomatic events	Include costs for trial-defined asymptomatic events	-56	-2,934	0.004	0.006	Dmab Domt	Dmab Domt
SRE costs	Based on NHS reference costs	-8	-2,874	0.004	0.006	Dmab Domt	Dmab Domt
SRE utilities	Based on TTO	-43	-2,918	0.004	0.006	Dmab Domt	Dmab Domt
	Based on Weinfurt 2005	-43	-2,918	0.002	0.003	Dmab Domt	Dmab Domt
AE utilities	Normal model	-43	-2,918	0.004	0.006	Dmab Domt	Dmab Domt
Starting age	Starting age = 50	-43	-2,935	0.004	0.006	Dmab Domt	Dmab Domt
	Starting age = 70	-44	-2,863	0.004	0.006	Dmab Domt	Dmab Domt
IV dosing frequency	Based on UK treatment patterns of Q3-4W dosing	-157	-3,176	0.004	0.006	Dmab Domt	Dmab Domt
Denosumab setting	Community (district nurse)	-130	-3,004	0.004	0.006	Dmab Domt	Dmab Domt
Disodium pamidronate efficacy	No efficacy (placebo treatment effect)	-43	-3,181	0.004	0.011	Dmab Domt	Dmab Domt
Discontinuation	Zero for all treatments	-469	-2,274	0.008	0.018	Dmab Domt	Dmab Domt
	0.025 per cycle for all treatments	-282	-1,385	0.005	0.011	Dmab Domt	Dmab Domt
Discounting	0% for costs and benefits	-40	-3,112	0.004	0.006	Dmab Domt	Dmab Domt
	0% for costs and 6% benefits	-40	-3,112	0.004	0.006	Dmab Domt	Dmab Domt

Note: Dmab Domt, denosumab dominant. Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Analysis 5 - Other solid tumours, no pain or pain and no history of a prior SRE

Table 30. Scenario analyses: Other solid tumours, no pain or pain and no history of a prior SRE [without PAS]

Description		Incremental costs for denosumab with comparator (£)	Incremental QALYs for denosumab with comparator	ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)
		BSC	**BSC**	**BSC**
Base-case		2,530	0.021	122,499
Time horizon	Time = 2 years	2,446	0.018	136,172
	Time = 5 years	2,534	0.020	124,913
21-day window	Without 21 day-window	2,442	0.024	101,160
Asymptomatic events	Include costs for trial-defined asymptomatic events	2,483	0.021	120,233
SRE costs	Based on NHS reference costs	2,659	0.021	128,772
SRE utilities	Based on TTO	2,530	0.013	188,300
	Based on Weinfurt 2005	2,530	0.005	467,106
AE utilities	Normal model	2,530	0.021	122,024
Starting age	Starting age = 50	2,534	0.021	122,280
	Starting age = 70	2,517	0.020	123,192
Denosumab setting	Community (district nurse)	2,443	0.021	118,301
Discontinuation	Zero for all treatments	5,973	0.042	141,722
	0.025 per cycle for all treatments	3,705	0.029	128,398
Discounting	0% for costs and benefits	2,584	0.021	120,340
	0% for costs and 6% benefits	2,584	0.020	128,422

Abbreviations: BSC, best supportive care; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

Table 31. Scenario analyses: Other solid tumours, no pain or pain and no history of a prior SRE [with PAS]

Description		Incremental costs for denosumab with comparator (£)	Incremental QALYs for denosumab with comparator	ICERs for denosumab with comparator (ΔCost (£)/ΔQALY)
		BSC	**BSC**	**BSC**
Base-case		1,730	0.021	83,763
Time horizon	Time = 2 years	1,683	0.018	93,698
	Time = 5 years	1,735	0.020	85,522
21-day window	Without 21 day-window	1,642	0.024	68,020
Asymptomatic events	Include costs for trial-defined asymptomatic events	1,683	0.021	81,497
SRE costs	Based on NHS reference costs	1,859	0.021	90,036
SRE utilities	Based on TTO	1,730	0.013	128,757
	Based on Weinfurt 2005	1,730	0.005	319,401
AE utilities	Normal model	1,730	0.021	83,439
Starting age	Starting age = 50	1,732	0.021	83,606
	Starting age = 70	1,721	0.020	84,263
Denosumab setting	Community (district nurse)	1,643	0.021	79,565
Discontinuation	Zero for all treatments	4,109	0.042	97,505
	0.025 per cycle for all treatments	2,538	0.029	87,963
Discounting	0% for costs and benefits	1,765	0.021	82,207
	0% for costs and 6% benefits	1,765	0.020	87,728

Abbreviations: BSC, best supportive care; TTO, time trade-off; SRE, skeletal-related event; AE, adverse event; NHS, National Health Service; ICER, incremental cost-effectiveness ratio

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

Analysis 1: Breast cancer

Table 32. PSA results: breast cancer [without PAS]

	Denosumab	ZOL	PAM	IBA
Total costs	£[redacted]	£[redacted]	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]	£[redacted]	£[redacted]
Total QALYs	1.911	1.904	1.897	1.905
95%lower CL	1.767	1.759	1.753	1.762
95% upper CL	2.051	2.044	2.038	2.045
INB of denosumab versus comparator:		-£1,269	£1,888	£155
95%lower CL		-£1,710	£989	-£1,075
95% upper CL		-£833	£2,952	£1,860

Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; IBA, ibandronic acid; INB, incremental net benefit; calculated with a cost-effectiveness threshold of £30,000; ICER, incremental cost-effectiveness ratio

Table 33. PSA results: breast cancer [with PAS]

	Denosumab	ZOL	PAM	IBA
Total costs	£[redacted]	£[redacted]	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]	£[redacted]	£[redacted]
Total QALYs	1.909	1.902	1.896	1.903
95%lower CL	1.779	1.772	1.765	1.773
95% upper CL	2.039	2.030	2.024	2.034
INB of denosumab versus comparator:		£700	£3,853	£2,130
95%lower CL		£318	£2,932	£921
95% upper CL		£1,082	£4,897	£3,764

Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; IBA, ibandronic acid; INB, incremental net benefit; calculated with a cost-effectiveness threshold of £30,000; ICER, incremental cost-effectiveness ratio

Figure 1. Cost-effectiveness scatter plot: breast cancer [without PAS]

