# JNHB Submission Dossier Template

For Health Technology Assessment of Medicinal Products

Version 2.0 March 2025

| | |
|---|---|
| **Company** | |
| **Medicinal Product (INN, Brand®)** | |
| **Relevant therapeutic indication** | |
| **Company contact** | *Name and email address* |
| **Date of submission** | |

# Document history

| Version | Valid from* | Description of key changes |
|---------|-------------|----------------------------|
| 2.0 | March 2025 | Updated after feedback received from associations of pharmaceutical industry from the Nordic countries. Mainly minor wording adjustments. |
| 1.0 | June 2024 | First published version of a submission template by JNHB. |

*The document and its updates must be adapted by DMC, Fimea, Landspitali, NOMA and TLV in consensus to be valid.

# Background and introduction to the submission template

This template outlines the preferred overall structure and content of the written submission to JNHB. The JNHB submission template is based on the guidelines by the Health Technology Assessment (HTA) bodies part of the JNHB. The template is updated periodically. Please refer to the webpage [Joint Nordic HTA-Bodies](#) to obtain the most recent version of the template prior to your submission.

It is not mandatory to follow this template. Following the template and guidance will however ease the validation and lead to a smoother assessment process. The submission template contains guidance to the content and preferred modelling throughout the relevant sections. JNHB generally encourage pre-submission meetings, to offer further guidance and discussion regarding preparation of the documentation for the HTA. This template also contains the list of required documents on page 8.

For some of the input parameters, the Nordic HTA-bodies have different preferences for what should be included in the model. This is described in the relevant sections of this template as country-specific input. The submitted model should be flexible enough to allow adjustments for country-specific input. In this dossier, the company base case can be reported in any currency used in the JNHB countries.

Prior to final submission, please make sure to include the required documents, listed at page 8.

In case the predefined headings or subheadings are not relevant for your submission, please keep the main headings and simply state: "not applicable due to..". You may delete the subheadings and bullet points under each heading.

When inserting tables and figures, avoid using picture formats (jpeg, etc) to the extent possible. To make JNHB's reports as accessible as possible to individuals with impaired vision, ensure that included pictures have a high enough resolution.

# Table of contents

# List of Tables

# List of figures

# List of required documents

- Submission dossier as a Word file
- Attachments to the dossier as PDF or Word files
- Health economic model as an Excel workbook
  - The submitted model should be adjustable to all countries involved as assessors, co-assessors and reviewers in the assessment.
- Summary of Product Characteristics (EPAR SmPC)
- EPAR public assessment report for the relevant indication
- Full text of the clinical studies used in the assessment including studies/reports that are considered to be <u>central</u> for the health economic modelling
  - Full text for other studies should be available upon request
  - If "data on file" is used as documentation in the assessment, the relevant part of the documentation must be sent in separately, marked "data on file".
- Approval for market authorisation
- Nordic Article Number*
  *Medicines marketed in Denmark, Finland, Iceland, Norway and Sweden must have a Nordic Article Number, which must be stated on the packaging. Nordic item numbers are administered by Lääketietokeskus OY in Finland.

For IT security reasons, DMC strongly encourage that the Excel workbook with the health economic model is signed with a certificate if the model contains macros, see link for more information on how to sign [Digitally sign your VBA macro project - Microsoft Support.](#)

In addition to the items listed below, the person representing the company is required to have a power of attorney, stating that they are authorised to represent the company in this matter.

The dossier can be submitted before the product is granted market authorization, but the application will only be considered complete after market authorisation approval.

# List of Abbreviations

| Abbreviation | Definition |
|---|---|
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |
|  |  |

