Guidance on the Reporting Format and Layout of Pharmacoeconomic Submissions to the National Centre for Pharmacoeconomics

September 2014

Version 1.4

Record of Updates

Version	Date	Description of changes
1.0	27.10.2010	
1.1	17.01.2013	Page 3: provision of working versions of models is required. The word “Recommendation” has been changed to guideline throughout text.
1.2	15.02.2013	Page 19, Section 5.2: the disaggregated PSA results should be presented within the working version of the economic model. These results will be used in the calculation of the Expected Value of Perfect Information.
1.3	01.10.2013	Page 12, Section 2.5: Evidence synthesis models should be replicable by the review group, i.e. model code and inputs should be provided.
1.4	30.09.2014	Page 13, Section 3.1: The basecase discount rate is made explicit. Page 23, Section 6.4: The uncertainty to be applied to the discount rate is made explicit.

Introduction

The following document outlines the guidelines for the preferred reporting format and layout of manufacturer submissions to the National Centre for Pharmacoeconomics (NCPE).

Guidance on data to be included and method of inclusion are provided. All data used to demonstrate clinical and cost-effectiveness must be presented clearly and include details of data sources. Tabular and graphical presentation guidelines are discussed where appropriate and necessary. The guidance in this document should be used in conjunction with the Guidelines for the Economic Evaluation and the Budget Impact Analysis Guidelines for Health Technologies in Ireland 2010 (available at: www.hiqa.ie).

The submission should be divided into core sections as follows:

Executive Summary
Section 1 – Background
Section 2 – Clinical Evidence
Section 3 – Description of Economic Evaluation
Section 4 – Results of Cost-Effectiveness Analysis
Section 5 – Analysis of Uncertainty
Section 6 – Budget Impact Analysis
Section 7 – Conclusion
Bibliography
Appendices

Please Note: Provision of the economic and budget impact models in an easy-to-use format to allow in-house data validation is required for reviewers at the NCPE.

This document may be updated periodically, therefore please refer to www.ncpe.ie to obtain the most recent version.

Executive Summary

An executive summary consisting of no more than two pages should preface the document encompassing an overview of the submission and the main findings of the economic evaluation.

Section 1 – Background Information

Text Requirements[1]	Recommended Tables and Figures
1.1 Describe the condition - Provide an overview of the clinical condition - Include standard diagnostic criteria/testing devices where appropriate - Disease classification (define subclasses where necessary and relevant) - Outline the proposed target population for the pharmacoeconomic assessment	
1.2 Epidemiology: - Provide details on the incidence and prevalence data (for each class/stage where appropriate). Use Irish data where possible - Outline the natural history including prognosis, mortality and progression features	**Figure:** Natural history of the condition

[1] Depending on the particular technology, not all points in this section need to be included.

Text Requirements	Recommended Tables and Figures
1.3 Pathophysiology of condition: - Describe briefly with particular reference to mode of action of the technology - Describe the symptoms and clinical consequences of disease	
1.4 Current treatment strategy/strategies: - Present current best-practice guidelines / consensus guidelines / literature-based sources for the condition - Provide details of the relevant comparator(s) used for the indication under review and justify rationale	
1.5 Treatment of condition in Irish setting: - Describe accepted treatment strategies i.e. routine clinical practice and recommended standard of care in the Irish setting	**Figure:** Algorithm of treatment for condition in the Irish setting.

Text Requirements	Recommended Tables and Figures

1.6 Description of technology[2]
- State relevant regulatory information:
  o License information for the technology for the indication(s) specified in the submission as detailed in the summary of product characteristics
  o Any other existing or potential future indication(s)
  o License status of the product for the proposed indication(s) specified in the submission
  o Potential or actual launch date for the technology for the indication(s) specified in the submission
- Review:
  o mode of action and pharmacology
  o clinically relevant interactions
  o pharmacokinetics
  o dosing and administration guidelines
  o pharmaceutical form
  o administration requirements
  o recommended monitoring requirements
- State anticipated place in therapy of new technology
	Table: Description of technology to include:
	a) information on approved name
	b) brand name
	c) pharmaceutical form(s)
	d) strengths available
	e) route of administration
	f) pack/package size

[2] Generic name should be used throughout submission in preference to proprietary name.

Section 2 – Clinical Evidence

An explicit outline of the method of locating and selecting the studies used for the clinical evidence assessment should be provided. Where a systematic review is conducted, provide an **appendix** outlining the method of conducting the systematic review (refer to PRISMA guidelines 2009, available at: http://www.prisma-statement.org/). Include search terms, databases searched, time frame, inclusion and exclusion criteria in an appendix. There should be a clear rationale for selecting and rejecting specific studies to demonstrate evidence of clinical benefits.

