Beneluxa
Initiative on Pharmaceutical Policy

Applicant Submission Template

Type of submission:

Comparative effectiveness and budget impact ☐

Comparative effectiveness, pharmacoeconomic model and budget impact ☐

International non-proprietary name:

Brand:

Formulation(s):

ATC-Code:

Therapeutic indications:

Applicant Company:

Applicant company representative: Name

                                           Signature

Date of submission:

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Version Control

Version	Date
1.0	15/05/20
2.0	08/12/2020

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This document outlines the content and format of the written submission via the Beneluxa process. Commercial- or academic-in-confidence data should be highlighted throughout the document. Please note that this is a living document and will be updated periodically. Please refer to www.Beneluxa.org to obtain the most recent version prior to submission.

Double-sided printing should be used when preparing the completed applicant template for submission. All pages in the submission, including appendices, should be numbered. While additional sub-headings may be included in the submission, do not otherwise alter the heading structure provided.

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Abbreviations

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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.

1. Disease and its management

1.1 Description of the disease/condition

- Provide a brief description of the disease/condition including an overview of the natural history of the disease, diagnosis, symptoms and clinical outcomes, causes or risk factors, disease-specific mortality etc.

1.2 Epidemiology of the disease/condition in Beneluxa countries

- Tabulate the incidence and prevalence of the disease/condition in each of the Beneluxa countries, in the general population and among relevant subgroups.

1.3 Treatment guidelines and clinical pathway for patients

- Describe how the disease/condition is managed and if this differs between the Beneluxa countries i.e. other available treatments, current standard of care (routine care) and best practice, supported by data confirming how this was established. Include both licensed and unlicensed therapies where applicable.
- Summarise local treatment/disease guidelines if available. Summarise other international and regulatory guidelines which are followed in Beneluxa countries and describe any variation in disease management, supported by data confirming how this was established.
- Where evidence is based on expert opinion, provide a detailed description of the methods and results of the expert elicitation process (see Appendix 1).
- Please describe the outcomes considered most relevant in the condition with supporting evidence and where proposals are made for including or excluding outcomes please provide adequate validation of these choices; in particular make reference to outcomes most relevant to patients with supporting evidence.

2. Intervention under assessment

2.1 Therapeutic indication

- State the regulatory approval status of the intervention. Specify the date of authorisation or CHMP opinion. Ensure that the European public assessment report (EPAR) is submitted in the reference file.

- State the therapeutic indication as approved by the EMA, including relevant conditions or restrictions. Indicate if the licensed therapeutic indication in the EMA varies from other jurisdictions. State all other indications for which the intervention is currently licensed, or for which additional indications are anticipated in the future.

- Indicate if the intervention has an orphan designation from the EMA, and if the intervention is a generic/biosimilar medicinal product.

- Include a description of the specific subgroup if the Applicant is applying for reimbursement for a 'smaller' indication.

2.2 Description of the intervention

- State the international non-proprietary name (INN), proprietary name, formulation, licensed dose, frequency, route of administration and duration of use of the intervention.

- Indicate if specific tests or investigations are required for targeted therapy e.g. biomarker testing, companion diagnostics etc.

- Indicate if there are particular requirements for dispensing or administration of the intervention or if co-prescribed drugs are required.

- State the ATC code and drug class. Summarise the mode of action and pharmacology, clinically relevant interactions and pharmacokinetics.

2.3 Anticipated place in therapy

- State the anticipated place in therapy of the intervention with respect to other available therapeutic options, supported by data confirming how this was established. Identify relevant comparators for the comparative evaluation.
- Where evidence is based on expert opinion, provide a detailed description of the methods and results of the expert elicitation process (see Appendix 1).
- Provide details of any current use of the intervention in Beneluxa countries e.g. as part of a clinical trial or early access programme, or in an unlicensed capacity.

2.4 Previous economic evaluations/assessments of relevance to the current assessment

- Describe the outcome of any previous comparative or cost-effectiveness assessments of the intervention/comparator(s) for this/other indication(s).

