NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single technology appraisal

[Evaluation title and ID number]

Company evidence submission

**[Month year]**

|  |  |  |  |
| --- | --- | --- | --- |
| **File name** | **Version** | **Contains confidential information** | **Date** |
|  |  | **Yes/no** |  |

# Instructions for companies

This is the template for submission of evidence to the National Institute for Health and Care Excellence (NICE) as part of the single technology appraisal (STA) process. Please note that the information requirements for submissions are summarised in this template; full details of the requirements for pharmaceuticals and devices are in the [STA and highly specialised technologies evaluation: User guide for company evidence submission template](https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/technology-appraisal-guidance/technology-appraisal-submission-templates-and-supporting-documents).

This submission must not be longer than 150 pages, excluding appendices and the pages covered by this template. If it is too long it will not be accepted.

Companies making evidence submissions to NICE should also refer to the [NICE health technology evaluations manual.](https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation)

|  |
| --- |
| In this template any information that should be provided in an appendix is listed in a box. |

### Highlighting in the template (excluding the contents list)

Square brackets and grey highlighting are used in this template to indicate text that should be replaced with your own text or deleted. These are set up as form fields, so to replace the prompt text in [grey highlighting] with your own text, click anywhere within the highlighted text and type. Your text will overwrite the highlighted section.

To delete grey highlighted text, click anywhere within the text and press ’delete’.

Grey highlighted text in the footer does not work as an automatic form field, but serves the same purpose – as prompt text to show where you need to fill in relevant details. Replace the text highlighted in [grey] in the header and footer with appropriate text. (To change the header and footer, double click over the header or footer text. Double click back in the main body text when you have finished.)

# Contents

[Please adapt this contents list to your evidence submission.]

[Tables and figures 4](#_Toc177741130)

[1 Decision problem, description of the technology and clinical care pathway 5](#_Toc177741131)

[2 Clinical effectiveness 10](#_Toc177741132)

[3 Cost effectiveness 15](#_Toc177741133)

[4 References 26](#_Toc177741134)

[5 Appendices 27](#_Toc177741135)

[Appendix A: Summary of product characteristics (SmPC) and UK public assessment report 28](#_Toc177741136)

[Appendix B: Identification, selection and synthesis of clinical evidence 29](#_Toc177741137)

[Appendix C: Subgroup analysis 31](#_Toc177741138)

[Appendix D: Adverse reactions 32](#_Toc177741139)

[Appendix E: Published cost-effectiveness studies 33](#_Toc177741140)

[Appendix F: Health-related quality-of-life studies 34](#_Toc177741141)

[Appendix G: Cost and healthcare resource identification, measurement and valuation 35](#_Toc177741142)

[Appendix H: Clinical outcomes and disaggregated results from the model 36](#_Toc177741143)

[Appendix I: Price details of treatments included in the submission 39](#_Toc177741144)

#  Tables and figures

[Include a list of all tables and figures here with page references]

1. Decision problem, description of the technology and clinical care pathway
	1. Decision problem

[Please choose the text below that is most applicable to your submission and adapt as needed:]

The submission covers the technology’s full marketing authorisation for this indication.

The submission focuses on part of the technology’s marketing authorisation [for example, explain if this affects details of the pathway position or population, such as ‘people with 2 previous relapses only’ or ‘people with severe disease’]. The proposed [position in the treatment pathway/population] is narrower than the marketing authorisation because [please include the relevant option from the list below]:

* This is relevant to NHS clinical practice; [technology] would not be used [elsewhere/in a wider population].
* The evidence base on [technology] is limited to [this position/population].
* This [position/population] optimises the cost effectiveness of [technology], because [please provide rationale].
* This [position/population] reflects where [technology] provides the most clinical benefit.
* [Technology] is not [clinically/cost] effective in [add position/population].

[Specify the decision problem that the submission addresses in the table below.]