# 1. Background

## 1.1. Overview

*Table 1. Overview of intervention and submission*

| | | |
|---|---|---|
| **Medicinal product** | *INN, Brand®* | |
| **ATC-code** | | |
| **Pharmaceutical class** | | |
| | **For the indication relevant for the submission, state:** | |
| **Indication approved by EMA** | | |
| **Patient population relevant for assessment (if different from indication)** | | |
| **Posology** | | |
| **Route of administration** | | |
| **Conditional approval** | If applicable, specify: | |
| **Does treatment require prior biomarker testing, companion diagnostics etc.?** | If applicable, specify: | |
| | **Information on the clinical documentation:** | |
| **Pivotal/main studies for the indication under review** | e.g. *OVERVIEW-101 NCT10101010* | Study design, numbers included, data cuts, etc.. |
| | e.g. *OVERVIEW-101 OLE-study NCT10101011* | |
| | e.g. *OVERVIEW-102 NCT10101010* | |
| | e.g. *OVERVIEW-102 OLE-study NCT10101011* | |
| **Type of economic model: e.g., paritioned survival model, Markov model, or other (please specify)** | | |
| **Result of economic model using country-specific setting of Health Technology Developer (HTD) choice** | LY-gained | |
| | QALY-gained | |
| | Incremental costs | |
| | Cost pr. LY | |
| | Cost pr. QALY | |

Please state the name of clinical experts consulted for preparation of this submission.

*Table 2. Clinical experts contacted for preparation of the submission package.*

| Name | Place of employment |
|---|---|
|  |  |
|  |  |

## 1.2. Description of the disease and patient population

- Provide a brief description of the disease/condition including an overview of natural history of the disease, diagnosis, symptoms, clinical outcomes, causes or risk factors, disease-specific mortality, influence on quality of life etc.
- Provide a brief description of patient characteristics, including age, gender, risk-groups e.g. prognostic factors, in a Nordic setting. Please specify, if any differences in patient characteristics are expected between the Nordic countries.
- If there are any subpopulations relevant for the assessment, describe specific characteristics that differentiate between (sub)populations. Provide a rationale for the subgroup selection and indicate whether these groups were pre-defined (and how) in the clinical studies.
- Briefly describe any diagnostic tests and methods used for patient selection. Will the new intervention require altered testing compared to today's clinical practice?
- Estimate number of patients in each country, eligible to the new treatment (prevalence and yearly incidence)

*Table 3. Estimated numbers of patients eligible to the new treatment in the different countries*

| Country | Prevalence | Yearly incidence |
|---------|-----------|------------------|
| Denmark | N=xx | |
| Finland | | |
| Iceland | | |
| Norway | | |
| Sweden | | |

## 1.3. Current treatment practice

- Describe how the disease/condition is currently managed in the Nordic countries including available treatments and current standard of care.
- Illustrate with a diagram if appropriate.
- Describe any variation in disease management between patients and between countries.
- Descriptions should be supported by literature, guidelines and/or input from Nordic clinical experts.

## 1.4. Description of the intervention, anticipated place in the treatment pathway

- Provide a brief description of the intervention. Dosage regimen, route of administration etc.
- State the anticipated place in the clinical pathway of the intervention with respect to other available therapeutic options.
- Describe and explain any treatment(s) that would be replaced by the introduction of the intervention.
- Justify the choice of comparator(s) for the assessment based on the above and the similarity between Nordic countries.
- Descriptions should be supported by literature, guidelines and/or input from Nordic

clinical experts.

# 2. Clinical evidence

## 2.1. Overview of literature

- All clinical efficacy and safety evidence included in the submission should be identified following an information retrieval process including a systematic literature search and reported according to the PRISMA guidelines.

## 2.2. Summary of clinical evidence

- Describe the studies included for the intervention.
- Describe the studies included for the comparators.
- Summarise in tables below. Add or remove sections to/from the table as necessary.

*Table 4. Summary of clinical efficacy studies*

| **\<Name of clinical study 1\>** | |
|---|---|
| Study ID (NCT number) | |
| Study design | |
| Intervention | |
| Comparator | |
| Primary endpoint | |
| Important secondary endpoint(s) | |
| Observation time | |
| Data cuts *primary analysis and later planned analyses* | |
| **\<Name of clinical study 2\>** | |
| Study ID (NCT number) | |
| Study design | |
| Intervention | |
| Comparator | |
| Primary endpoint | |
| Important secondary endpoint(s) | |
| Observation time | |
| Data cuts *primary analysis and later planned analyses* | |

- Provide a summary of supportive studies of relevance to the decision problem including relevant and central studies supporting the health economic analysis. Add sections to the table if needed (i.e. more than one supportive study).
- A more detailed description of these studies and how they are used in the modelling

should be described in later sections.