3. Clinical/Pharmacotherapeutic evidence

Where a joint comparative effectiveness report has been completed by EuNetHTA and has been deemed as sufficient for all members of the Beneluxa initiative this may be included in this section.

All clinical efficacy and safety evidence included in the submission should be selected following a systematic literature search to identify relevant data sources, and reported in accordance with PRISMA guidelines. Justify the selection of specific sources. Where evidence is based on expert opinion, provide a detailed description of the methods and results of the expert elicitation process (see Appendix 1).

3.1 Clinical efficacy evidence

- Provide a brief overview of the clinical development programme supporting product registration. Summarise the programme under the headings in Table 1.

Table 1. Summary of clinical development programme

Study	Methodology	No. of Patients	Inclusion criteria	Treatments	Primary endpoints	Secondary endpoints	Duration of follow-up

- Describe the main studies from Table 1 in further detail. Studies directly comparing the intervention with the comparator(s) of interest to the decision-maker are of most relevance. Provide the rationale for selection of studies for detailed description. Describe each of the studies under the following headings *(may be tabulated as appropriate)*:

  ➢ Design and methodology
  ➢ Inclusion and exclusion criteria
  ➢ Treatments, allocation and retention
  ➢ Study endpoints
    Include both directly measured clinical outcomes and quality of life outcomes where measured. Justify the use of alternative endpoints. Discuss the validity of surrogate markers where included
  ➢ Analysis
    Describe data analysis methods including the statistical approach to missing data and to specific trial design features e.g. crossover, switching, responder

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> *enrichment etc.*

➢ Population

➢ Results

> *Please provide a summary of all results in tabulated form.*

	X (new intervention) (n)	Y (comparator) (n)	Treatment effect estimate (e.g. hazard ratio), confidence interval, p-value
Primary outcomes			
Secondary outcome			

➢ Quality assessment

> *Use a validated quality assessment tool, including risk of bias. Results of the quality assessment may be included in an appendix*

➢ Discussion of results and limitations

> *Include a discussion of the relevance to the population for the indication under review*

• Provide details of supporting studies of relevance to the decision problem including randomised/non-randomised observational studies, phase IV post-marketing studies etc.

3.2 Synthesis of evidence of comparative effectiveness

Complete this section if evidence synthesis methods were used to combine multiple sources of evidence to estimate comparative effectiveness and/or safety e.g. a pairwise meta-analysis, indirect comparison or network meta-analysis. If not applicable, write "N/A".

3.2.1 Study selection and data extraction

• Describe the process of study selection and data extraction, including a flowchart of the study selection process.

• Provide a clear list of excluded studies with reasons for exclusion.

- Where direct and indirect evidence were combined, present a diagram of the evidence network.

- Tabulate the details of each study selected for inclusion including study identifier, design, interventions, population, outcome definitions, analysis methods, baseline characteristics and results. Tabulate the individual study data extracted for inclusion in the evidence synthesis analysis *(This may be included in an appendix and a summary included in the main submission).*

- Assess the similarity of studies within the evidence network and discuss any implications for the evidence synthesis methodology, sensitivity analysis, results or interpretation.

3.2.2   Quality assessment

- Discuss the quality of the evidence network and any implications for the evidence synthesis methodology, sensitivity analysis, results or interpretation.

3.2.3   Data synthesis methodology

- Describe the type of analysis conducted i.e. pairwise meta-analysis, indirect comparison, adjusted indirect comparison, network meta-analysis or other type of analysis. Provide the rationale for the type of analysis.

- Define the outcome measure(s) used in the analysis. Where more than one outcome measure exists, justify the exclusion of alternative measures.

- Describe the statistical model(s) used for each outcome. Specify if a fixed-effects or random-effects model was used and justify the choice of model(s).

- For Bayesian analyses, provide details on priors, convergence and number of iterations.

- Describe how statistical heterogeneity was measured.

- Describe how consistency between the direct and indirect evidence was assessed.