Table [X] The decision problem

|  |  |  |  |
| --- | --- | --- | --- |
|  | Final scope issued by NICE | Decision problem addressed in the company submission | Rationale if different from the final NICE scope |
| **Population** |  |  |  |
| **Intervention** |  |  |  |
| **Comparator(s)** |  |  |  |
| **Outcomes** |  |  |  |
| **Economic analysis** | [please delete row if economic analysis is as per the scope] |  |  |
| **Subgroups to be considered** | [please delete row if not applicable] |  |  |
| **Special considerations including issues related to equity or equality** | [please delete row if not applicable] |  |  |

* 1. Description of the technology being evaluated

|  |
| --- |
| In appendix A include the summary of product characteristics or information for use, and the UK public assessment report, scientific discussion or drafts. |

[Describe the technology being evaluated in the table below.]

Table [X] Technology being evaluated

|  |  |
| --- | --- |
| UK approved name and brand name |  |
| Mechanism of action |  |
| Marketing authorisation/CE mark status | [Indicate whether the technology has a UK marketing authorisation/CE marking for the indications detailed in this submission. If so, give the date on which this was granted. If not, state the current UK regulatory status, with relevant dates. [(For example, date of application and/or expected date of approval from the MHRA)][Please confirm which regulatory process are you following, for example MHRA national procedure, European Commission Decision Reliance Procedure (ECDRP) or other recognition routes.] |
| Indications and any restriction(s) as described in the summary of product characteristics (SmPC) | [Give the (anticipated) indiciation(s) in the UK. For devices, provide the date of (anticipated) CE marking, including the indication for use. If a submission is based on the company's proposed or anticipated marketing authorisation, the company must advise NICE immediately of any difference between the anticipated and the final marketing authorisation approved by the regulatory authorities. Include the (draft) SmPC for pharmaceuticals or information for use (IFU) for devices in appendix A. Provide the (draft) UK Public Assessment Report for pharmaceuticals or a (draft) technical manual for devices in appendix A.] |
| Method of administration and dosage |  |
| Additional tests or investigations | [State whether additional tests or investigations are needed (for example, diagnostic tests to identify the population for whom the technology is indicated in the marketing authorisation).] |
| List price and average cost of a course of treatment |  |
| Patient access scheme (if applicable) | [Indicate if there is a patient access scheme agreed with NHS England and whether this is a simple discount or complex arrangement.] |

* 1. Health condition and position of the technology in the treatment pathway

[Provide a brief overview of the disease or condition for which the technology is indicated.]

[Summarise the clinical pathway of care in a diagram showing the context and the proposed placement of the technology within the pathway.]

[Describe location or setting of care (for example, primary or secondary care).] [See section 1.3 of the user guide for full details of the information required here.]

* 1. Equality considerations

[Provide an assessment of whether the use of this technology is likely to raise any equality issues.]

[See section 1.4 of the user guide for full details of the information required here.]

1. Clinical effectiveness
	1. Identification and selection of relevant studies

See appendix B for full details of the process and methods used to identify and select the clinical evidence relevant to the technology being evaluated.

|  |
| --- |
| * In appendix B describe the process and methods used to identify and select the clinical evidence relevant to the technology being evaluated.
* See section 2.1 of the user guide for full details of the information required in appendix B.
 |

* 1. List of relevant clinical effectiveness evidence

[Provide details of the studies that provide evidence of the clinical benefits of the technology. These should be based on the best evidence available, preferably from randomised controlled trials (RCTs). Non-randomised and non-controlled evidence may be needed to supplement RCT data. Include details on additional and supporting evidence, including expert elicitation, expert opinion, real world evidence or natural history data used to support any severity assumptions. A suggested table format for each study is presented below. Additional and supporting evidence may be presented as a written description.]

[See section 2.2 of the user guide for full details of the information required here.]

Table [X] Clinical effectiveness evidence

| Study  | [Clinical trial name or primary author surname (year published)] |
| --- | --- |
| Study design |  |
| Population |  |
| Intervention(s) |  |
| Comparator(s) |  |
| Indicate if study supports application for marketing authorisation | YesNo |
| Indicate if study used in the economic model | YesNo |
| Rationale if study not used in model |  |
| Reported outcomes specified in the decision problem | [Please mark in bold the outcomes that are incorporated into the model] |
| All other reported outcomes | [Please mark in bold the outcomes that are incorporated into the model] |

[Sections 2.2 to 2.6 of the submission should include only the studies that were included in the economic model. If you wish to include additional studies in sections 2.2 to 2.6, which were not included in the economic model but are relevant to your submission (for example, natural history data to support severity assumptions), please provide your rationale below, in the following format:]

[Study name] was not used to populate the economic model but is included in sections 2.2 to 2.6. The results of this study support [please include details of why they are relevant]. This study was not included in the economic model because [please add rationale].