Table 5. Summary of relevant supportive studies used in health economic modelling.

| <Name of supportive study 1> | |
|---|---|
| Study ID (NCT number) | |
| Study design | |
| Population | |
| Intervention | |
| Comparator | |
| Observation time | |
| Data cuts *primary analysis and later planned analyses* | |
| How is the data from this study used in the assessment? | |

- List and briefly describe relevant ongoing studies.

## 2.3. Efficacy results per study (intervention and comparator)

- Describe the studies from table 4 above, including a description of the study design and methodology (statistical analyses), population, most important inclusion and exclusion criteria, treatments and concomitant medications, subsequent treatments, and study endpoints.
- Refer to guidelines from EU-HTAR to ensure that proper methods are applied consistently.
- Provide a summary of the key efficacy findings for each study included in the comparative analysis (intervention and comparator studies) in table format.
    - Highlight results used in later cost-effectiveness analysis.
- Include results from subpopulations, when relevant
- Provide a short discussion on results and limitations of results.
- Discuss validity of surrogate markers if they are included.
- Describe and report the HRQoL outcomes measured during the clinical development program for the intervention and the comparators.

## 2.4. Evidence synthesis methods

- Complete this section if evidence synthesis methods (pair-wise meta-analyses or indirect comparisons) are used to estimate comparative effectiveness.
- Refer to guidelines from EU-HTAR to ensure that proper methods are applied consistently.
- The documentation should be based on the systematic literature search.
- Identify and discuss any between-study differences, particularly those which relate to potential prognostic variables and treatment-effect modifying variables.
- The following could be considered and discussed:
    - definition of endpoints
    - statistical analysis

- o duration of follow-up
- o types and distributions of a subsequent treatment received in the study,
- o etc
- Describe data synthesis methodology (statistical analyses)
- Present results of the evidence synthesis. Highlight results used in later cost-effectiveness analysis.
- Include a discussion on results, internal validity, external validity, assumption of exchangeability, and limitations.

## 2.5. Clinical safety

- Report adverse events (AE) and serious AEs in the clinical evidence for the intervention and comparator.
- Report treatment discontinuation, interruptions, and dose modification due to AE's in the clinical evidence for the intervention and comparator.
- Summarise the results in tables.
- Summarise associated risk management requirements.
- Discuss the differences in safety profiles between the intervention and comparator(s)

# 3. Health economic analysis

- The submitted model should be adjustable to all countries taking active part in the assessment to allow for an easy way to get results for all countries.
- All relevant variables and parameters in the model must be adjustable for the assessment team.
- The model must be flexible to allow adjustments for country-specific inputs.
- Preferably country-specific input should be included and can be modelled in the form of a "drop-down menu".
- Country-specific input variables are described in the latter sections.

## 3.1. Model structure and applicability

- Describe the type of model used, time horizon, cycle length, and perspective.
- Give a detailed description and justification of the chosen model-type in the context of the intervention for the relevant population in question.
- 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.
- Include a model diagram and description of the health states.
- The time horizon should be long enough to capture all health benefits and costs.
- The perspective should be limited societal perspective but not all countries include patient costs and indirect cost (such as productivity loss). Please include these country-specific costs in a "drop-down menu", when relevant.

*Table 6. Perspective and formalities applied in the health economic analysis.*

| Topic | Description |
|---|---|
| Model type | |
| Cycle length | |
| Half cycle correction | |
| Time horizon | |
| Perspective | |

## 3.1.1. Discounting

- The Nordic countries use different discount rates. Please allow for the model to switch between the different discount rates as country-specific input (preferable in the form of a "drop-down menu"). The discount rates are shown below.