- Outline the approach taken to sensitivity analysis and scenario analysis in order to explore uncertainty in the evidence and/or the analysis base, including uncertainty

related to bias, heterogeneity and/or inconsistency.

- Discuss the role for bias adjustment in the presence of imbalances in potential treatment effect modifiers, or heterogeneity in relative treatment effects.

- Provide details of the statistical software and code used to conduct the analysis *(This may be included in an appendix and a summary included in the main submission).*

3.2.4 Results

- Tabulate and present forest plots and/or posterior distributions of the mean treatment effects and 95% confidence/credible intervals of each treatment versus the common/reference comparator for each outcome, including measures of between-study heterogeneity for random effects models.

- Tabulate and present forest plots and/or posterior distributions of the mean treatment effects and 95% confidence/credible intervals of the intervention versus the comparator(s) for each outcome.

- If absolute treatment effects parameters are required for the economic model, tabulate the absolute treatment effects and 95% confidence/credible intervals for each treatment and outcome.

- Tabulate a comparison of the direct and indirect evidence – present results of pairwise comparisons from the evidence synthesis alongside corresponding results from direct comparative studies, and pairwise meta-analysis if appropriate.

- Present results of model diagnostics to justify model selection.

- Provide the results of the statistical assessment of heterogeneity in the relative treatment effects and inconsistency in the evidence network.

- Present the results of sensitivity analyses, including any adjustments to the analysis as a result of bias, heterogeneity and/or inconsistency.

3.2.5 Discussion

- Discuss the results of the analysis, including the internal and external validity of the analysis, and the assumptions regarding study similarity and evidence consistency.

3.3 Clinical safety

- Provide details of the adverse events occurring in the identified studies, in terms of absolute and relative statistical measures, specifying the population to which the results relate, and highlighting significant differences between the intervention and comparator(s).
- Summarise the key safety issues related to the intervention, and associated risk management requirements.
- Summarise the differences in safety profiles between the intervention and comparator(s), including results of any evidence synthesis analyses.

4. Experience, applicability and usability

- Experience

  Summarize the experience with the drug under investigation vs. the comparator. The experience is categorized as limited (<3 years on the market or <100,000 prescriptions with a not chronic indication / <20,000 with chronic medication), sufficient (>3 years on the market or >100,000 prescriptions with a not chronic indication / >20,000 with chronic medication or broad (>10 years on the market).

- Applicability

  Contra-indications, specific groups (elderly, renal/hepatic impairment, paediatrics), interactions and warnings and precautions of the drug under investigation/assessment and the comparator drug should be included.

- Usability

  Route of administration and the administration frequency and other point for discussion should be mentioned. Claims about a better usability should be supported by study results.

Sections 5-7 are to be completed if a full pharmacoeconomic assessment has been requested

5. The decision problem and model structure

5.1 Population

- Define the population included in the economic evaluation including subgroups if relevant. Provide justification if this does not reflect the licensed therapeutic indication. Provide a comparison on generalisability to the country specific populations under consideration.

- Populations or population subgroups should not be defined on the basis of response/non-response to treatment. This is more appropriately captured in the model using a treatment stopping-rule following response assessment.

5.2 Intervention

- Define the intervention included in the economic evaluation in terms of international non-proprietary name, proprietary name, formulation, dose, frequency, route of administration and duration of use. Provide justification if this does not reflect the licensed therapeutic indication.

- If treatment discontinuation is based on the observed duration of use in a clinical trial, or the application of a responder rule, describe the relevance of treatment discontinuation assumptions to clinical practice.

5.3 Comparators

- List all the relevant comparators included in the economic evaluation in terms of international non-proprietary name, proprietary name, formulation, dose, frequency, route of administration and duration of use. Provide justification if these details do not reflect the licensed therapeutic indication(s), posology and method of administration.

- Provide the rationale for the inclusion (and exclusion) of relevant comparators identified in Sections 2.iii) and 3.iii).

