

**NCPE Rapid Review Applicant Submission Template**

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| --- | --- |
| **Drug:** | INN/Brand® |
| **Therapeutic indication:** |  |
| **Applicant Company:** |  |
| **Submission checklist complete:** | Yes/No |
| **Applicant company representative:** | Name and email address |
|  | Signature |
| **Second company contact:** | Name and email address |
| **Date of submission:** |  |

**Version Control**

|  |  |  |
| --- | --- | --- |
| **Version** | **Date** | **Description of key changes** |
| 2.0 | 02/02/21 | New template |

This document outlines the content and format of the written submission to the NCPE as part of a Rapid Review. The submission should be concise, consisting of summary information, with more detailed information provided in supplementary appendices, if necessary. Inclusion of confidential information should follow guidance outlined in Appendix 4 of this Template. This document may be updated periodically. Please refer to www.ncpe.ie to obtain the most recent version prior to submission.

All pages in the submission, including appendices, should be numbered. Do not alter the heading/table structure provided, unless otherwise specified.

All files included in the submission should be named in accordance with the specified file-naming convention and saved in the specified format, as outlined below. The international non-proprietary name (INN) should be included at the start of all filenames. Please do not use all capital letters or use underscores in the filename.

**File naming convention and format**

|  |  |  |
| --- | --- | --- |
| Type of file | File naming convention | File format |
| Applicant template | <INN RR Applicant Template>  e.g. Aspirin RR Applicant Template | .docx and .pdf |
| References | <INN RR references>  e.g. Aspirin RR references | .ris |
| Submission checklist | <INN RR Submission checklist>  e.g. Aspirin RR Submission Checklist | .pdf |

**Submission Checklist**

Prior to starting the Rapid Review assessment, the NCPE Review Group will ensure that the Applicant submission includes:

* a completed Rapid Review Submission Template in both .docx and .pdf format, including all Appendices
* an Appendix 2 .xls file showing drug cost calculations
* Full text copies of all references in .pdf format
* RIS file of all references
* a draft SPC, if the rapid review is submitted at CHMP positive opinion, as the SPC and EPAR will not be published.

If the submission is incomplete, the Applicant will be requested to submit the missing element(s). If errors are identified in the drug cost and/or budget impact calculations, the Applicant will be requested to correct the errors and resubmit the relevant files within three working days of the request.

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List of Abbreviations

1. Details of the Intervention

*Where applicable, Table 1 should be populated directly from the EMA/competent authority website (Table 1a), and the Summary of Product Characteristics (Table 1c).*

|  |  |
| --- | --- |
| **Table 1: Details of the Intervention** | |
| **1a: Regulatory status** | |
| International non-proprietary name: |  |
| Proprietary Name: |  |
| Therapeutic indication: |  |
| Currently designated an orphan medicine by the EMA: | Yes/No |
| Date of marketing authorisation: | DD/MM/YY  *If applicable, include one of the following:*  CHMP positive opinion  Conditional MA. Conditions include… |
| Other EMA/HPRA/FDA approved indication(s), or license extensions under EMA assessment (date of approval/status of assessment) | *Delete as appropriate:*  EMA licensed indications:  FDA licensed indications:  EMA Indications under assessment:  None |
| *Additional comment(s) on regulatory status may be added as narrative footnotes, in the following order \*, †, ‡, §, |, ¶.* | |
| **1b: Reimbursement status** | |
| Requested reimbursement setting: | *Please select from the options and delete others*  Hospital/National Drug Management System  High Tech Drug Arrangement (HT)  Oncology Drug Management Scheme (ODMS)  Community Drug Schemes (CDS)  Other: *please specify* |
| Current reimbursement status: | *Please select from the options and delete others*  Not currently reimbursed  Reimbursed on [X] scheme for [Y] indication |
| Other reimbursed formulations: |  |
| *Additional comment(s) on reimbursement status may be added as narrative footnotes, in the following order \*, †, ‡, §, |, ¶.* | |
| **1c: Description of drug** | |
| Formulation (pack size) |  |
| Dose and frequency |  |
| Route of administration |  |
| Store in a refrigerator | Yes/No |
| Duration of use | *If applicable, include details of response assessment recommendations and stopping criteria.* |
| ATC code |  |
| Mechanism of action |  |
| Other | *If applicable, Include details of specific tests or investigations required for targeted therapy, relevant pharmacokinetics, or specific dispensing/administration requirements.* |
| *Additional comment(s) on the drug description may be added as narrative footnotes, in the following order \*, †, ‡, §, |, ¶.* | |