Text Requirements	Recommended Tables and Figures
2.1 Clinical efficacy data for technology - Review clinical studies included providing evidence of clinical benefits of the technology i.e. Phase III studies (randomised controlled trials (RCTs)), Phase I/II studies, open-label extension studies etc. - Provide an explicit overview of trials including study design, patient selection criteria (inclusion / exclusion), primary and secondary outcomes - Discuss the validity of use of surrogate markers where included - Discuss the patient populations studied and their generalisability to the intended population for the licensed technology - Provide an in-depth analysis of the primary and relevant secondary outcomes of trials	**Table**: Overview of all clinical studies reviewed for technology with following headings: - Reference source - Acronym (where applicable) - Study type i.e. phase I, II, III, open-label etc. - Study description (safety, efficacy, dose-ranging etc.) - Comparator in study (and dose where applicable) - Patient population studied (including sample size and inclusion / exclusion - criteria)

Text Requirements	Recommended Tables and Figures
- Specify where results are based on interim analyses - Where subgroup analyses are undertaken clearly present the rationale this and any potential limitations - Results should be presented in terms of absolute and relative risk with appropriate statistical summaries (including 95% confidence intervals) - Describe any limitations of the sources of the clinical efficacy data - Provide details of any ongoing studies for the technology in the indication(s) under review	– Primary and relevant secondary outcome(s) **Table**: Analysis of results of primary and relevant secondary outcomes in included studies: – Details of treatment arms and relevant baseline characteristics and results of primary and relevant secondary outcome(s) – Absolute and relative risk with appropriate statistical summaries
2.2 Safety data for technology - Detail sources of data for clinical adverse effects of the technology i.e. case reports, observational or controlled trials - Where subgroup analyses are undertaken, clearly present the rationale for this and any potential limitations - Results should be presented in terms of absolute and relative risk with appropriate statistical summaries - Describe any additional safety issues for the technology	**Table**: Summary of safety data, include absolute and relative risk with appropriate statistical summaries

Text Requirements	Recommended Tables and Figures
2.3 Efficacy/effectiveness data for comparator(s) - Review clinical studies included providing evidence of clinical benefits of the technology i.e. Phase III studies (RCTs), Phase I/II studies, open-label extension studies and relevant post-marketing studies etc. - Provide an explicit overview of trials including study design, patient selection criteria (inclusion / exclusion), primary and secondary outcomes - Discuss the validity of use of surrogate markers where included - Discuss the patient populations studied and their generalisability to the intended population for the indication under review - Provide an in-depth analysis of the primary and secondary outcomes of trials - Specify where results are based on interim analyses - Where subgroup analyses are undertaken clearly present rationale for same and limitations - Results should be presented in terms of absolute and relative risk with appropriate statistical summaries - Describe any limitations of the trials that may affect the quality of the evidence included in the submission	**Table**: Same as for tables recommended in section 2.1 above

Text Requirements	Recommended Tables and Figures
2.4 Safety data for comparator(s) - Detail sources of data for clinical adverse effects (method of location and selection) of the technology i.e. case reports, observational or controlled trials - Where subgroup analyses are undertaken, clearly present rationale for same and limitations - Results should be presented in terms of absolute and relative risk with appropriate statistical summaries – Describe any additional safety issues for the comparator(s)	**Table**: Same as for tables recommended in section 2.2 above
2.5 Recommendations on summarising the evidence - Provide details of the rationale supporting the choice of studies to provide the clinical evidence. Outline criteria for including / excluding trials from the evidence base - Clearly outline the methods used to combine data from different studies - Methods used to conduct meta-analysis of direct evidence from head-to-head studies should be clearly described - Indirect comparisons may be required if no head to head clinical trials with active comparators are available	**Table**: Summary of studies included **Figure**: Network diagram of selected studies for indirect comparison **Figure** – Forest plot of results using RR, OR or absolute findings (or regression analysis where applicable)

Text Requirements	Recommended Tables and Figures
- Provide details of the studies used in the indirect comparison and include a network diagram of selected studies. - The method of deriving an estimate of clinical benefit or adverse effects should be clearly described - Heterogeneity between studies and quality of the primary studies should be discussed - Results should be presented in terms of absolute risk and relative risk with appropriate statistical summaries - Evidence synthesis models should be replicable by the review group, i.e. model code and inputs should be provided.	