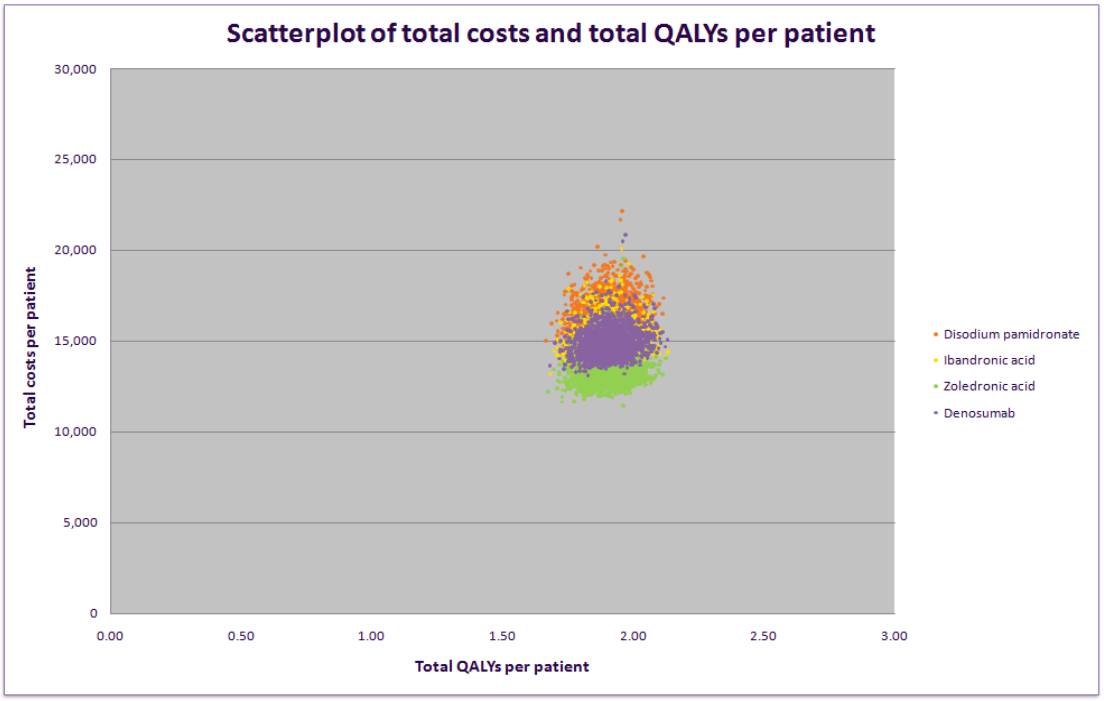


Figure 2. Cost-effectiveness scatter plot: breast cancer [with PAS]

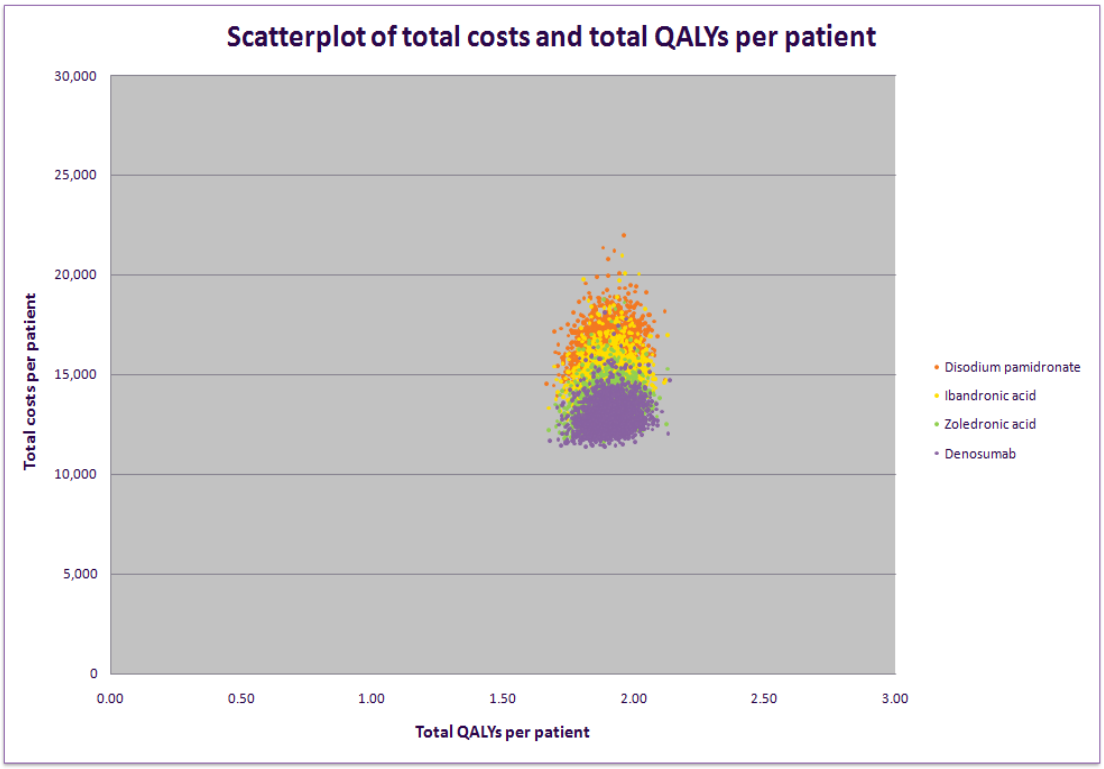


Figure 3. Cost-effectiveness acceptability curve: breast cancer [without PAS]

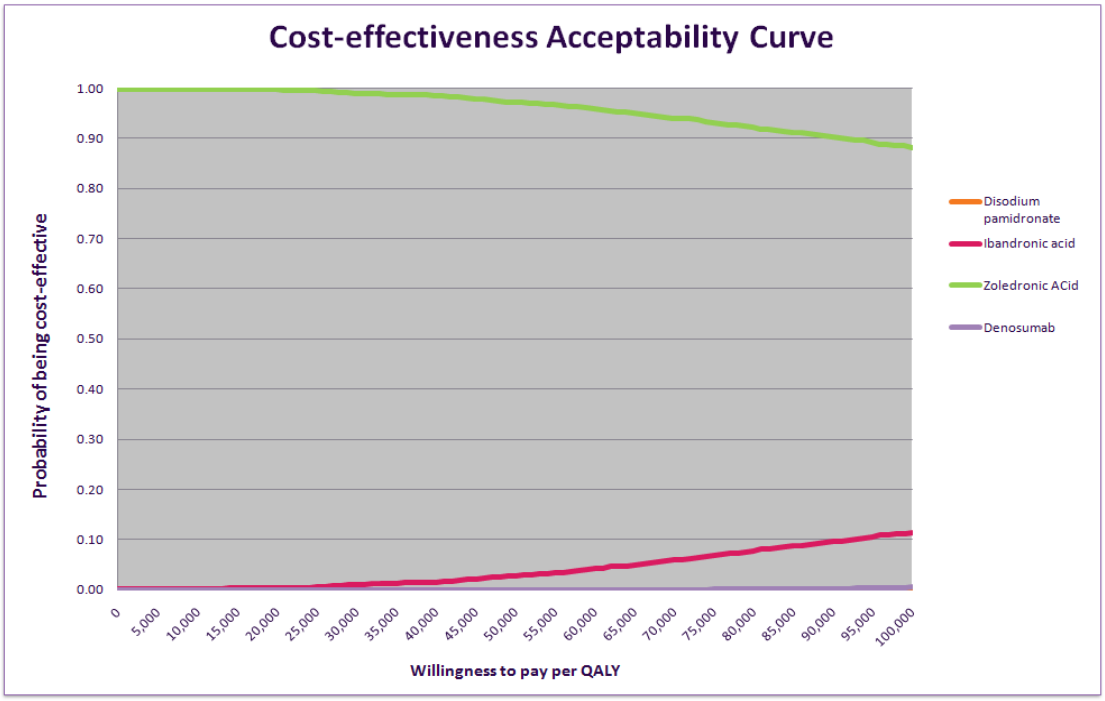
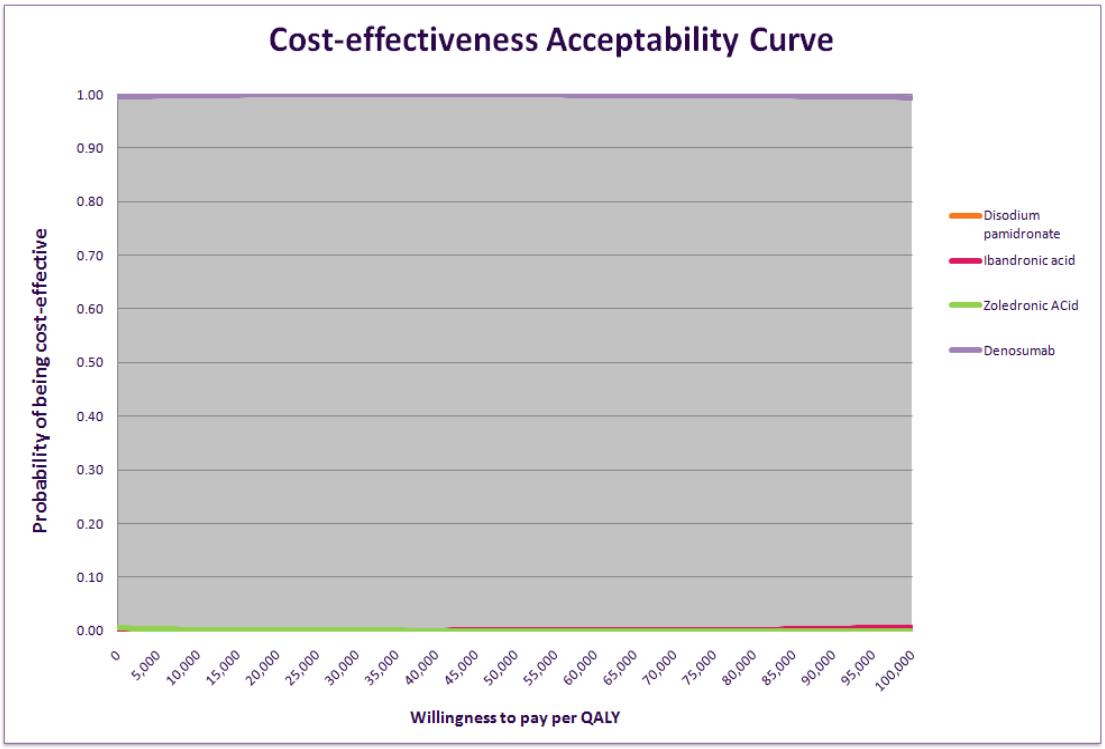