5.4 Model structure

- Describe the type of model used, time horizon and cycle length. State if a half-cycle correction was applied. Provide the rationale for these model choices.
- Describe the model structure and provide a model diagram.
- If a state transition model was used, describe the model health states, patient pathways through the model and clinical outcomes.
- Provide the rationale for the model structure in terms of the natural course of the disease/condition and the clinical relevance/importance of model outcomes to patients.
- If progression through the model is based on a surrogate marker, provide the rationale and evidence base for use of the marker.
- Describe all methods and assumptions used to derive baseline model transition probabilities including a description of the systematic search employed to identify relevant sources. Present the transition probability matrix.
- Justify the relevance of the model to the population in question.
- A comprehensive suite of quality assurance checks should be conducted and reported, to ensure the internal and external validity of the model. Provide details and results of all model verification, external validation and quality assurance exercises.
- In tabular format, clearly detail and justify all assumptions regarding the model structure.

5.5 Perspective

- The perspective of the analysis should be both payer (base case) and societal (please refer to country specific guidelines). State the perspective of the primary analysis and of any secondary analyses conducted.

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6. Economic model inputs

Select economic model inputs following a systematic literature search to identify relevant data sources, and report search results in accordance with PRISMA guidelines. Justify the selection of specific sources. Where evidence is based on expert opinion, provide a detailed description of the methods and results of the expert elicitation process (see Appendix 1). Model inputs should be derived from the population in question, where available. All parameter values should be presented together with measures of precision e.g. mean value and 95% confidence interval.

6.1 Treatment effectiveness

- Describe the mechanism by which the intervention alters the disease course in the model.
- Describe the application of treatment effects in the model.
- Describe the source of treatment effects for the intervention and comparator(s) in the model, including a description of the systematic search employed to identify relevant sources.
- If treatment effects were determined by patient-level data, analysed using non-parametric or parametric survival analysis methods, present a range of models within the written submission and electronic model and systematically assess model fit. Provide the corresponding summary outcomes predicted by the models e.g. mean overall survival, mean progression free survival etc, and compare with equivalent outcome results from clinical trials.
- If treatment effects were extrapolated over the model time horizon, describe the persistence or durability of treatment effects of both the intervention and comparator(s). Provide the rationale and evidence to support the extrapolation of treatment effects.
- Provide details of all analyses conducted to derive and extrapolate treatment effects.
- Clearly detail and justify all assumptions regarding treatment effectiveness.
- Tabulate the mean parameter values and ranges applied in probabilistic analyses and deterministic sensitivity analyses, including justification for the chosen ranges and

probability distributions.

- Outline the approach taken to sensitivity analysis and scenario analysis in order to explore uncertainty in treatment effectiveness.

6.2 Health-outcomes

- Describe the health outcomes captured by the model in terms of the expected health-related benefits and harms represented by model health states and/or events. The preferred evaluation type is a cost-utility analysis with the outcomes expressed in quality-adjusted life years (QALYs).The EQ-5D descriptive system is the preferred method of measuring health-related quality of life (HRQoL), with utilities derived from an EQ-5D relevant country value set valuation set from a representative sample of the general population (please see country specific guidelines on versions to be used per country i.e. 3L or 5L). Additional outcomes such as life years gained may also be presented.

- Justify the inclusion or exclusion of selected benefits and harms (adverse events) in the model.

- Describe the sources of HRQoL utility data used in the model, including a description of the systematic search employed to identify relevant studies. Provide the rationale for the choice of data sources.

- If HRQoL outcomes were measured during the clinical development programme, describe the methods and results of the analysis. Provide rationale for inclusion/omission of trial results in the model.

- Provide details of all analyses conducted to estimate utility values including details of the population, the timepoint of measurement, response rates, the instrument and valuation methods, the approach to missing data and mapping technique if used. Discuss the relevance of the population from which estimates were derived to the Beneluxa population in question.

- Clearly detail and justify all assumptions regarding the application of utility values in the model.

- Tabulate the mean parameter values and ranges applied in probabilistic analyses and

deterministic sensitivity analyses, including justification for the chosen ranges and probability distributions.