Section 3 – Description of Economic Evaluation

Text Requirements	Recommended Tables and Figures
3.1 Introduction - Clearly define the study question addressed (objective) - Detail the type of evaluation e.g. Cost-utility analysis (CUA) - State the perspective of the study i.e. HSE[3] for reference case - State the comparator(s) for the base case and any additional scenarios - State time period over which costs and benefits measured (time horizon) with appropriate rationale - State whether discounting for costs and benefits was undertaken. The discount rate (for costs and benefits) should be 5%.	**Table**: Summary of parameter estimates, with base case values, range, distributions and sources
3.2 Base case / scenario details - State the reimbursement scheme under which the base case is undertaken (e.g. GMS* scheme or HTDS*) - Detail alternative scenarios investigated where appropriate (e.g. DP* scheme, hospital only)	

[3] Health Service Executive - publicly-funded health and social care system in Ireland
* GMS: General Medical Services, HTDS: High Tech Drug Scheme, DP: Drug Payments

Text Requirements	Recommended Tables and Figures
– Provide details of the outcome of the analysis e.g. o cost per quality-adjusted life year (cost/QALY) o cost per life years gained (cost/LYG) o cost per adverse event avoided o cost per hospitalisation avoided etc. - Indicate the primary (i.e. QALY) and secondary outcomes (e.g. LYG) of the analysis	
3.3 Model description - Provide a clear description of the economic model - Methods for the quality assurance of the model should be described and details of the model validation provided (include model development history where appropriate) - Baseline estimates of survival should be derived from published population-based sources (i.e. Irish life tables; www.cso.ie). - Outline the method(s) of sensitivity analysis undertaken (i.e. one-way / probabilistic)	**Figure**: Diagram of model structure

Text Requirements	Recommended Tables and Figures
3.4 Model inputs **a) Effectiveness data** - Where modelling of efficacy / effectiveness data is undertaken to populate the model, provide a clear explanation of the methodology or methodologies used and the rationale - State the source of the effectiveness estimates used and cross-reference to section 2 (clinical evidence) of the submission - Provide a summary of **key assumptions** surrounding efficacy, effectiveness and safety / tolerability at the end of this section	
b) Measurement of resource use and costs - Describe the method used to identify, measure and value resource use (e.g. hospitalisations, primary care visits, management of adverse events, costs associated with waning efficacy and switching treatments etc.) and unit cost data. Include justification and source of data. Irish data should be used where possible - if data are applied from other jurisdictions, justify the rationale. - Where cost data are obtained from the literature, methods used	**Table:** Cost data including description of resource use data, quantity of resources, unit costs, and source of resource use and unit cost data

Text Requirements	Recommended Tables and Figures
to identify data should be described. Where several sources are available, justification should be provided for the choice of cost - Report resource use items and unit costs separately - Provide a clear description of the drug cost data for the new technology, the comparator (s), and concurrent medication (e.g. to manage adverse events). Include a description of relevant margins and pharmacy dispensing fees in disaggregated form[4]. - Provide a summary of **key assumptions** used to estimate resource use and cost data at the end of this section	
c) Valuing health-related quality of life (HRQoL) - Detail the health states that are assigned a utility weight - Include source of data and justification for selection of utility values. Irish data should be used where possible. If data are applied from other jurisdictions, justify the rationale - Where utility values are derived from the literature, methods used to identify data should be described. Details of any systematic reviews of the literature should be presented in an accompanying appendix. All utility values reported in the literature should be	**Table**: Utility scores assigned to parameters and sources of data

[4] Refer to NCPE drug cost guidelines available at www.ncpe.ie

Text Requirements	Recommended Tables and Figures
clearly described and the rationale for the value included in the evaluation provided - Ensure health states reported in the literature reflect the health state in the submitted economic evaluation - Where mapping of HRQoL from a disease-specific instrument to a generic instrument is undertaken, provide the rationale for doing this and a clear explanation of methods used - Provide a summary of **key assumptions** surrounding HRQoL inputs at the end of this section	

Section 4 – Results of Cost-Effectiveness Analysis

Note: all results should be presented in a disaggregated and aggregated form (e.g. hospitalisations avoided, LYG, HRQoL and QALYs).

Text Requirements	Recommended Tables and Figures
4.1 Base case Incremental Cost-Effectiveness Ratio (ICER) - Detail explicitly the base case analysis and the resultant ICERs for the comparator(s)	**Table**: Costs, incremental costs, expected QALYs, incremental QALYs and ICER (i.e. incremental cost per QALY) **Figure:** Cost-effectiveness plane of results for base case scenario (QALYs on x axis, costs on y axis)
4.2 Scenario ICER results - Provide individual scenario ICER results (which can include the societal perspective)	**Table:** Costs, incremental costs, expected QALYs, incremental QALYs and ICER may be required for each scenario as appropriate **Figure(s) –** Cost-effectiveness plane of results for alternative scenarios (QALYs on x axis, costs on y axis) may be required for each scenario as appropriate

Section 5 – Analysis of Uncertainty

State the areas of uncertainty concerning the cost-effectiveness of the intervention (refer to key assumptions in Section 3 above).