Figure 4. Cost-effectiveness acceptability curve: breast cancer [with PAS]



Analysis 2: Prostate cancer – pain and history of a prior SRE

Table 34. PSA Results: Prostate cancer - pain and history of a prior SRE [without PAS]

	Denosumab	ZOL
Total costs	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]
Total QALYs	1.087	1.081
95%lower CL	1.003	0.997
95% upper CL	1.174	1.169
INB of denosumab versus comparator:		-£742
95%lower CL		-£1,077
95% upper CL		-£378

Abbreviations: ZOL, zoledronic acid; INB = incremental net benefit, calculated with a cost-effectiveness threshold of £30,000

Table 35. PSA Results: Prostate cancer - pain and history of a prior SRE [with PAS]

	Denosumab	ZOL
Total costs	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]
Total QALYs	1.158	1.152
95%lower CL	1.061	1.055
95% upper CL	1.262	1.256
INB of denosumab versus comparator:		£465
95%lower CL		£164
95% upper CL		£828

Abbreviations: ZOL, zoledronic acid; INB = incremental net benefit, calculated with a cost-effectiveness threshold of £30,000

Figure 5. Cost-effectiveness scatter plot: Prostate cancer - pain and history of a prior SRE [without PAS]

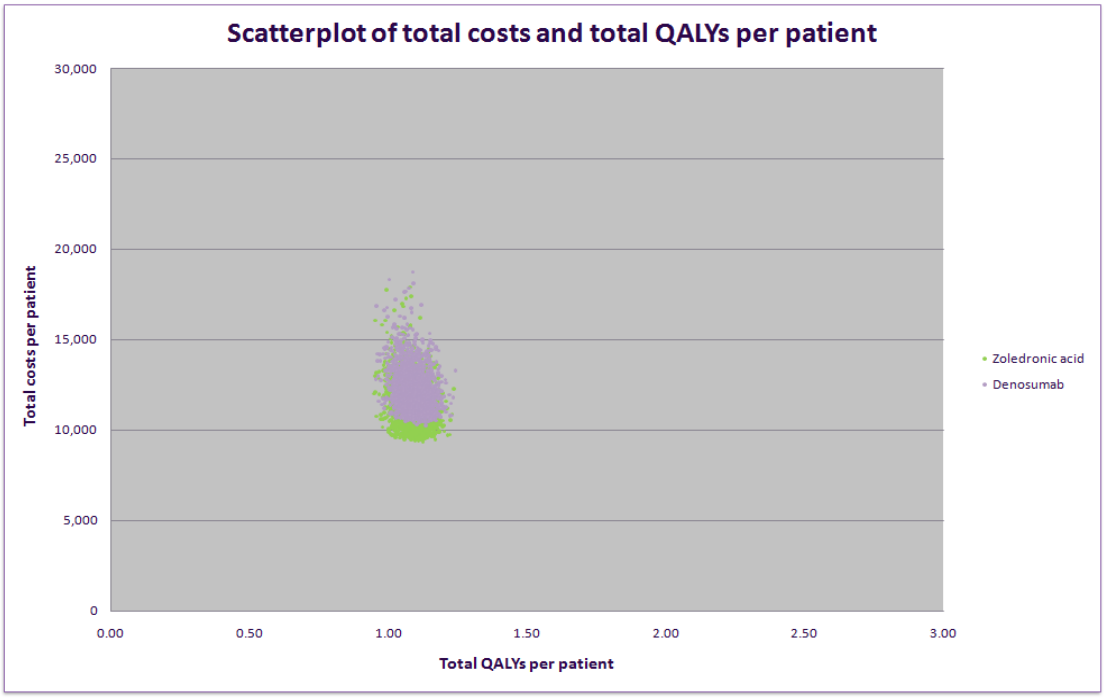


Figure 6. Cost-effectiveness scatter plot: Prostate cancer - pain and history of a prior SRE [with PAS]

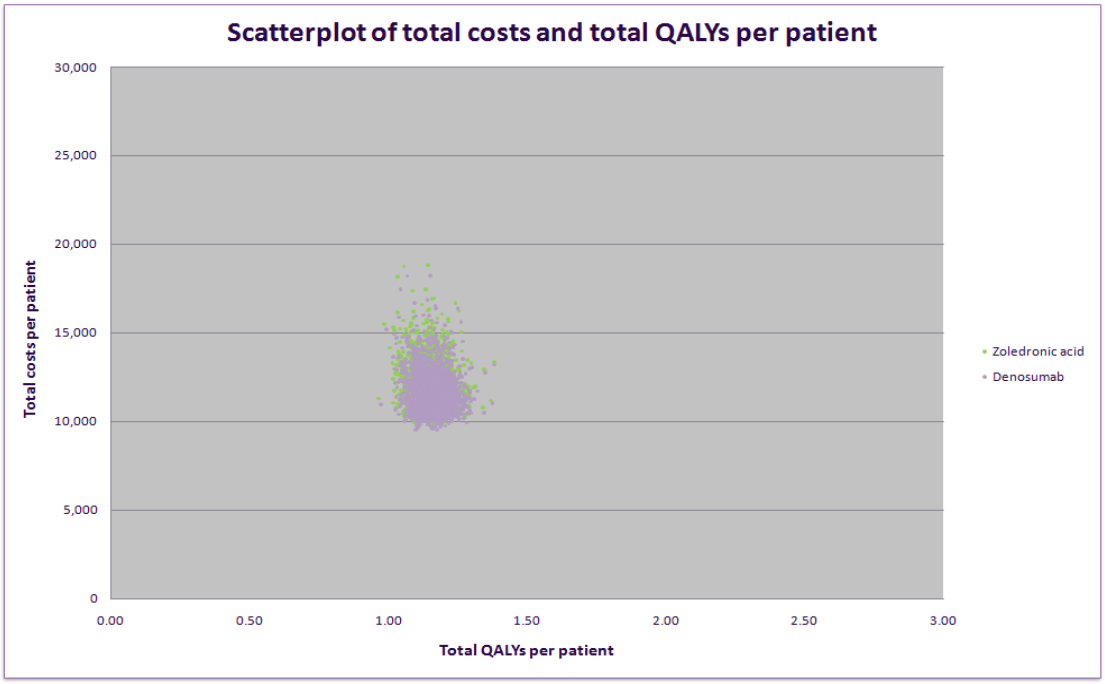


Figure 7. Cost-effectiveness acceptability curve: Prostate cancer - pain and history of previous SREs [without PAS]