*Table 7. Country-specific input for discounting*

| Country | Description |
|---|---|
| Denmark | 3,5 % annually |
| Finland | 3 % annually |
| Iceland | 3,5 % annually |
| Norway | 4 % the first 40 years, then 3 % annually for the next 35 years |
| Sweden | 0 %, 3 % and 5 % annually |

## 3.1.2. Model requirements

- Model requirements
  - Microsoft Excel is the preferred software for HTA submission.
  - A description of function and purpose of each sheet in the excel model must be provided.
  - In all models delivered, the sources for input data in the model must also be stated in the respective spreadsheet.
  - If the model uses macros, a description of the macros used should be provided. Visual Basic for Applications (VBA) code should include brief description of all actions. Make sure all macros run successfully before submitting .
  - Spreadsheets must be transparent, fully user modifiable and change of input variables should automatically update results, preferably with a reset button to return to original setting.
  - Spreadsheets should not contain password protected sheets or cells, contain no hidden cells, or utilise proprietary or non-transparent programmes and/or programming language.
  - All sheets should include visible headers by default. When possible, do not hide rows, columns, or sheets that are not used. If sheets (or parts of sheets) are not used but cannot be easily deleted (due to offset functions, macros, etc.), this should be clearly stated/highlighted.

- Provide a selected number of plots (plot of Markov-traces and /or other plots) that can aid assessors evaluate the modelling assumptions.
- When survival analysis techniques are applied, KM-curves and all extrapolations could be visualized within the same graph, within the health economic model. Include all-cause mortality for the general population from <u>any</u> of the Nordic countries (country of HTD choice).
- Attach the model technical report if relevant.

## 3.2. Population

- Summarise and compare the populations from the clinical studies, the relevant Nordic population, and the modelled population.
  - o Include discussion on subpopulations when relevant.
- Deviations must be discussed and justified with respect to transferability of results from the clinical study to the Nordic setting.

## 3.3. Intervention

- Describe / discuss the relevance of any deviations between how the intervention is prescribed in a Nordic setting and how it was used in the clinical studies, e.g., differences in dosing, frequency, route of administration, relative dose intensity, etc.
- Deviations must be discussed and justified with respect to transferability of results from the clinical study to the Nordic setting.
- Include description and discussion of subsequent treatments and background medication

## 3.4. Comparator(s)

- Describe / discuss the relevance of any deviations between how the comparator(s) is prescribed in a Nordic setting, in the clinical studies and in the model, e.g. study medication, differences in dosing, frequency, form of administration, etc.
- Deviations must be discussed and justified with respect to transferability of results from the clinical study to the Nordic setting.
- Include description and discussion of subsequent treatments and background medication

## 3.5. Modelling of treatment effectiveness

- This section describes the clinical parameters and variables included in the cost-effectiveness analysis.
- A complete and transparent description of how the outcomes from clinical studies/other reports are subsequently included in the health economic model.
- In general terms, describe and justify how the clinical data was implemented in the model, including how transitions between health states are modelled, sources of transition probabilities, assumptions made to model long-term efficacy beyond the study period.
- State the sources of clinical data included in the model; data-cut, follow-up time, population
- For time-to-event data describe the approach for fitting parametric curves and extrapolation.

- Structure this section with subheadings for each outcome, see examples below.
- For each subsection consider the following:

  General:
  o Clearly define what data have been used to inform the transitions.
  o Specify data-cut and population.
  o If surrogate outcomes are used, describe how these are linked to final outcomes.
  o If treatment effects were extrapolated over the model time horizon, describe the persistence or durability of treatment effects of both the intervention and comparator
  o Provide the rationale and evidence to support the extrapolation of treatment effects.
  o Describe how the clinical effects of potential subsequent treatments are modelled.
  o Discuss applicability of the parameters in Nordic clinical practice
  o Discuss uncertainty regarding the estimation of the input and modelling of treatment effects.

  Survival analyses:
  o If survival analysis techniques are used, describe the selection and applications of the techniques and validation of the clinical parameters. Describe and justify parametrisation and extrapolation and which criteria guided the choice of parametric model (such as AIC/BIC, visual fit, hazard plots, clinical plausibility, external data etc).
  o Include graphical presentation of time to event data curves, where both Kaplan-Meier (KM) data and the parametric distribution are shown in the same figure (in the spreadsheet).
  o Provide the 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.
  o Adjust accordingly for background mortality using data from <u>any</u> of the Nordic countries (choice of HTD).
  o If adjustment for treatment switching (crossover) is applied, see NOMA guidelines chapter 9 [submission-guidelines-april2024.pdf (dmp.no)](submission-guidelines-april2024.pdf).