- Outline the approach taken to sensitivity analysis and scenario analysis in order to explore uncertainty in health-related benefits and harms.

6.3 Resource use and costs

Describe all costs captured by the model including intervention and comparator costs (drug acquisition, administration, monitoring etc.), adverse event, health state and other costs. Direct costs relevant to the healthcare payer should be included in costs. Non-healthcare/wider societal costs, productivity losses associated with informal care, absenteeism from work etc. should be included as a scenario for the Netherlands. Justify the inclusion or exclusion of selected costs in the model.

6.3.1 Intervention and comparator costs

- State the ex-manufacturer price of the intervention (per pack) exclusive of tax. Alternative prices may be included in a sensitivity analysis. State the ex-manufacturer price of the comparator(s).If a Patient Access Scheme (PAS) or confidential discount is in place for a comparator, include a plausible range of prices in sensitivity analysis. State whether value-added-tax (VAT) is payable on the intervention/comparator(s).
- Include a table using the headings described in Table 2 outlining the price per year (or treatment course as applicable) of the intervention and comparator(s) detailing ex-manufacturer price, wholesale margin, fees, rebates and final reimbursement price under the relevant reimbursement scheme (exclusive of VAT). Include a separate table for each country.

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Table 2. e.g. For Ireland – this will need adjustment per country.

Price* per patient per year (or per treatment course) for the intervention and comparator(s).

Drug	Strength	Pack size	a. Price to wholesaler (PTW)	b. Pharmacy purchase price	c. Plus pharmacy fee	d. Less Rebate 5.25% on PTW	Total reimbursement price per pack	Cost/ patient/ year or treatment course
							b+c-d	

*Price should be list price per country and include relevant fees or mark-ups/margins as appropriate and in line with country specific cost guidance.

- Describe and provide the rationale for any assumptions regarding the dose of the intervention/comparator(s) and the duration of treatment/rate of discontinuation applied in the model.

- Where applicable the length of treatment should be determined from the mean treatment duration as opposed to the median. If the source informing the mean duration of treatment is not fully mature this should be noted in the submission.

- Describe the measurement and valuation of administration and monitoring costs associated with the intervention and comparator(s).

- Please provide a scenario analysis with indirect medical costs; medical costs of unrelated diseases due to living longer. For example the cost of breaking a hip for a patient who lived longer due to a heart transplant. To calculate these costs a tool used in the Netherlands can be used; Practical Application to Include future Disease costs (PAID, https://www.imta.nl/paid/).

6.3.2   Health state, adverse event and other costs

- Describe the sources of resource use and unit cost (refer to country specific guidelines) data used in the model, including a description of the systematic search employed to identify relevant studies. Provide the rationale for the choice of data sources.

- If resource utilisation was measured during the clinical development programme, describe the methods and results of the analysis, and discuss the relevance of the trial protocol to standard practice in Beneluxa countries. Provide rationale for inclusion or omission of trial results in the model.

- Describe the methods of converting costs from a different year or reported for a different country, if relevant.

- Clearly detail and justify all assumptions regarding the application of resource use and cost data in the model.

- Tabulate the mean parameter values and ranges applied in probabilistic analyses and deterministic sensitivity analyses, including justification for the chosen ranges and probability distributions.

- Outline the approach taken to sensitivity analysis and scenario analysis in order to explore uncertainty in resource use and costs.

6.4 Discount rate

- State the discount rate applied to costs and benefits/harms, and the range of discount rates applied in sensitivity analysis. The discount rate varies between countries and the appropriate rate should be applied in the scenario relevant to the specific country. (See country specific guidelines)

6.5 Parameter Summary

- Tabulate all parameters used in the model including values, range/confidence intervals and probability distributions applied in probabilistic analyses and deterministic sensitivity analyses, and sources. Cross-reference parameter details to relevant sections in the written submission, and indicate the location of parameters in the electronic model

- Indicate that each parameter has been included in both probabilistic and deterministic analysis. Justify the exclusion of any parameter from probabilistic or deterministic analysis.