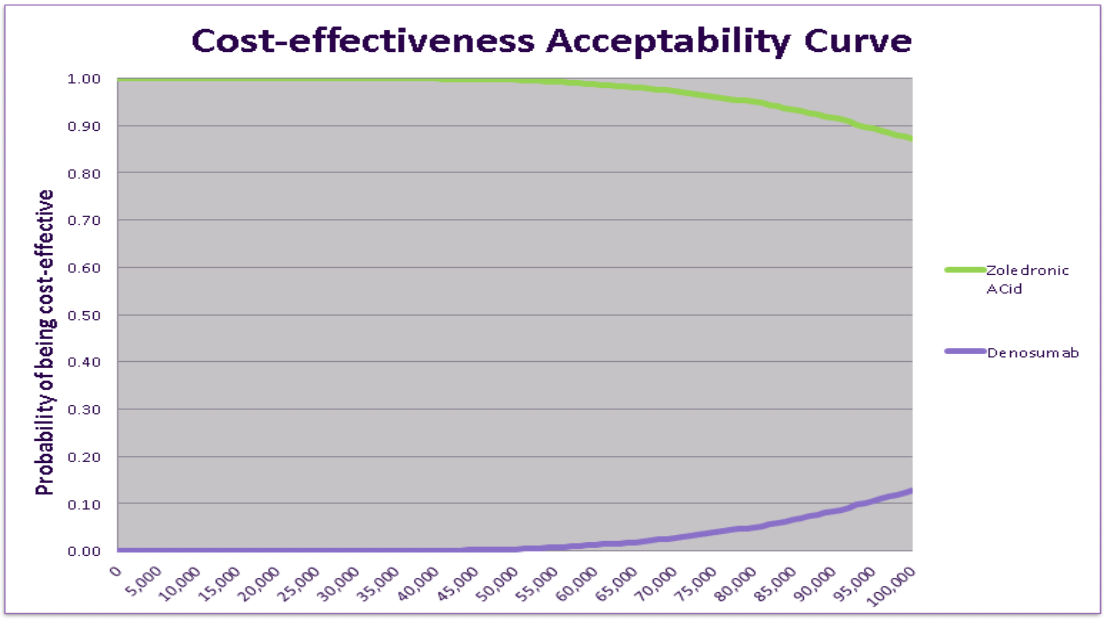


Figure 8. Cost-effectiveness acceptability curve: Prostate cancer - pain and history of previous SREs [with PAS]

Analysis 3: Prostate cancer - no pain or pain and no history of a prior SRE

Table 36. PSA Results: Prostate cancer - no pain or pain and no history of a prior SRE [without PAS]

	Denosumab	BSC
Total costs	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]
Total QALYs	1.190	1.150
95%lower CL	1.107	1.053
95% upper CL	1.275	1.245
INB of Denosumab versus comparator:		-£2,711
95%lower CL		-£4,091
95% upper CL		-£889

Abbreviations: BSC, best supportive care; INB, incremental net benefit; calculated with a cost-effectiveness threshold of £30,000; ICER, incremental cost-effectiveness ratio

Table 37. PSA Results: Prostate cancer - no pain or pain and no history of a prior SRE [with PAS]

	Denosumab	BSC
Total costs	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]
Total QALYs	1.190	1.151
95%lower CL	1.107	1.052
95% upper CL	1.275	1.245
INB of Denosumab versus comparator:		-£1,589
95%lower CL		-£2,952
95% upper CL		£181

Abbreviations: BSC, best supportive care; INB, incremental net benefit; calculated with a cost-effectiveness threshold of £30,000; ICER, incremental cost-effectiveness ratio

Figure 9. Cost-effectiveness scatter plot: prostate cancer – no pain or pain and no history of a prior SRE [without PAS]

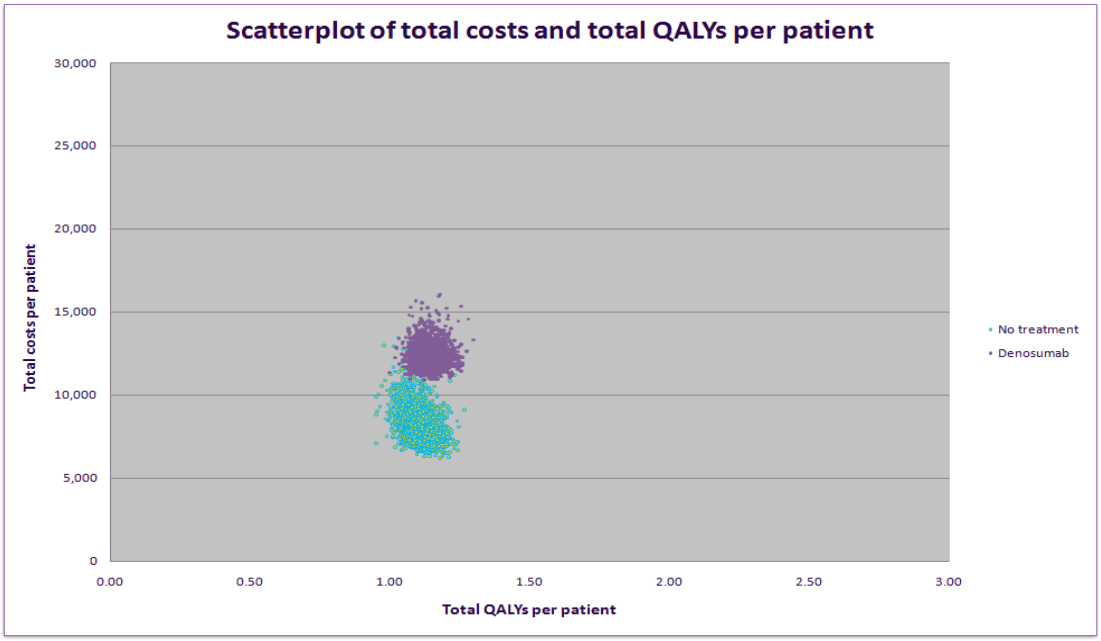


Figure 10. Cost-effectiveness scatter plot: prostate cancer – no pain or pain and no history of a prior SRE [with PAS]