1. The Disease and Place in Therapy

*Where evidence is based on expert opinion, provide an appendix describing the methods and results of the expert elicitation process (see Appendix 1-Clinical Opinion).*

* 1. The disease/condition
* Provide a brief description of the disease/condition
  1. Epidemiology of the disease in Ireland
* State the incidence and prevalence of the disease/condition in Ireland, in the general population and among relevant subgroups.
  1. Clinical guidelines and standard of care in Ireland
* Summarise Irish treatment/disease guidelines if available. Summarise other international guidelines which are followed in Ireland.
* Describe how the disease/condition is managed in Ireland i.e. other available treatments, current standard of care (routine care) and best practice, and describe any variation in disease management, supported by data confirming how this was established. Include both licensed and unlicensed therapies where applicable.
  1. Place in therapy
* State the anticipated place in therapy of the intervention with respect to other available therapeutic options, outlining any perceived advantages/disadvantages of the drug over current standard of care, supported by data confirming how this was established. Do not include details of clinical efficacy in this section.
  1. Comparators
* Identify relevant comparators for the Rapid Review comparison of clinical evidence, costs and budget impact, supported by data confirming how this was established. The preferred comparator(s) is that which is most widely used in clinical practice in Ireland in the target population. Unlicensed drugs may also be relevant comparators if they are part of standard of care.

1. Clinical evidence 
   1. Study Design

* Briefly summarise the clinical trial programme for the drug for the indication in question, including the number of trials conducted. Identify the **pivotal** trial(s) and indicate if it is ongoing and if so, when it is expected to be completed and, if applicable, when the next data-cut is expected. A summary of the **pivotal** trial(s) design should be presented in Table 2.1 (and subsequent tables, as necessary if there is more than one pivotal trial). The general structure of Table 2.1 should be retained, though adjustments may be made for the sake of clarity and simplicity. Studies directly comparing the intervention with the comparator(s) of interest to the decision-maker are of most relevance. In the absence of such studies, comment on the feasibility of conducting an indirect treatment comparison (ITC).

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| **Table 2.1: [Trial#1 name] trial design** | | |
| **clinicaltrials.gov identifier: [#]** | **[Trial design e.g. Phase III, double-blind, randomised controlled trial]** | |
| **Treatments** | **Key inclusion and exclusion criteria** | **Endpoints** |
| Intervention:  [Drug1, dose, duration, stopping rules etc]  [n=X]  Control:  [Drug2, dose, duration, stopping rules etc]  [n=X]  [Other relevant details of treatments or procedures] |  | Primary endpoint:  Key secondary efficacy endpoint(s):  Health-related Quality of Life endpoint(s): |
| [Abbreviations]  *Additional comment(s) on the trial design may be added as narrative footnotes, in the following order \*, †, ‡, §, |, ¶.* | | |

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| **Table 2.2 [Trial#2 name] trial design** |
| *Complete trial details as above* |

* 1. Clinical efficacy
* Provide a very brief summary of baseline demographics of the pivotal trial(s). Indicate if patient characteristics were well-balanced between the treatment arms or if any imbalances were observed.
* Present clinical outcomes from the pivotal trial(s) in Table 3, clearly showing the results of the primary and key secondary endpoint(s) for each study arm, in addition to relative effect measures and significance tests. Health-related quality of life measures should also be included, if available. Indicate if the results pertain to an interim or final analysis of the trial data and, if applicable, when results of the final data analysis will be available. If the trial is ongoing, indicate whether new patients are still being recruited. Specify the type of analysis underpinning the results e.g. ITT, mITT etc. The general structure of Table 3 should be retained, though adjustments may be made for the sake of clarity and simplicity. Additional tables, in the same format, may be added for relevant subgroups.