* 1. Summary of methodology of the relevant clinical effectiveness evidence

[Provide details of the methodology of the RCTs and non-randomised and non-controlled evidence identified in section 2.2 as relevant to your submission.]

[Provide a summary of the baseline characteristics of study participants, if relevant.]

[Please provide a description of the methods used for expert elicitation or expert opinion.]

[See section 2.3 of the user guide for full details of the information required here.]

* 1. Statistical analysis and definition of study groups in the relevant clinical effectiveness evidence

[State the primary hypothesis or hypotheses under consideration and provide methods used for testing hypotheses for each study identified in section 2.2 as relevant to your submission.]

|  |
| --- |
| In appendix B, provide details of the numbers of participants eligible to enter the studies. |

[See section 2.4 of the user guide for full details of the information required here.]

* 1. Critical appraisal of the relevant clinical effectiveness evidence

[Provide a quality assessment for each of the sources of clinical evidence identified in section 2.2 as relevant to your submission.]

|  |
| --- |
| In appendix B, provide the complete quality assessment for each study. |

[Provide a discussion on the limitations of the evidence base presented.]

[See section 2.5 of the user guide for full details of the information required here.]

* 1. Clinical effectiveness results of the relevant studies

[Provide results for all outcomes included in the economic model and all outcomes specified in the NICE scope, for all studies identified in section 2.2 as relevant to your submission (including real-world studies where applicable). The primary outcome of the studies must be reported.]

[See section 2.6 of the user guide for full details of the information required here.]

* 1. Subsequent treatments used in the relevant studies

[Provide details of the subsequent treatments used in each arm of the studies identified in section 2.2 as relevant to your submission.]

[See section 2.7 of the user guide for full details of the information required here.]

* 1. Subgroup analysis

[Provide details of any subgroup analyses that were carried out and specify the rationale and whether they were pre-planned or post-hoc.]

[See section 2.8 of the user guide for full details of the information required here.]

|  |
| --- |
| Provide a summary of the results for the subgroups in appendix C. |

* 1. Meta-analysis

[Provide results of any meta-analyses carried out. If a meta-analysis is not considered appropriate, a rationale must be given and a qualitative overview provided.]

[See section 2.9 of the user guide for full details of the information required here.]

* 1. Indirect and mixed treatment comparisons

|  |
| --- |
| In appendix B include full details of the methodology for the indirect comparison or mixed treatment comparison. |

[Provide the results of any indirect and/or mixed treatment comparisons.]

[See section 2.10 of the user guide for full details of the information required here.]

### Uncertainties in the indirect and mixed treatment comparisons

[Describe and explain any uncertainties in the inputs and assumptions of the indirect and mixed treatment comparisons described above. Please provide a summary of any sensitivity analyses conducted to explore these uncertainties]

* 1. Adverse reactions

[Provide details of all adverse reactions experienced with the technology in relation to the decision problem and reported in the studies identified in section 2.2.]

|  |
| --- |
| In appendix D, provide details of any studies that report additional adverse reactions to those reported in the studies in section 2.2. |

[See section 2.11 of the user guide for full details of the information required here.]

* 1. Ongoing studies

[Provide details of all completed and ongoing studies that should provide additional evidence in the next 12 months for the indication being appraised.]

* 1. Interpretation of clinical effectiveness and safety evidence

[Make brief conclusions about the clinical effectiveness and safety of the technology compared with the comparators specified in the final scope issued by NICE, including any subgroups.]

[See section 2.13 of the user guide for full details of the information required here.]