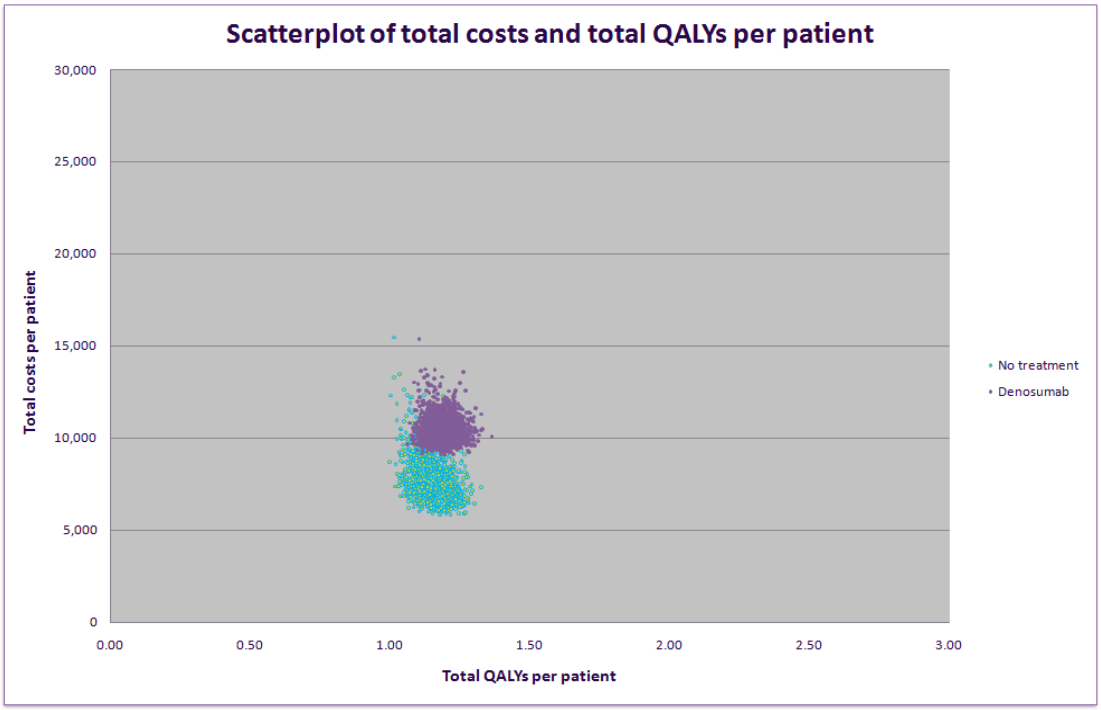


Figure 11. Cost-effectiveness acceptability curve: prostate cancer – no pain or pain and no history of a prior SRE [without PAS]

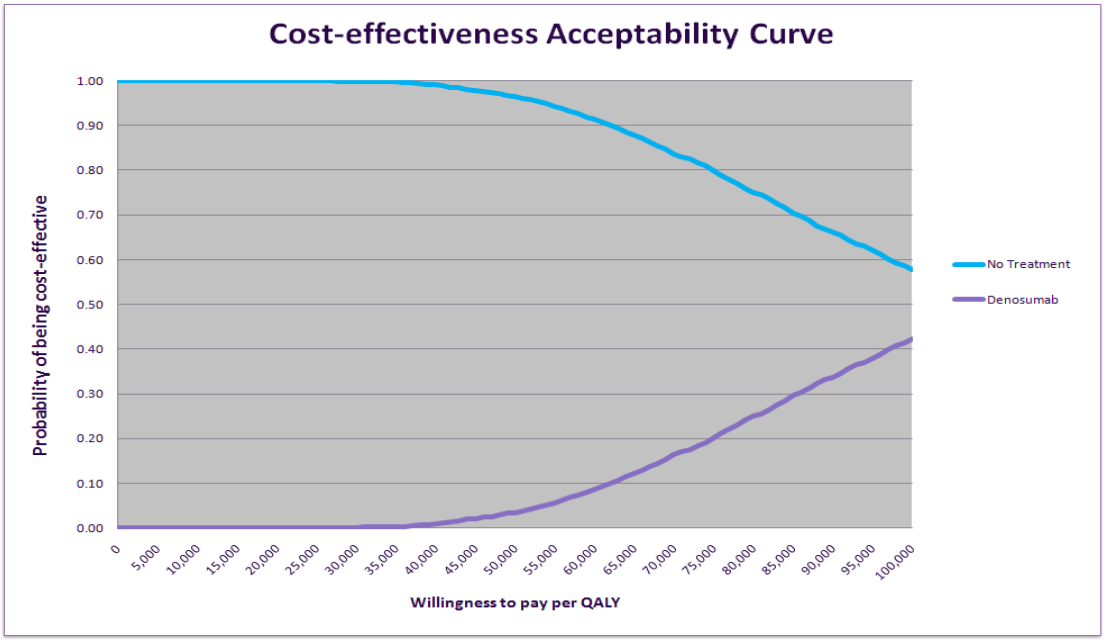
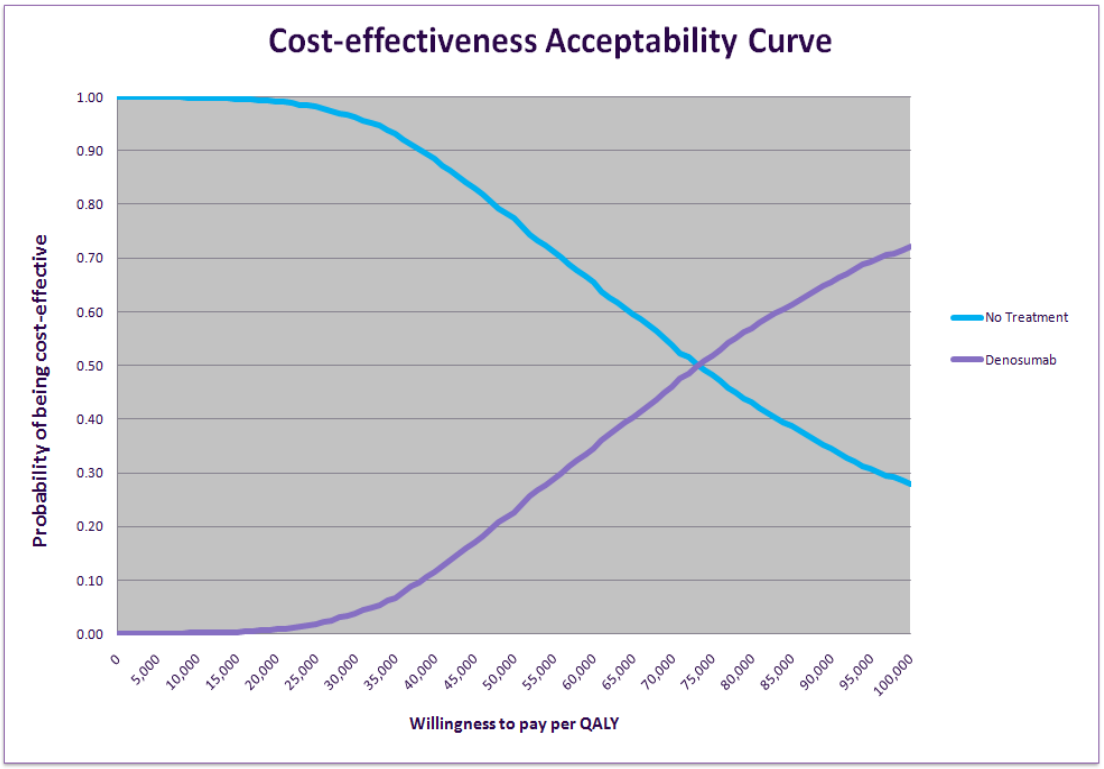


Figure 12. Cost-effectiveness acceptability curve: prostate cancer – no pain or pain and no history of a prior SRE [with PAS]



Analysis 4: Other solid tumours - pain and history of a prior SRE

Table 38. PSA Results: Other solid tumours - pain and history of a prior SRE [without PAS]

	Denosumab	ZOL	PAM
Total costs	£[redacted]	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]	£[redacted]
Total QALYs	0.763	0.759	0.750
95%lower CL	0.703	0.699	0.689
95% upper CL	0.825	0.822	0.815
INB of denosumab versus comparator:		-£636	£2,560
95%lower CL		-£901	£1,324
95% upper CL		-£372	£4,093

Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; INB, incremental net benefit; calculated with a cost-effectiveness threshold of £30,000; ICER, incremental cost-effectiveness ratio

Table 39. PSA Results: Other solid tumours - pain and history of a prior SRE [with PAS]