Text Requirements	Recommended Tables and Figures
5.1 One-way sensitivity analysis (SA) - State key parameters explored in the one-way sensitivity analysis and ranges over which parameters are varied. Provide justification for choice of variables and ranges for individual parameters.	**Table**: Parameters examined, base case value, range over which parameters are varied and resultant effect on ICER **Figure**: Tornado diagram to display the results of one-way sensitivity analysis
5.2 Probabilistic sensitivity analysis (PSA) - Present clear methodology of probabilistic sensitivity analysis - Undertake analysis to demonstrate cost-effectiveness of the technology at a range of threshold levels - The disaggregated PSA results should be presented within the working version of the economic model. These PSA results will be used in the calculation of the Expected Value of Perfect Information.	**Table:** Probability of cost-effectiveness at a range of threshold ICER values **Figure(s)**: Probabilistic sensitivity analysis. Cost-effectiveness scatter plots (incremental QALYs on y axis, incremental costs on x axis) **Figure(s)**: Cost-effectiveness acceptability curve(s) (CEACs) (ICER threshold on x axis, probability of cost-effectiveness on y axis)

Section 6 – Budget Impact Analysis

Text Requirements	Recommended Tables and Figures
6.1 Target population - Clearly state the method of estimating the budget impact of the intervention in the Irish setting. State sources of data and any assumptions. Justify any assumptions that have been made. - Include data on: o An estimate of the total number of patients who have the condition relating to the indication under consideration (**prevalence**) o An estimate of the number of newly diagnosed patients with the condition over the first five years after introduction (**Annual incidence**) o Estimated number of patients eligible for treatment per year (prevalent cases + incident cases less those who recover or die) o Where specific sub-group addressed include number of eligible patients o Provide an estimate of the number of patients currently treated for the condition	**Table:** Estimated number of eligible patients who have the condition, estimated number of newly treated patients with proposed intervention, estimated number of patients switched to proposed intervention from an existing treatment(s) from years 1 to 5.

Text Requirements	Recommended Tables and Figures
○ Provide an estimate of the number of patients likely to be treated with the proposed technology (these may be newly treated patients or patients who are switched from an existing treatment). Include any assumptions related to market share and forecasted uptake. - Assess annual number of eligible patients over five year horizon	
6.2 Costing – Include the annual direct costs associated with the new treatment including: ○ Average dose and duration of therapy (range) ○ Average cost per patient per year over five year period – Report resource use and unit cost data separately – Include a description of relevant margins and pharmacy dispensing fees in disaggregated form[5]. – Include any direct cost savings associated with the new treatment over time. In general this would include cost offsets from switching from an alternative therapy, potential savings if switching from a parenteral to an oral product.	**Table:** Drug costs for the proposed new intervention and existing treatment(s).

[5] Refer to NCPE drug cost guidelines available at www.ncpe.ie

Text Requirements	Recommended Tables and Figures
6.3 Budget impact – Provide a summary of the total and incremental budget impact in each of the first five years following introduction. – The total budget impact should include annual costs associated with the introduction of the new technology. – The incremental budget impact should reflect the annual cost of introducing the new technology and the impact of replacing existing technologies and other potential cost offsets.	**Table:** Total budget impact of introducing proposed new intervention from years one to five. **Table:** Incremental budget impact (including replacement costs of existing treatments and any potential cost offsets) from years one to five.
6.4 Analysis of uncertainty – Uncertainty around key parameters should be explored. At a minimum the following parameters should be included in a one-way sensitivity analysis: o Number of eligible patients per year o Uptake rate of new technology o Rate of replacement of existing technology(ies) o Cost of new technology o Cost of comparator where uncertainty exists (e.g. comparator not currently reimbursed or published prices not available)	**Table**: Parameters examined, base case value, range over which parameters are varied and resultant effect on budget impact.

Text Requirements	Recommended Tables and Figures
○ Cost of other potential cost offsets ○ The discount rate (costs and benefits) should be varied to 0% and 10%. – Scenario analyses may also be required to explore the impact of reimbursement under alternative reimbursement schemes. – Justification should be provided for the range of values included in the sensitivity analysis.	

Section 8 – Conclusion

An overview of the main findings of the submission may be provided.

Bibliography

- References can be presented in Vancouver or Harvard style.
- References used for any systematic review(s) may be provided in the relevant appendix.

Appendices

The following may be included as supplementary appendices:

- Details of systematic reviews
- Summary of product characteristics
- Any other relevant supporting data

Please submit the following information to the NCPE Review Group:

1. Electronic copy of submission
2. Electronic copy of the cost-effectiveness and budget impact models
3. Three bound paper copies of the submission
4. Electronic copies of the references included in the bibliography

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