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| --- | --- | --- |
| **Table 3.1: [Trial name] clinical outcomes** | | |
| Date of [*interim/final*] analysis | |  |
| Expected date of final analysis (if applicable) | |  |
| **Outcome** | **[Drug]** | **[Comparator]** |
| [Primary endpoint] |  |  |
| [Key secondary endpoint(s)] |  |  |
| [HRQoL endpoint(s)] |  |  |
| [Abbreviations]  *Footnotes \*, †, ‡, §, |, ¶.* | | |

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| **Table 3.2: [Trial name] clinical outcomes** |
| *Complete trial details as above* |

* Provide a brief narrative summary of other clinical evidence of relevance. This may include other non-pivotal randomised studies, observational studies, long term extension studies etc.
* If an ITC has been conducted, a brief summary of the feasibility assessment (if not previously discussed), methods and findings of the ITC may be submitted. However, it is outside the scope of the NCPE Rapid Review process to fully appraise an ITC.
  1. Clinical safety
* Summarise safety data, including a list of the most frequent adverse events observed in clinical trials and observational cohorts, and the incidence of Grade 3-5 adverse events.
* Summarise specific safety concerns and key warnings and precautions for use.
* Comment on the comparative safety versus relevant comparators of interest.

1. Comparative costs

* Details of all calculations and assumptions underpinning the drug costs should be included in a .xls file, Appendix 2-Drug cost calculations. Complete Table 4 and Table 5 with values extracted directly from Appendix 2. Detailed guidance on drug cost calculations is outlined in NCPE Guidelines for Inclusion of Drug Costs in Pharmacoeconomic Evaluations ([www.ncpe.ie](http://www.ncpe.ie)), and a drug cost calculator is also included in the NCPE Budget Impact Model Template.
* Please add/remove additional columns to/from Table 4 depending on the number of pack types that will be available e.g. different strengths, formulations, pack sizes etc. Update the column titles in the header row of Table 4 to reflect the different pack types.
* Where there are multiple presentations and strengths, it may be useful to add a row in Table 5 to represent an expected weighted average price of the drug. Provide information on how the weights are derived. For treatments which have a variable but limited duration of treatment, provide information on the expected mean duration of treatment and how this has been derived. For treatments which have variable dosing options (e.g. weight, body surface area) please justify values used in the analysis.

Costs included in Table 4 and Table 5 represent publicly-available “list” prices. If a confidential patient access scheme (PAS) is included in the submission, this information should be presented here also, using confidential tables 4-5, with full details of the PAS and its proposed implementation. Both list price and PAS price calculations are required.

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| **Table 4:Total drug cost per pack of [drug name] to the HSE** | | | |
|  | **Pack #1** | **Pack #2** | **Pack #3** |
| Strength |  |  |  |
| Pack size |  |  |  |
| Price to wholesaler\* |  |  |  |
| Reimbursement scheme |  |  |  |
| Total drug cost† per pack excluding pharmacy fees, excluding VAT |  |  |  |
| Total drug cost† per pack excluding pharmacy fees, including VAT |  |  |  |
| [Abbreviations]  *\*Based on the pricing application form (PAF) submitted to the HSE-CPU on [XX/XX/XXXX] OR \*Awaiting PAF*  *† including relevant fees and rebates, excluding pharmacy fees*  *‡ Footnote indicating that there is a 0% rate of VAT on oral medicines, if applicable*  *§ Footnote indicating that a PAS applies/is on offer, if applicable* | | | |

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| **Table 5: Total comparative drug cost to the HSE for the intervention and comparator(s)** | | | |
|  | **Total cost per patient per [year/treatment course†]\*** | | |
|  | Including VAT | Excluding VAT | Source |
| [Drug] Pack#1 |  |  |  |
| [Drug] Pack#2 |  |  |  |
| [Drug] Pack#3 |  |  |  |
| [Comparator] |  |  |  |
| [Abbreviations]  *\*Including all relevant fees and rebates*  †*Footnote indicating duration (and clear justification) if cost per year has been replaced with cost per treatment course*  *‡ Footnote indicating that there is a 0% rate of VAT on oral medicines, if applicable*  *§ Footnote indicating that a PAS applies to a particular drug, if applicable* | | | |