	Denosumab	ZOL	PAM
Total costs	£[redacted]	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]	£[redacted]
Total QALYs	0.763	0.759	0.757
95%lower CL	0.701	0.697	0.695
95% upper CL	0.825	0.822	0.819
INB of denosumab versus comparator:		£157	£3,096
95%lower CL		-£90	£2,052
95% upper CL		£410	£4,316

Abbreviations: ZOL, zoledronic acid; PAM, disodium pamidronate; INB, incremental net benefit; calculated with a cost-effectiveness threshold of £30,000; ICER, incremental cost-effectiveness ratio

Figure 13. Cost-effectiveness scatter plot: other solid tumours – pain and history of a previous SRE [without PAS]

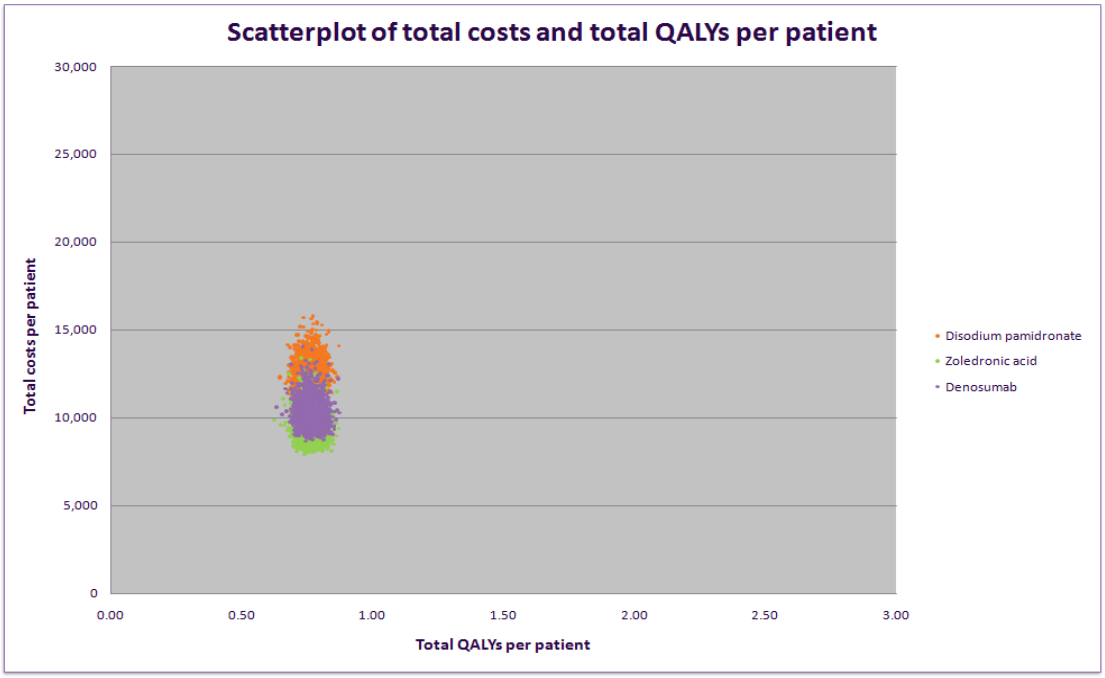


Figure 14. Cost-effectiveness scatter plot: other solid tumours – pain and history of a prior SRE [with PAS]

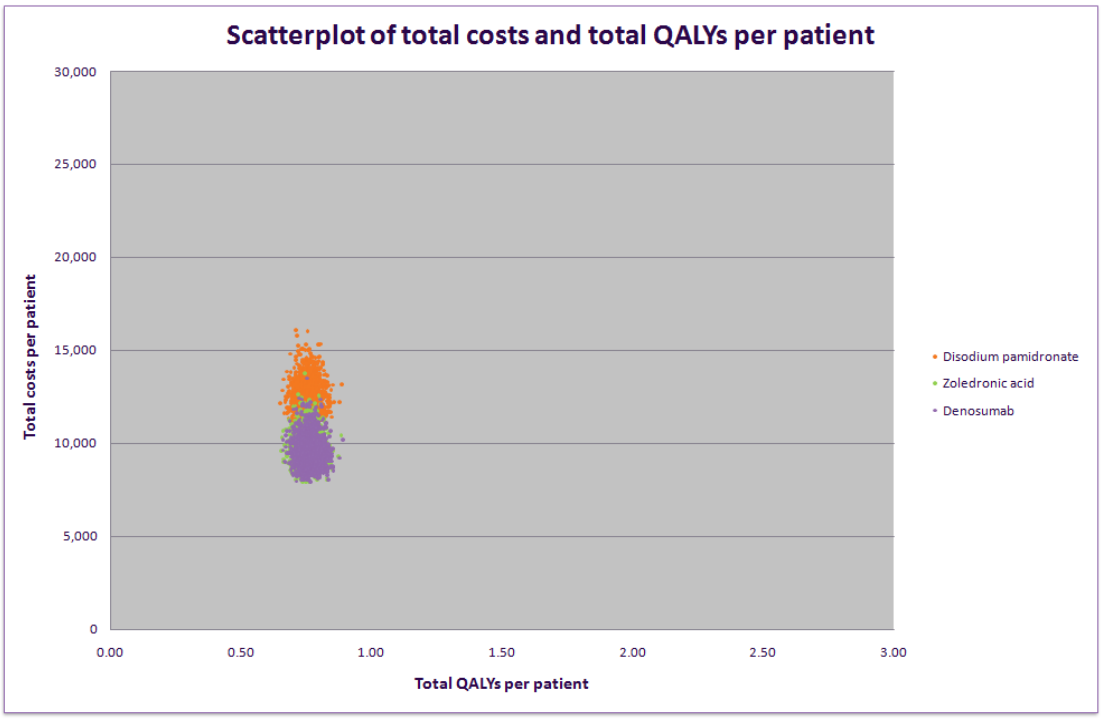


Figure 15. Cost-effectiveness acceptability curve: other solid tumours – pain and history of a prior SRE [without PAS]