  Transition probabilities:
  o Describe how transition probabilities were calculated from the clinical data
  o Provide Markov-traces and /or other plots that can aid reviewers critically appraise the modelling assumptions.
  o If appropriate, provide the transition matrix

  External data:
  o Describe how external data sources have been used to model disease progression, transition probabilities, background mortality, etc.
  o Selection of external data used to model natural disease progression (as a result of a systematic literature review).

### 3.5.1. Outcome 1 (e.g. Modelling of overall survival)

**Study outcome**
- Present the efficacy results from the clinical studies/other reports for the relevant populations.

**Modelling of study outcome (intervention and comparator)**
- Describe and justify specific choices related to how <u>this</u> input is modelled. Including, but not limited to, parameterisation and extrapolation, assumptions made on transitions, treatment effect, discontinuation, external validation, clinical opinion, etc.

### 3.5.2. Outcome 2 (e.g Modelling of short-term transition between health state X and Y)

**Study outcome**

**Modelling of study outcome (intervention and comparator)**

### 3.5.3. Outcome 3 (e.g. Modelling of subsequent treatment effect)

**Study outcome**

**Modelling of study outcome (intervention and comparator)**

### 3.5.4. Modelling of time to treatment discontinuation – intervention and comparator
- Time-to-treatment discontinuation (TTD) should be described here.
- State which population is used to calculate TTD.
- Describe and justify parametrisation and extrapolation if this is applied and which criteria guided the choice of model.
- Describe and justify assumptions regarding response/discontinuation rates, waning treatment effects, stopping rules, subsequent treatments, and other relevant factors, that impact results.

### 3.5.5. Relevant supportive outcomes not used in the health economic model
- Study outcomes that are not modelled in the cost-effectiveness analysis, but support assumptions or claims of clinical benefit may be presented in this section. This could for example be a primary composite outcome where the individual outcomes are modelled separately.

## 3.6.  Modelling of safety events
- Describe how AEs have been implemented in the health economic model and report disutility for each AE and duration of modelled AE.

- Justify the inclusion/exclusion of the modelled adverse events.

## 3.7. Health-related quality of life (HRQoL)

- EQ-5D is the preferred instrument in JNHB.
- If values from alternative instruments are used, they should preferentially be mapped to EQ-5D values using validated methods accompanied by a transparent description of the methods and the results should be compared to published quality-of-life data for the relevant patient group.

- The Nordic countries have different preferences for EQ-5D instrument and the source of the tariffs. Please allow the model to switch between country-specific input, when possible (preferable in the form of a "drop-down menu"). Table below shows the preferred instruments and tariffs for utility values in each country.

*Table 8: Country-specific preferences for EQ-5D instrument and tariffs*

| Country | Preference for utility calculation |
|---------|-----------------------------------|
| Denmark | EQ-5D-5L with Danish tariffs |
| Finland | No preference |
| Iceland | No preference |
| Norway | EQ-5D-3L with UK tariffs |
| Sweden | EQ-5D-3L with UK tariffs and EQ-5D-3L Swedish tariff in sensitivity analysis |

- Describe the methods and provide details of all analyses conducted to estimate utility values, including:
    o Number of subjects who responded to the questionnaires (compliance rates by visit and by treatment), including reasons for missing data, and differences, if any, between non-responders and responders.
    o The choice of statistical model for HRQoL analyses (e.g. regression model), including the full model equation, with a justification of variable selection, and description and justification of the correlation structure.
    o Handling of missing data
- Provide a description of external studies and data used for informing the model for each state in the model (using a systematic literature review).
    o Discuss applicability and limitations of external data in relation to a Nordic setting.

- Tabulate the parameter values used in the model (including SE/95%CI), and if relevant values gathered from other literature.
- Describe and justify all assumptions regarding the application of utility values in the model. Please consider the following:
    o Justify the choice of values, including strengths and weaknesses of the possible alternative choices.
    o Justify the inclusion or exclusion of selected outcomes in the model. All outcomes that impact patients' HRQoL should be included.