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7. Results of incremental cost-effectiveness analysis

7.1 Incremental analysis of costs and outcomes

- Calculate and present total costs and outcomes, incremental costs and outcomes and incremental cost-effectiveness ratios (ICERs) using both probabilistic (mean total costs and outcomes) and deterministic analysis, for the full population and relevant subgroups. If more than one comparator is included, present ICERs for each comparator compared with standard-of-care or baseline, followed by a fully incremental analysis with exclusion of treatments subject to dominance and extended dominance.

- Justify the number of replications conducted in probabilistic analysis.

- Explain any differences between the ICERs calculated using probabilistic and deterministic analysis.

- A burden of disease calculation should be included here for the Netherlands using the proportional shortfall method.

7.2 Analysis of Uncertainty

- Present the results of the probabilistic analysis using a scatter-plot of simulated cost and effect pairs on the incremental cost-effectiveness plane, and using cost-effectiveness acceptability curves and tables illustrating the probability of cost effectiveness at a range of willingness to pay thresholds as per country specific thresholds.

- Present the results of deterministic sensitivity analyses and scenario analyses in tabular format and using a tornado diagram. Conduct analyses for the full population and relevant subgroups. Discuss the key drivers of cost effectiveness.

- Ensure that all relevant information has been submitted, in the appropriate format, to allow analysis to be re-run and results to be reproduced.

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- Present a value of information analysis to explore whether additional research will reduce the uncertainty about specific model outcomes.

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Sections 8-12 are to be completed for *all* assessments under the Beneluxa Initiative

8. Budget Impact Analysis

8.1 Eligible population and market share

- State the estimated eligible population over the next five years and the proportion of market share predicted for the intervention, supported by data confirming how these estimates were established. Eligible population should comprise both the incident (newly diagnosed) and prevalent population. The eligible population should be provided both individually per country and cumulatively.

8.2 Gross drug budget impact

- Based on the eligible population and predicted market share, state the estimated gross budget impact (i.e. inclusive of fees, margins, rebates and VAT as applicable) in year 1, 2, 3, 4, and 5 (ensure at least five full calendar years are included). It is necessary to ensure that a full 5 year budget impact is included (i.e. Year 1 to be the 1st rolling 12 months). The gross budget impact estimates should only include the drug acquisition cost. Other costs, such as costs of administration or concomitant medication may be presented in section 8 (iv).
- Please also provide a scenario where it is assumed that on average patients start the treatment in the middle of the year, unless there is reason to assume this will not be the case (e.g. a therapy patients have desperately been waiting for). This means that the treatment duration in the first year will be for six months.
- Where applicable the length of treatment should be determined from the mean treatment duration as opposed to the median. If the source informing the mean duration of treatment is not fully mature this should be noted in the submission.

8.3 Net drug-budget impact

- Describe the potential drug costs and cost-offsets anticipated from the increased utilisation and/or displacement of other drugs. Present the net drug-budget impact analysis taking account of potential drug cost-offsets in year 1, 2, 3, 4, and 5.

- The net budget impact estimates should only include the drug acquisition cost. Other costs, such as costs of administration or concomitant medication may be presented in section 8 (iv).

8.4 Additional costs and cost-offsets

- Describe the potential for additional costs and cost-offsets which may impact the wider healthcare budget e.g. administration, monitoring, adverse event costs etc., supported by data confirming how these estimates were established. Present the net healthcare budget impact analysis taking account of potential wider healthcare costs in year 1, 2, 3, 4, and 5.

8.5 Analysis of Uncertainty

- Explore the impact of parameter uncertainty on the budget impact analysis using deterministic one-way sensitivity for each parameter/scenario analysis, providing clear rationale for the range of values applied.

9. Evaluations and reimbursement status in other jurisdictions

- Describe the reimbursement status of the intervention in other European countries, including the level of reimbursement, any restrictions on reimbursement, and any patient access schemes which may apply. Include the EU-average price and a list/table of international prices of the intervention (per pack, per strength) detailing ex-manufacturer price , rebates/local discounts if applicable, package size; Indicate the

outcome/status of HTAs of the intervention in other European countries.