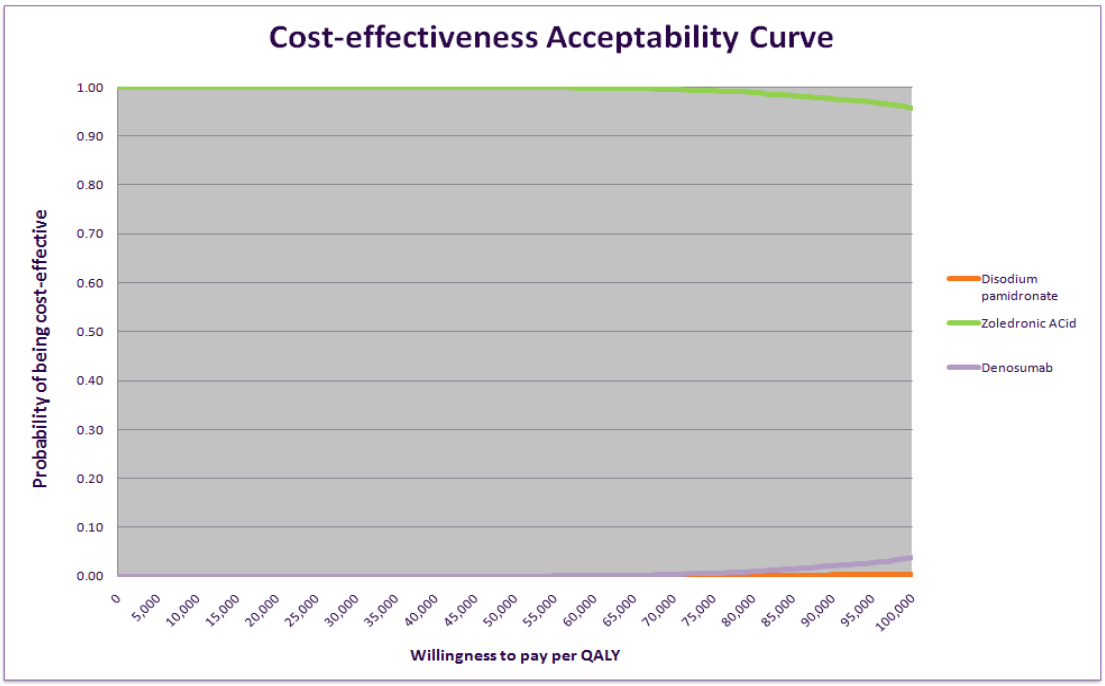
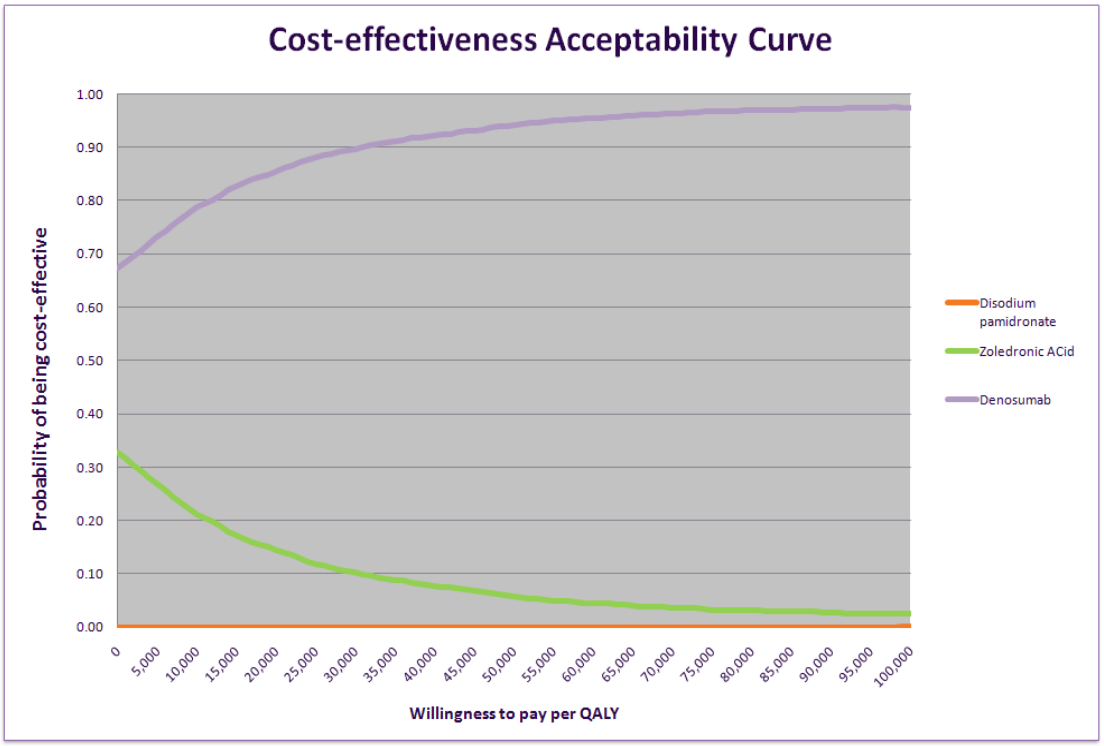


Figure 16. Cost-effectiveness acceptability curve: other solid tumours – pain and history of a prior SRE [with PAS]



Analysis 5: Other solid tumours, no pain or pain and no history of a prior SRE

Table 40. PSA Results: Other solid tumours - no pain or pain and no history of a prior SRE [without PAS]

	Denosumab	BSC
Total costs	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]
Total QALYs	0.801	0.780
95%lower CL	0.745	0.719
95% upper CL	0.859	0.843
INB of denosumab versus comparator:		-£1,861
95%lower CL		-£2,605
95% upper CL		-£1,010

Abbreviations: BSC, best supportive care; INB, incremental net benefit; calculated with a cost-effectiveness threshold of £30,000; ICER, incremental cost-effectiveness ratio

Table 41. PSA Results: Other solid tumours - no pain or pain and no history of a prior SRE [with PAS]

	Denosumab	BSC
Total costs	£[redacted]	£[redacted]
95%lower CL	£[redacted]	£[redacted]
95% upper CL	£[redacted]	£[redacted]
Total QALYs	0.802	0.781
95%lower CL	0.744	0.717
95% upper CL	0.862	0.845
INB of denosumab versus comparator:		-£1,099
95%lower CL		-£1,818
95% upper CL		-£189

Abbreviations: BSC, best supportive care; INB, incremental net benefit; calculated with a cost-effectiveness threshold of £30,000; ICER, incremental cost-effectiveness ratio

Figure 17. Cost-effectiveness scatter plot: other solid tumours – no pain or pain and no history of a prior SRE [without PAS]

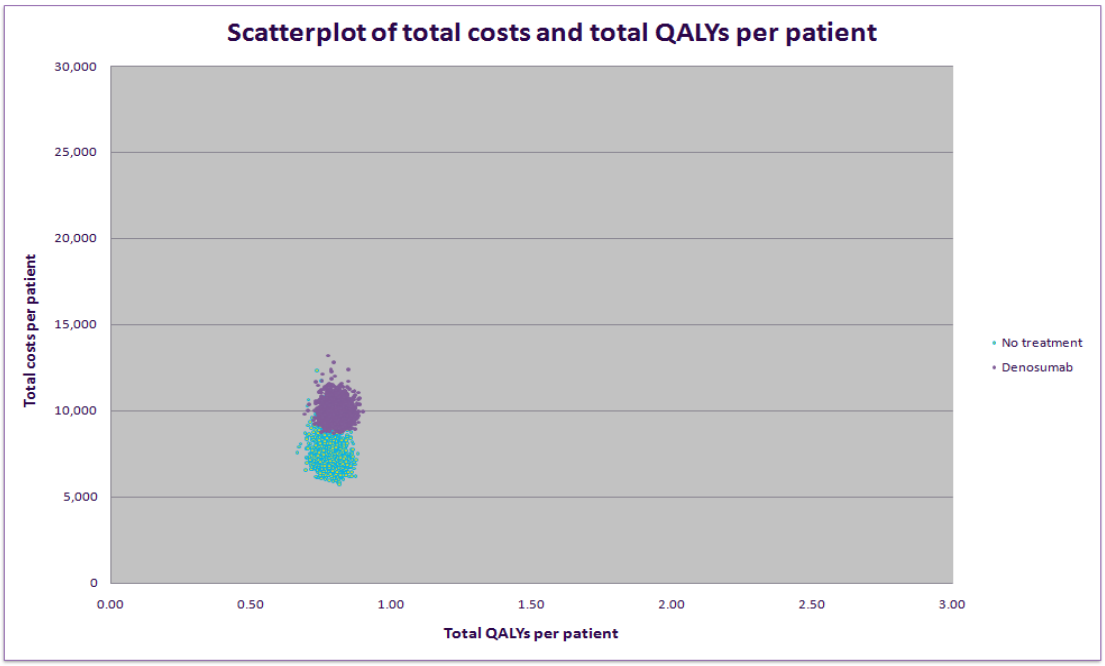


Figure 18. Cost-effectiveness scatter plot: other solid tumours – no pain or pain and no history of a prior SRE [with PAS]