- o Describe adjustments made to utility values, e.g. baseline HRQoL value or age adjustments.
- To account for changes in morbidity and mortality in the general population with increasing age, development of HSUV over time must be age adjusted using the multiplicative method, using data from any of the Nordic countries (choice of HTD). Lack of age-adjustment should be justified.
- If treatment specific HSUV are used, this must be comprehensively justified and documented in clinical studies and have a clinical rationale

- Disutilities: Describe how disutilies have been calculated similar to above

## 3.8. Resource use and costs

**General information:**
- The company can select which country will serve as the basis for their health economic analysis in terms of references to resource use and unit prices (price lists) .
- Currencies for all actively participating HTA-bodies should be included in the model.
- For medicine acquisition cost, public prices are to be included for all countries in local currencies (DKK, SEK, ISK, NOK and EUR).
- For all other cost the HTD can choose
  - o To include country specific unit prices for all cost *or*
  - o To incorporate a feature in the model that allows for conversion between different currencies. It should be evident how currency conversion are handled in the model and what rates are used (DKK, EUR, ISK, NOK, SEK).
- If there are certain cost items that have a significant impact on the results, country specific unit prices should be included in the model to allow the assessor to estimate the impact in the different countries.
  - o JNHB will ask for country-specific unit prices if the cost has an impact on the analysis.
- For costs that have limited impact on the decision problem, the source of data can be of <u>any</u> country (choice of HTD).

### 3.8.1. Medicine acquisition costs
- Include country-specific public prices for medicine acquisition costs in the model.
- Information should also be presented in tables, se example below.
  - o For all countries describe/tabulate medicine acquisition costs including costs for intervention, comparators for subsequent and/or concomitant treatments.
  - o Include product numbers if available. Add a table for each country or include columns for all countries.

*Table 9. Medicine acquisition costs [country] (or add columns for all countries)*

| | Product number | Strength | Pack size | Public price* pr. Pack [country] |
|---|---|---|---|---|

| Non-proprietary name (proprietary name) | *e.g., 595728* | *e.g., 500 mg* | *e.g., 60 tablets* | *e.g., EURO 199* |
|---|---|---|---|---|
| Non-proprietary name (proprietary name) | | | | |
| Non-proprietary name (proprietary name) | | | | |

- Include "Cost per day" or other suitable/applicable unit
- All cost input should be changeable to allow each HTA bodies to add their own (non-public) prices.
- If multiple strength, dosages, and pack sizes are available, be explicit about assumptions regarding how medicine acquisition costs are applied in the model.
- Be explicit about assumptions related to wastage.
- Be explicit about assumptions regarding how costs are applied in the model.
- Justify and describe the inclusion/exclusion of subsequent treatment costs.
- Describe the data source from which the subsequent treatment is based on.
- Discuss limitations and uncertainties.

## 3.8.2. Medicine administration costs

- Describe any relevant medicine administration costs associated with the treatments included in the analysis. Describe the tariffs used for the administration cost.
- The costs incurred by patients (and caregivers), as a consequence of the medicine treatment (time spent including transportation time) should be included in a "drop-down menu", when relevant.
- Discuss whether the cost for medicine administration may differ substantially between Nordic countries taking into consideration the impact of this input on the decision problem

## 3.8.3. Health state and event costs

- Describe/tabulate costs (resource use and unit prices) associated with each health state and/or events, including costs components associated with each state/event.
  - E.g. Cost per hospitalisation and number of hospitalisations in each health state.
- If costs incur across health states, this must be clearly stated.
- Include sources for each state and event.
- The costs incurred by patients (and caregivers), as a consequence of the health state/event (time spent including transportation time) should be included in a "drop-down menu", when relevant.
- Discuss whether the costs may differ substantially between Nordic countries taking into consideration the impact of this input on the decision problem.

## 3.8.4. Adverse events costs

- Describe/tabulate the costs (resource use and unit prices) and cost components for the adverse events included in the model.

- The costs incurred by patients (and caregivers), as a consequence of the adverse event (time spent including transportation time) should be included in a "drop-down menu", when relevant.
- Discuss whether the costs may differ substantially between Nordic countries taking into consideration the impact of this input on the decision problem.

### 3.8.5. Miscellaneous costs

- Describe/tabulate the costs and cost components for monitoring and/or other costs included in the model, e.g. end-of-life costs.
- Discuss whether the costs may differ substantially between Nordic countries taking into consideration the impact of this input on the decision problem.