1. Cost effectiveness
	1. Published cost-effectiveness studies

|  |
| --- |
| * In appendix E, describe and compare the methods and results of any published cost-effectiveness analyses available for the technology and/or the comparator technologies (relevant to the technology evaluation).
* See section 3.1 of the user guide for full details of the information required in appendix E.
 |

[Summarise the published cost-effectiveness studies using a table similar to the one below:]

Table X Summary list of published cost-effectiveness studies

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Study | Year | Summary of model | Patient population (average age in years) | QALYs (intervention, comparator) | Costs (currency) (intervention, comparator) | ICER (per QALY gained) |
| Study 1 |  |  |  |  |  |  |
| Study 2 |  |  |  |  |  |  |
| [Add more rows as needed] |  |  |  |  |  |  |

Abbreviations: ICER, incremental cost-effectiveness ratio; QALYs, quality-adjusted life years

* 1. Economic analysis

[Summarise how the cost-effectiveness studies identified in appendix E inform the economic analysis.]

[If a de novo model economic model is included in the submission, please justify why this is necessary.]

### Patient population

[Provide details about the patient population included in the cost-effectiveness analysis.]

[See section 3.2.1 of the user guide for full details of the information required here.]

### Model structure

[Provide details about the model structure of the cost-effectiveness analysis.]

[If there have been NICE technology evaluations for the same indication, please summarise the main inputs to the economic models accepted by evaluation committees in the table below. If the model in this evaluation uses different inputs, give a rationale for this.]

[See sections 3.2.2 to 3.2.4 of the user guide for full details of the information required here.]

Table X Features of the economic analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Factor | Previous evaluation, TAXXX | Previous evaluation, TAXXX | Current evaluation, chosen values | Current evaluation, justification |
| Time horizon |  |  |  |  |
| Treatment waning effect? |  |  |  |  |
| Source of utilities |  |  |  |  |
| Source of costs |  |  |  |  |

### Intervention technology and comparators

[Provide details about the intervention technology and comparator technologies included in the cost-effectiveness analysis, including position in the treatment pathway and location or setting of care.]

[See sections 3.2.5 and 3.2.6 of the user guide for full details of the information required here.]

* 1. Clinical parameters and variables

[Provide details about the clinical parameters and variables included in the cost-effectiveness analysis. This includes describing whether intermediate outcomes were linked to final outcomes, methods of extrapolation, estimation and application of transitional probabilities (when relevant), the use and selection of the most appropriate survival analysis techniques and whether any validation of the clinical parameters has been carried out.]

[See section 3.3 of the user guide for full details of the information required here.]

* 1. Measurement and valuation of health effects

[See section 3.4 of the user guide for details of supporting documents on measuring and valuing health benefits.]

### Health-related quality-of-life data from clinical trials

[Provide details of the health-related quality-of-life data available from the clinical trials.]

[See section 3.4.1 of the user guide for full details of the information required here.]

### Mapping

[Provide details of any mapping techniques used to estimate health-related quality-of-life data. If health-related quality-of-life data were collected in the clinical trials but not mapped onto a generic outcome measure, explain why.]

[See section 3.4.2 of the user guide for full details of the information required here.]

### Health-related quality-of-life studies

|  |
| --- |
| In appendix F describe how systematic searches for relevant health-related quality-of-life data were done. |

[Provide details of the health-related quality-of-life data available from published (and unpublished) studies.]

[See section 3.4.3 of the user guide for full details of the information required here.]

### Adverse reactions

[Provide details of how adverse reactions associated with the technology have an impact on health-related quality of life.]

[See section 3.4.4 of the user guide for full details of the information required here.]

### Health-related quality-of-life data used in the cost-effectiveness analysis

[Provide details of the health-related quality-of-life data used in the cost-effectiveness analysis, including a description of patient experience in the health states of the analysis and whether the utility values have been adjusted and validated.]

[See sections 3.4.5 to 3.4.11 of the user guide for full details of the information required here.]

[Provide the utility values used in the analysis in the table below.]