10.   Conclusion

- Provide an overview of the main findings of the submission.

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11.   References

- Format all references in a standardised style (based on Vancouver), and list at the end of the submission. Verify that all in-text references correspond to the final reference list prior to submission.

- Where a reference is used to support specific evidence e.g. data point, parameter, other piece of information, the primary data source should be referenced rather than secondary sources such as other economic evaluations which have used the data. The relevant line/table/section should be highlighted within the primary reference source.

- Submit electronic full-text copies and an RIS formatted file of all references.

- Where data from clinical study reports are used please provide an electronic copy.

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12.   Appendices

- Additional information, details of search strategies, summaries of product characteristics and other supporting documentation may be submitted as appendices, as appropriate.

13.   Electronic models

- Microsoft Excel is the preferred software for Beneluxa submissions. A full Technical Specification Document, with sufficient detail to facilitate evaluation and reproduction, should accompany all electronic models. The specification document should include but not be limited to, guidance for model-users on how to use/adapt the model, and detail on the basic functioning, background calculations, and underlying assumptions of the model structure. At a minimum, the document should 1) define the role and describe the content of each tab of the Excel spreadsheet, and 2) list and describe all of the macros used in the model and define their relationship to the various tabs of the spreadsheet.
- Due to the complexities of parameters involved for the different countries it would be useful to set the model with a front interface allowing choice of country which will then automatically change the parameters e.g. discounting, utility etc. One model is preferred, incorporating all countries.

13.1   Cost-effectiveness model

- Where pharmacoeconomic modelling has been done the Applicant should submit a fully executable electronic copy of the cost-effectiveness model, ensuring that the model structure and all parameters values are as specified in the written submission.
- In Microsoft Excel models, all parameter values directly feeding into the deterministic and probabilistic calculation of costs and benefits should be listed in consecutive rows on a single worksheet.

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- Disaggregated probabilistic results i.e. all simulated cost and effect pairs, should be presented in the model, in addition to summary measures.

13.2   Budget Impact Model

- Where a budget impact model is submitted it should be fully programmable so that the Beneluxa assessment Group can easily examine the impact of a change in any of the parameters to the budget impact.
- Tabulate the price of the intervention and comparator(s) inclusive of wholesale margin, fees, rebates and VAT if applicable, per pack and per year (or treatment course as applicable).
- Please provide a separate (stand alone) excel model for the budget impact.
- Tabulate all parameters used in the model in consecutive rows on a single worksheet. Include the reference source and measures of uncertainty where available.

Appendix 1

Guidance on the use of clinical opinion as supporting evidence in the Applicant submission

Data inputs should be based on empirical data from randomised trials or nonrandomised studies. Where such data is lacking, expert opinion may be needed to supplement or support observed data. Expert opinion represents low level evidence and if used in a submission, **its inclusion should be justified**. Data collection should be systematically planned, documented and analysed, and reported in a transparent way. Applicant submissions which include data elicited through expert opinion should provide details of the elicitation process **including the following elements**:

1. A description of the criteria used for selecting the experts.
2. The numbers of experts approached.
3. The number of experts who participated.
4. A declaration of potential conflicts of interest from each expert whose opinion was sought.
5. The background information that was provided to the experts on the study and its consistency with the evidence provided in the submission.
6. Detailed method used to collect opinions e.g. either individually or through a meeting.
7. The medium used to collect opinions e.g. direct interview, questionnaire, telephone.
8. The questions asked (including a copy of the questionnaire or outline of the interview).
9. Numbers of responses received for each question.
10. The analytic approach used to collate the opinion, including the variability in opinion.

References:

Hunger et al. Using Expert Opinion in Health Technology Assessment: A Guideline Review. Int J Technol Assess Health Care. 2016 Jan;32(3):131-9

Australian Government Department of Health. Guidelines for preparing a submission to the Pharmaceutical Benefits Advisory Committee (PBAC Guidelines), version 5.0.