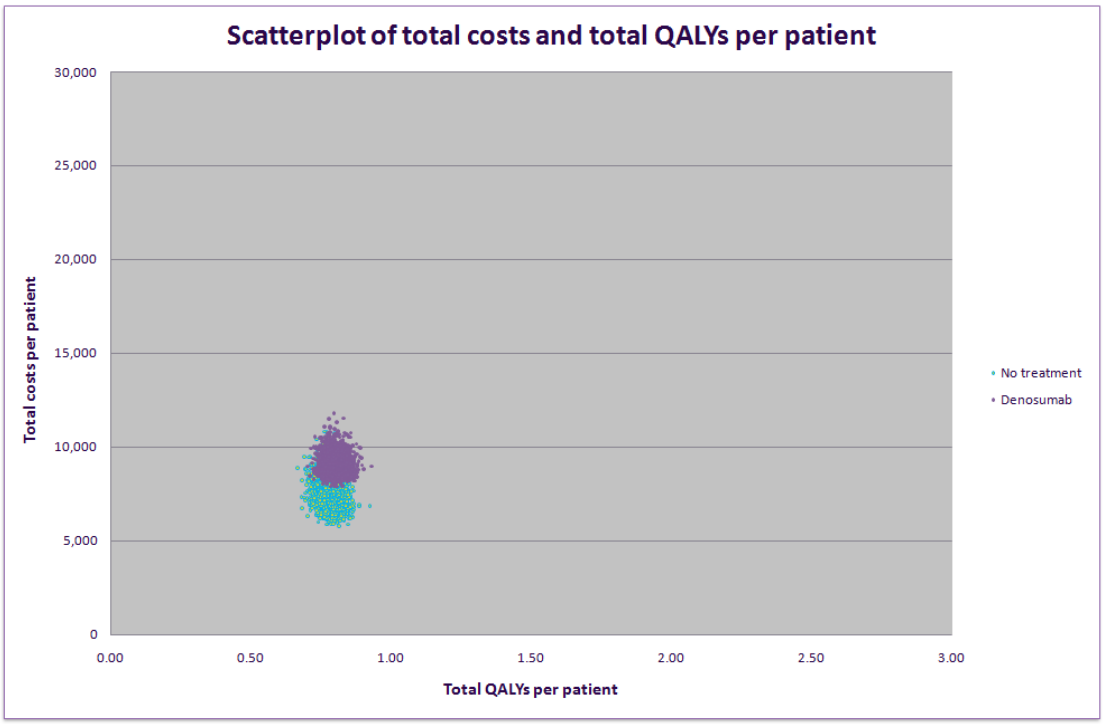


Figure 19. Cost-effectiveness acceptability curve: other solid tumours – no pain or pain and no history of a prior SRE [without PAS]

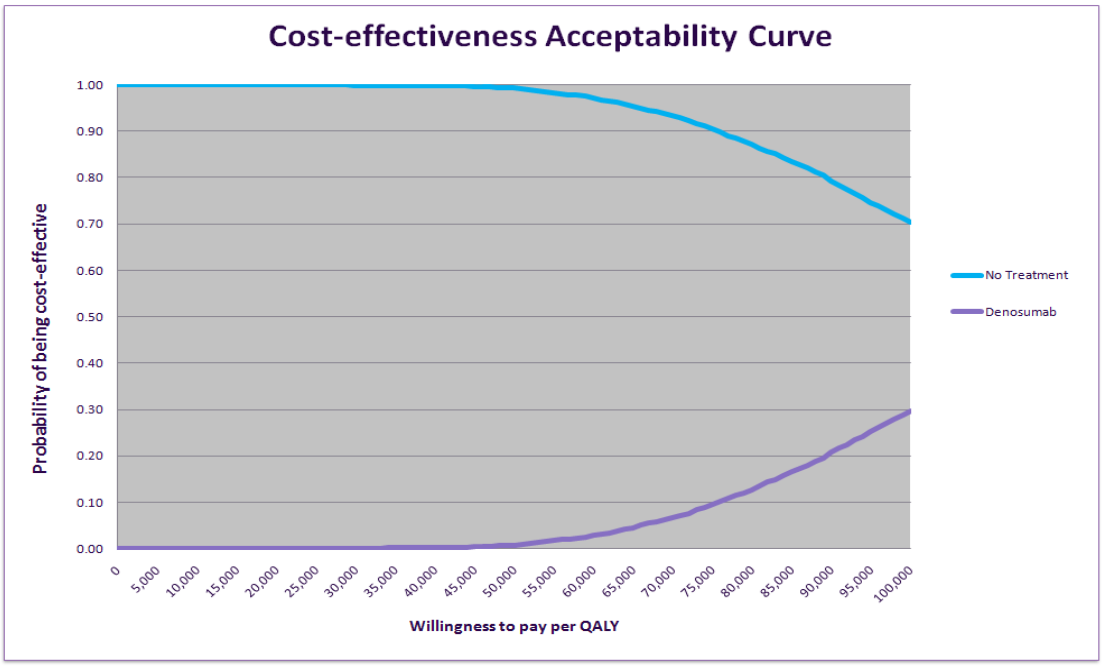
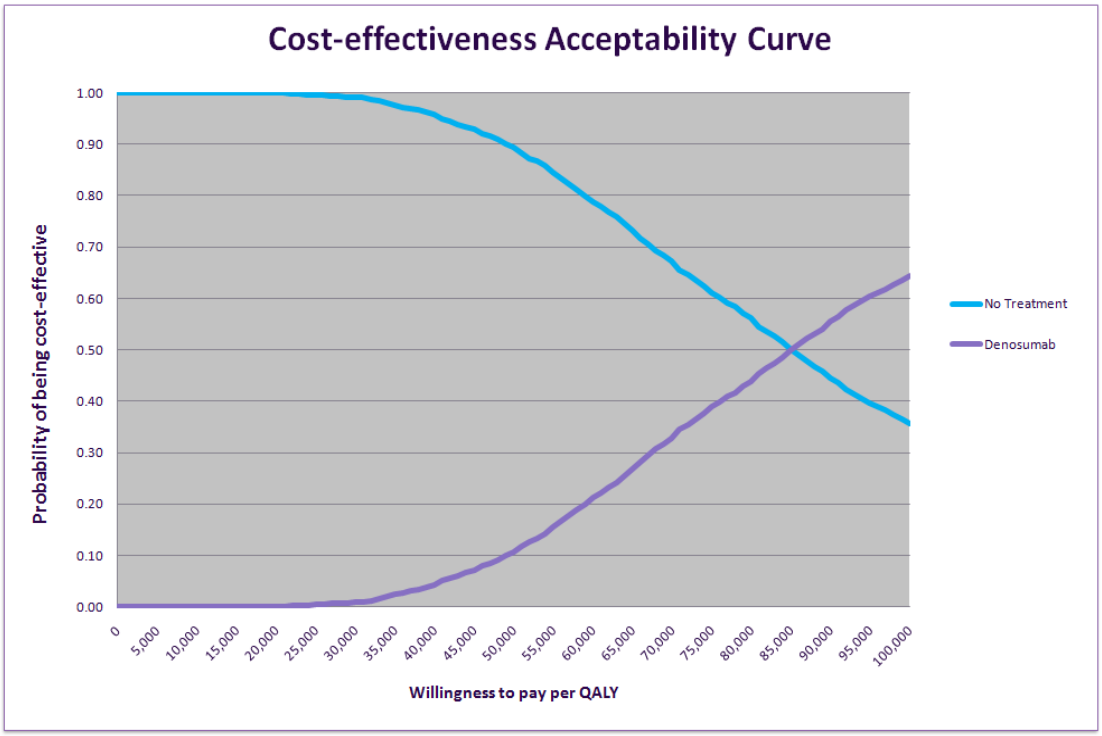


Figure 20. Cost-effectiveness acceptability curve: other solid tumours – no pain or pain and no history of a prior SRE [with PAS]



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

Scenario analyses are included in 4.9

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.