Table X Summary of utility values for cost-effectiveness analysis

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| State | Utility value: mean (standard error) | 95% confidence interval | Reference in submission (section and page number) | Justification |
| Health state 1  | Health state 1 |  |  |  |
| Health state 2 | Health state 2 |  |  |  |
| [Add more rows as needed] |  |  |  |  |
| Adverse reaction 1 | Adverse reaction 1 |  |  |  |
| Adverse reaction 2 | Adverse reaction 2 |  |  |  |

* 1. Cost and healthcare resource use identification, measurement and valuation

[See section 3.5.1 of the user guide for full details of the information required here.]

|  |
| --- |
| In appendix G describe how relevant cost and healthcare resource data were identified. |

### Intervention and comparators’ costs and resource use

[Describe and tabulate the costs and resource use associated with the intervention technology and comparator technologies included in the cost-effectiveness analysis. This should include drug acquisition costs, administration costs and monitoring costs.]

[See sections 3.5.4 to 3.5.6 of the user guide for full details of the information required here.]

### Health-state unit costs and resource use

[Describe and tabulate the unit costs and resource use associated with the health states included in the cost effectiveness analysis.]

[See section 3.5.7 of the user guide for full details of the information required here.]

### Adverse reaction unit costs and resource use

[Describe and tabulate the unit costs and resource use associated with the adverse reactions included in the cost effectiveness analysis.]

[See section 3.5.8 of the user guide for full details of the information required here.]

### Miscellaneous unit costs and resource use

[Describe and tabulate any other unit costs and resource use that have been included in the cost effectiveness analysis.]

[See section 3.5.9 of the user guide for full details of the information required here.]

* 1. Severity

[If relevant, include a statement on whether this technology meets the criteria for a severity weight. Provide details about the calculation of QALY shortfall, including source of population EQ-5D data and survival data. Present supporting evidence and validation of model outcomes. Complete the tables below and where relevant cross reerence to where this information is found in the company submission.]

[Provide a list of the assumptions in the model that are key to severity and justify each assumption.]

[See section 3.6 of the user guide for full details of the information required here.]

Table [X] summary features of QALY shortfall analysis

|  |  |  |
| --- | --- | --- |
| Factor | Value (reference to appropriate table or figure in submission) | Reference to section in submission |
| Sex distribution |  | [Patient characteristics section x]  |
| Starting age  |  | [Trial results section x]  |

Table X summary list of QALY shortfall from previous evaluations

|  |  |  |  |
| --- | --- | --- | --- |
| TA | Expected total QALYs for the general population  | Expected total QALYs that people living with a condition would be expected to have with current treatment | QALY shortfall |
| TAXXX |  |  |  |
| [Add more rows as needed] |  |  |  |

Table X summary of health state benefits and utility values for QALY shortfall analysis

|  |  |  |
| --- | --- | --- |
| State | Utility value: mean (standard error) | Undiscounted life years |
| Health state 1  | Health state 1 |  |
| Health state 2 | Health state 2 |  |
| [Add more rows as needed] |  |  |

Table X summary of QALY shortfall analysis

|  |  |  |
| --- | --- | --- |
| Expected total QALYs for the general population  | Total QALYs that people living with a condition would be expected to have with current treatment | QALY shortfall |
|  | Comparator A |  |
| [Add more rows as needed] | Comparator B |  |

* 1. Uncertainty

[If relevant, include a statement on how the nature of this condition or technology impacts the ability to generate high-quality evidence.]

* 1. Managed access proposal

[A managed access proposal may be made for any technology that is eligible for the Cancer Drugs Fund or the Innovative Medicines Fund. This section may be deleted if not relevant.]

[See section 3.8 of the user guide for full details of the information required here.]

* 1. Summary of base-case analysis inputs and assumptions

### Summary of base-case analysis inputs

[Summarise and tabulate the inputs and variables of the cost-effectiveness analysis.]

[See sections 3.9.1 to 3.9.2 of the user guide for full details of the information required here.]

[Summarise the base-case analysis inputs in the table below.]

Table X Summary of variables applied in the economic model

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable**  | **Value (reference to appropriate table or figure in submission)** | **Measurement of uncertainty and distribution: confidence interval (distribution)** | **Reference to section in submission** |
| [Age] | [A years]  | [x to y (normal)]  | [Patient characteristics section x]  |
| [Overall survival]  | [B months]  | [x to y (Weibull)]  | [Trial results section x]  |
| [Add more rows as needed] |  |  |  |

### Assumptions

[Provide a list of all assumptions in the economic model and justify each assumption, particularly any assumptions that do not align with the reference case.]