1. Budget Impact Analysis

* It is preference of the NCPE that the NCPE Budget Impact Model Template (available at <http://www.ncpe.ie/submission-process/submission-templates/budget-impact-model-template/> ) is used to guide Applicants in the calculation of budget impact estimates.
* Details of all calculations and assumptions underpinning the budget impact analysis should be included in Appendix 3-Budget impact analysis calculations. Alternatively, a completed NCPE budget impact model template may be included with the submission. All drug costs included in the budget impact analysis should correspond with those submitted in Appendix 2.
* Complete Table 6 based on the costs presented in Table 5. The gross drug-budget impact only includes drug-acquisition costs of the intervention (inclusive of fees, margins, rebates and VAT, as applicable). Costs associated with administration of the drug should not be included here. The net drug-budget impact may include potential drug-acquisition cost offsets anticipated from changes in the utilisation of other drugs. If a confidential patient access scheme (PAS) is included in the submission, a supplementary Confidential Table 6 should be included in this section.
* The “Eligible population” should directly reflect the prevalence and incidence of the disease in Ireland, and be specific to the population covered by the Marketing Authorisation. All other assumptions such as diagnostic availability, levels of testing, treatment uptake and market share should be factored into “Proportion treated”.
* If applicable, briefly describe the potential impact on the wider healthcare budget e.g. administration costs, concomitant drug costs, monitoring costs, adverse event costs etc. Do not provide quantitative estimates of the wider healthcare budget impact.

|  |  |  |  |  |  |  |
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| **Table 6: Drug-budget impact** | | | | | | |
| **Population** | **Year 1** | **Year 2** | **Year 3** | **Year 4** | **Year 5** | **5-year cumulative** |
| Eligible population\* |  |  |  |  |  |  |
| Proportion treated (%) |  |  |  |  |  |  |
| Treated population |  |  |  |  |  |  |
| Gross drug-budget impact |  |  |  |  |  |  |
| Including VAT |  |  |  |  |  |  |
| Excluding VAT |  |  |  |  |  |  |
| Net drug-budget impact |  |  |  |  |  |  |
| Including VAT |  |  |  |  |  |  |
| Excluding VAT |  |  |  |  |  |  |
| [Abbreviations]  *\* Provide a definition of the “eligible population” for the purposes of the BIA*  *† Footnote indicating that there is a 0% rate of VAT on oral medicines, if applicable*  *‡ Footnote indicating that a PAS applies to a particular drug, if applicable* | | | | | | |

1. International HTA

Complete Table 7 including the status of HTAs in the specified agencies

|  |  |
| --- | --- |
| **Table 7: International HTA** | |
| **Organisation** | **Recommendation/Status (date)** |
| NICE, UK |  |
| SMC, Scotland |  |
| NIHDI, Belgium |  |
| ZIN, Netherlands |  |
| AIHTA, Austria |  |
| CADTH, Canada |  |
| PBAC, Australia |  |
| ICER, US |  |

1. References

* Format all references in the Vancouver style, 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 or other piece of information, the primary data source should be referenced. 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. Website links alone are not sufficient due to the potential for web addresses to change over time. Screenshots should be provided as “full-text” copies in these cases. The number of full-text references should match the number of references in the submission.

1. Appendices

* Appendix 1: Clinical opinion, should be submitted if any evidence in the submission is based on expert opinion. Information provided in this appendix should follow the “NCPE Guidance on the use of expert opinion as supporting evidence in the applicant submission”, located at the end of this document.
* Appendix 2: Drug cost calculations, must be completed with a description of all calculations and assumptions underlying the drug costs included in the submission
* Appendix 3: Budget impact analysis calculations, must be completed with a description of all calculations and assumptions underlying the budget impact estimates. Alternatively, the NCPE budget impact template may be included with the submission.
* Appendix 4: Confidential information, includes a Confidential Information template which must be completed if the submission contains confidential information.

## Appendix 1: Clinical opinion

**NCPE 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**. Expert opinion may be a qualitative expression of an individual’s judgement, or a quantitative expression of judgement used to define point estimates of key model parameters and characterise uncertainty (6). In the case of quantitative data, appropriate mathematical aggregation methods should be used. All studies or exercises used to obtain expert opinion should be well-designed to minimise bias and reported with clarity and transparency. Applicant submissions which include data based on expert opinion should provide details of the process used to obtain the data **including the following elements** (6, 7):

1. A description of the criteria used for selecting the experts.
2. The numbers of experts approached.
3. The details of experts who participated.
4. The date(s) on which the expert opinion was obtained.
5. A declaration of potential conflicts of interest from each expert whose opinion was sought.
6. The background information that was provided to the experts on the study and its consistency with the evidence provided in the submission.
7. Detailed method used to collect opinions e.g. either individually or through a meeting.
8. The medium used to collect opinions e.g. direct interview, questionnaire, telephone.
9. The questions asked (including a copy of the questionnaire or outline of the interview).
10. The numbers of responses received for each question.
11. The responses received for each question.
12. The analytic approach used to collate the opinion, including the variability in opinion. This is of particular importance where quantitative expert opinion has been used to inform a model input parameter, in which case all of the data used to derive the parameter in addition to a description of the mathematical method or process used to aggregate the data is required.