* 1. Base-case results

[See section 3.10.1 of the user guide for full details of the information required here.]

### Base-case incremental cost-effectiveness analysis results

[Describe and tabulate the base-case incremental cost-effectiveness results and, when appropriate, the expected net health benefits using values placed on a QALY gain of £20,000 and £30,000.]

[See section 3.10.2 of the user guide for full details of the information required here.]

[Present the base-case results in the table below.]

Table X Base-case results

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Technologies  | Total costs (£)  | Total LYG  | Total QALYs  | Incremental costs (£)  | Incremental LYG  | Incremental QALYs  | ICER versus baseline (£/QALY)  | ICER incremental (£/QALY)  |
|   |   |   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |   |   |

Abbreviations: ICER, incremental cost-effectiveness ratio; LYG, life years gained; QALYs, quality-adjusted life years

Table X Net health benefit

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Technologies  | Total costs (£)  | Total QALYs  | Incremental costs (£)  | Incremental QALYs  | NHB at £20,000 | NHB at £30,000  |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |
|   |   |   |   |   |   |   |

Abbreviations: ICER, incremental cost-effectiveness ratio; LYG, life years gained; NHB, net health benefit; QALYs, quality-adjusted life years

|  |
| --- |
| In appendix H please provide the following:* **Clinical outcomes from the model**
	+ Present the estimates of clinical outcomes included in the cost-effectiveness analysis (and compare with the clinical trial results).
	+ See section 3.10 of the user guide for full details of the information required here.
* **Disaggregated results of the base-case incremental cost effectiveness analysis**
	+ Describe and tabulate the disaggregated results of the base-case incremental cost-effectiveness analysis.
	+ See section 3.10 of the user guide for full details of the information required here.
 |

* 1. Exploring uncertainty

[Present an overall assessment of uncertainty, including the relative effect of different types of uncertainty on cost-effectiveness estimates, and an assessment of whether the uncertainties that can be included in the analyses have been adequately captured. Highlight the presence of uncertainties that are unlikely to be reduced by further evidence or expert input.]

### Probabilistic sensitivity analysis

[Describe the methods and present the results of the probabilistic sensitivity analysis.]

[See sections 3.11.2 to 3.11.6 of the user guide for full details of the information required here.]

### Deterministic sensitivity analysis

[If relevant, describe the methods and tabulate the incremental cost-effectiveness results of the deterministic sensitivity analysis.]

[See sections 3.11.7 to 3.11.10 of the user guide for full details of the information required here.]

### Scenario analysis

[Describe the methods and tabulate the incremental cost-effectiveness results of the scenario analyses carried out. Include the impact on the estimates of QALY shortfall when appropriate.]

[See sections 3.11.11 to 3.11.13 of the user guide for full details of the information required here.]

* 1. Subgroup analysis

[Provide details of any subgroup analyses explored in the cost-effectiveness analysis.]

[See sections 3.12.1 to 3.12.6 of the user guide for full details of the information required here.]

* 1. Benefits not captured in the QALY calculation

[If you consider that there are potential health benefits of the technology that have been inadequately captured and may therefore misrepresent the health utility gained, identify and present the data and provide a rationale for your decision.]

* 1. Validation

### Validation of cost-effectiveness analysis

[Describe any methods used to internally and externally validate the cost-effectiveness analysis.]

[See section 3.14 of the user guide for full details of the information required here.]

* 1. Interpretation and conclusions of economic evidence

[Provide a conclusion on the cost effectiveness of the technology.]

[See section 3.15 of the user guide for full details of the information required here.]

1. References

[Please use a recognised referencing style, such as Harvard or Vancouver. Trials should be identified by the first author or trial ID, rather than by relying on numerical referencing alone (for example, ‘TrialNCT123456/Trial ACRONYM/Jones et al.126' rather than ‘One trial126’).]

[Please also provide references as a separate RIS file.]

1. Appendices

[List the titles of the appendices here. All appendices should be provided as **separate documents to the main submission**.]

[See section 5 of the user guide for a list of the appendices that should be used to support the submission. Appendices A to I should be provided. Any additional appendices should start at appendix J.]

# Appendix A: Summary of product characteristics (SmPC) and UK public assessment report

## 1.1 SmPC

## 1.2 UK public assessment report

# Appendix B: Identification, selection and synthesis of clinical evidence

## 1.1 Identification and selection of relevant studies

[Describe the process and methods used to identify and select the studies relevant to:

* the technology being appraised
* comparator technologies, when an indirect or mixed treatment comparison is carried out.]

[See sections 2.1 and 2.9 of the user guide for full details of the information required here.]

### Search strategy

### Study selection

#### Complete reference lists for included studies and excluded studies

### Summary of trials used for indirect or mixed treatment comparisons

#### Methods and outcomes of studies included in indirect or mixed treatment comparisons

#### Methods of analysis of studies included in indirect or mixed treatment comparisons

#### Programming language for indirect or mixed treatment comparisons

#### Risk of bias of studies included in indirect or mixed treatment comparisons

## 1.2 Participant flow in the relevant randomised controlled trials

[Provide details of the numbers of participants who were eligible to enter the trials. Include the number of participants randomised and allocated to each treatment. Provide details of and the rationale for participants who crossed over treatment groups, were lost to follow-up or withdrew from the RCT. Provide a CONSORT diagram showing the flow of participants through each stage of each of the trials.]

[See section 2.4 of the user guide for full details of the information required here.]

## 1.3 Critical appraisal for each study

[See section 2.5 of the user guide for full details of the information required here.]

# Appendix C: Subgroup analysis

[See section 2.7 of the user guide for full details of the information required here.]

# Appendix D: Adverse reactions

[See section 2.10 of the user guide for full details of the information required here.]

# Appendix E: Published cost-effectiveness studies

[See section 3.1 of the user guide for full details of the information required here.]

# Appendix F: Health-related quality-of-life studies

Describe how systematic searches for relevant health-related quality-of-life data were done. Consider published and unpublished studies, including any original research commissioned for the technology. Provide the rationale for terms used in the search strategy and any inclusion and exclusion criteria used. The search strategy used should be provided in the appendix.

Tabulate the details of the studies in which health-related quality of life was measured. Include the following, but note that this list is not exhaustive:

* population in which health effects were measured
* information on recruitment (for example, participants of a clinical trial, approximations from clinical experts, utility elicitation exercises including members of the general public or patients)
* interventions and comparators
* sample size
* response rates
* description of health states
* adverse reactions
* appropriateness of health states given the condition and treatment pathway
* method of elicitation
* method of valuation
* mapping
* uncertainty around values
* consistency with reference case.

# Appendix G: Cost and healthcare resource identification, measurement and valuation

Describe how relevant cost and healthcare resource use data for England were identified. Evidence should be presented to demonstrate that resource use and cost data have been identified systematically. Include the search strategy and inclusion criteria, and consider published and unpublished studies. The search strategy used should also be provided in the appendix. If the systematic search yields limited data for England, the search strategy may be extended to capture data from other countries. Please give the following details of included studies:

* country of study
* date of study
* applicability to clinical practice in England
* cost valuations used in the study
* costs for use in the economic analysis
* technology costs.

When describing how relevant unit costs were identified, comment on whether NHS reference costs or payment-by-results (PbR) tariffs are appropriate for costing the intervention being appraised. Describe how the clinical management of the condition is currently costed in the NHS in terms of reference costs and the PbR tariff. Provide the relevant Healthcare Resource Groups and PbR codes and justify their selection with reference to section 2.

If clinical experts assessed the applicability of the cost and healthcare resource use values available, or approximated any of the values used in the cost-effectiveness analysis, provide the details (see section 3.3.4 of user guide).

# Appendix H: Clinical outcomes and disaggregated results from the model

1.1 Clinical outcomes from the model

[Present the estimates of clinical outcomes included in the de novo cost-effectiveness analysis (and compare with the clinical trial results).]

[See section 3.9 of the user guide for full details of the information required here.]

## 1.2 Disaggregated results of the base-case incremental cost-effectiveness analysis

[Describe and tabulate the disaggregated results of the base-case incremental cost-effectiveness analysis.]