## Appendix 2 (.xls file): Drug cost calculations

Details of all calculations and assumptions underpinning the drug costs should be included in an excel file labelled Appendix 2-Drug cost calculations. Values included in Table 4 and Table 5 of the submission, and any confidential costs, should be extracted directly from this file. Detailed guidance on drug cost calculations is outlined in NCPE Guidelines for Inclusion of Drug Costs in Pharmacoeconomic Evaluations ([www.ncpe.ie](http://www.ncpe.ie)), and a drug cost calculator is included in the NCPE Budget Impact Model Template.

## Appendix 3: Budget impact analysis calculations

Details of all calculations and assumptions underlying the budget impact estimates provided in Section 5 should be included in this Appendix. All drug costs included in the budget impact analysis should correspond with those submitted in Appendix 2. A clear explanation of how estimates of eligible population, treated population and market share were calculated should be included. All assumptions regarding treatment doses, durations and discontinuations should be clearly described and justified.The NCPE Budget Impact Model Template is available to guide Applicants in the calculation of the eligible patient population, drug acquisition costs and cost offsets, presentation of results and analysis of uncertainty.

A completed NCPE Budget Impact Model Template, showing the calculations underpinning the estimates in Table 6 may be submitted as an alternative to Appendix 3.

\*It is necessary to ensure that a full five-year budget impact is included (i.e. Year one to be the first rolling 12 months). Partial calendar years are not acceptable in budget impact models due to uncertainty in the exact date or month of introduction to the market.

## Appendix 4: Confidential information

**Submission of commercial/academic-in-confidence information**

In the interests of transparency of NCPE recommendations, all efforts should be made to ensure that information included in the Applicant Submission can be included, without redaction, in NCPE Rapid Review Assessment Reports. It is recognised, however, that certain information, for commercial or academic reasons, may be requested to be considered confidential, either by the Applicant, or other parties contributing to the Assessment. This type of data should be kept to a minimum in submissions. If confidential information is included in an Applicant Submission, it should be highlighted as such in all relevant documents, in accordance with the following convention: yellow for commercial-in-confidence, blue for academic-in-confidence. Submissions which include confidential information **must include a completed Table A4.1**, identifying all confidential information contained in the submission, the specific reason for identifying information as confidential, and the date/milestone on which the data may no longer be regarded as confidential. All information included in Table A4.1 will be reviewed by the NCPE Review Group. Any information which is not considered to warrant confidentiality will be highlighted by the NCPE Review Group during the assessment. Any information accepted as confidential by the NCPE Review Group, and subsequently included in the NCPE Rapid Review Assessment Report, will be highlighted as such.

*Types of information which* ***may*** *be considered confidential*

Detailed information must be provided to justify the identification of information as confidential in Table A4.1. It is insufficient to simply label information as “commercial-in-confidence” or “academic-in-confidence”. The following broad types of information may be considered confidential.

* Information which is not in the public domain, the publication of which may have a significant impact on the commercial interests of the Applicant.
* Scientific research findings which are not in the public domain, the publication of which may jeopardise the ability of the author(s) to publish the findings as a scientific paper.
* Price discounts/rebates submitted as part of PAS proposals.
* Budget-impact model outputs, estimated under the terms of a PAS.

*Types of information which* ***may not*** *be considered confidential*

* Information which is already in the public domain.
* Drug price (as outlined in Table 4)\*.
* Budget impact estimates including estimates of eligible patient population, treated patient population, gross drug-budget and net drug-budget impact\*.

*\*With the exception of prices and budget-impact model outputs, calculated/estimated under the terms of a PAS.*

**Table A4.1: Confidential information included in the Applicant Submission**

|  |  |  |
| --- | --- | --- |
| **Page and line number** | **Specific reason for confidentiality**  ***(identifying information as “commercial” or “academic” is insufficient”)*** | **Date/milestone after which information may not be regarded as confidential** |
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