[Provide (if appropriate) a graphical representation of how QALYs accrue over time in the economic model (for example, Markov trace, active partitioned survival curves or equivalent). Supply 1 for each comparator, showing the proportion of time spent in each health state over the full time horizon. Other time horizons may also be appropriate.]

[See section 3.10 of the user guide for full details of the information required here.]

Table X Summary of QALY gain by health state

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Health state | QALY intervention (X) | QALY comparator (Y) | Increment | Absolute increment | % absolute increment |
| [Health state 1]  | [XHS1]  | [YHS1]  | [XHS1 – YHS1]  | [|XHS1 – YHS1|] | [|XHS1 – YHS1|/(Total absolute increment)] |
| [Health state 2] | [XHS2]  | [YHS2]  | [XHS2 – YHS2]  | [|XHS2 – YHS2|] | [|XHS2 – YHS2|/(Total absolute increment)] |
| [Add more rows as needed] |  |  |  |  |  |
| Total  | [XTotal] | [YTotal] | [XTotal – YTotal] | Total absolute increment | 100% |

Abbreviations: HS1, health state 1; HS2, health state 2; QALY, quality-adjusted life year. Table dapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee

Table X Summary of costs by health state

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Health state | Cost intervention (X) | Cost comparator (Y) | Increment | Absolute increment | % absolute increment |
| [Health state 1 (HS1)]  | [XHS1]  | [YHS1]  | [XHS1 – YHS1] | [|XHS1 – YHS1|]  | [|XHS1 – YHS1| / (Total absolute increment)]  |
| [Health state 2] | [XHS2]  | [YHS2]  | [XHS2 – YHS2] | [|XHS2 – YHS2|]  | [|XHS2 – YHS2| / (Total absolute increment)]  |
| [Add more rows as needed] |  |  |  |  |  |
| Total  | [XTotal] | [YTotal] | [XTotal – YTotal] | Total absolute increment | 100% |

Abbreviations: HS1, health state 1; HS2, health state 2. Table adapted from Pharmaceutical Benefits Advisory Committee (2008) Guidelines for preparing submissions to the Pharmaceutical Benefits Advisory Committee (Version 4.3). Canberra: Pharmaceutical Benefits Advisory Committee

Table X Summary of predicted resource use by category of cost

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Item | Cost intervention (X) | Cost comparator (Y) | Increment | Absolute increment | % absolute increment |
| [Technology cost]  | [Xtech]  | [Ytech] | [Xtech – Ytech]  | [|Xtech – Ytech|]  | [|Xtech – Ytech| / (Total absolute increment)]  |
| [Mean total treatment cost]  | [Xtreat]  | [Ytreat] | [Xtreat – Ytreat]  | [|Xtreat – Ytreat|]  | [|Xtreat – Ytreat| / (Total absolute increment)]  |
| [Administration cost] | [Xadmin]  | [Yadmin] | [Xadmin – Yadmin]  | [|Xadmin – Yadmin|]  | [|Xadmin – Yadmin| / (Total absolute increment)] |
| [Monitoring cost]  | [Xmon]  | [Ymon] | [Xmon – Ymon]  | [|Xmon – Ymon|]  | [|Xmon – Ymon| / (Total absolute increment)] |
| [Tests] | [Xtests]  | [Ytests] | [Xtests – Ytests]  | [|Xtests – Ytests|]  | [|Xtests – Ytests| / (Total absolute increment)] |
| [Add more rows as needed] |  |  |  |  |  |
| Total | [XTotal] | [YTotal] | [XTotal – YTotal] | Total absolute increment | 100% |

Abbreviations: admin, administration; mon, monitoring; tech, technology; treat, treatment

# Appendix I: Price details of treatments included in the submission

## 1.1 Price of intervention, comparators and subsequent treatments

[See section 3.5 of the user guide for full details of the information required here.]

Table X Details of all costs, including intervention, concomitant, comparator and subsequent medicines, for each formulation used in the model

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Name | Form | Dose per unit | Pack size | List price | Source |  PAS price (if known) | eMIT price/date searched for (if available) |
| [Technology]  | [Mode of administration] |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| [Add more rows as needed] |  |  |  |  |  |  |  |

Abbreviations: eMIT, drugs and pharmaceutical electronic market information tool; PAS, patient access scheme