# 4. Health economic analysis - Results

## 4.1. Incremental analysis of costs and outcomes

### 4.1.1. Base case results

- Complete the following table for the main analysis choosing a currency and country-specific setting of HTD choice. Copy Table 10 table for any potential subgroup analysis. Results from any subgroup analysis requires a description of the analysis in the context of relevance and applicability to Nordic clinical practice.

*Table 10. Summary of results of the incremental cost-effectiveness analysis.*

| Per patient | \<Intervention\> | \<Comparator\> | Difference |
|---|---|---|---|
| **Life years gained** | | | |
| Total life years gained | | | |
| Life years gained \<health state A\> | | | |
| Life years gained \<health state B\> | | | |
| | | | |
| **QALYs** | | | |
| Total QALYs | | | |
| QALYs \<state A\> | | | |
| QALYs \<state B\> | | | |
| QALYs, disutilitites | | | |
| | | | |
| **Costs** | | | |
| Total costs | | | |
| Medicine costs | | | |
| Administrative costs | | | |
| Hospital admissions | | | |
| End of life costs | | | |
| Adverse reactions | | | |
| Other costs (specify) | | | |
| | | | |
| Incremental results | **Intervention vs. Comparator** | | |
| ICER (per QALY) | | | |
| ICER (per life year gained) | | | |

## 4.1.2. Sensitivity and scenario analysis related to the modelling uncertainty

### Deterministic sensitivity analysis

- It is not possible to give a general description or exhaustive list of how the company should address uncertainties in the health economic analysis, as this will depend on the disease, patient population, treatment and available data of each individual case
- Present relevant sensitivity/scenario analysis related to modelling uncertainty in tables, if relevant supplemented by corresponding/relevant figures, e.g. tornado diagram. Arbitrary intervals around the mean (e.g. +/- 20%) should generally be avoided but can in some instances be the only reasonable approach.
- Provide justifications/descriptions in text form, including details on relevant sensitivity and scenario analyses and why they may be plausible in this context.
- Country-specific scenarios do not need to be reported here

*Table 11. Deterministic sensitivity/scenario analysis example.*

| | Change | Reason / Rational / Source | Incremental cost (NOK) | Incremental benefit (QALYs) | ICER (NOK/QALY) |
|---|---|---|---|---|---|
| *Base case* | | | | | |
| *Efficacy outcome A intervention* | | | | | |
| *Efficacy outcome B intervention* | | | | | |
| *Hazard Ratio (HR) Overall Survival (OS)* | 0.71 | Lower C.I. | | | |
| | 1.83 | Upper C.I | | | |
| *Risk of hospitalisation* | | | | | |
| *Adverse reaction A* | | | | | |
| *Medicine costs of comparator* | 30 % down | | | | |
| | 50 % down | | | | |
| *Time horizon* | | | | | |
| | | | | | |
| | | | | | |
| *Administrative costs* | 500 | 50 % down | | | |
| | 1500 | 50 % up | | | |
| *QALY-weight (state A)* | 0.52 | Alt. source 1 | | | |
| | 0.67 | Alt. source 2 | | | |
| *Etc.* | | | | | |
| | | | | | |

### Probabilistic sensitivity analysis (PSA)

- Probabilistic sensitivity analysis is needed according to DMC guidelines and can be included in this submission template. The analysis should be performed according to dMC guidelines.

- Tabulate all parameters (point estimate, lower bound, upper bound) and distribution
- The PSA must contain all parameters from the model that are uncertain. Choice of parameters and the associated probability distributions must be justified.
- It should be easy to change the choice of distributions, e.g. via a drop-down list in the Excel model.
- It should be easy to switch parameters on and off in the PSA, e.g. via a drop-down list in the Excel model.
- If there are correlated parameters, these should be described, and correlation should be considered in the PSA. Describe the method used to account for correlated parameters.
- In cases where a parameter has not been estimated empirically, argumentation should be of how the uncertainty surrounding the estimate is determined. Avoid aarbitrary intervals around the mean (e.g., +/-20%).
- If data has been extrapolated in the analysis, parameters from all distributions must be included in the PSA module in the Excel model.
- In addition to the Scatter plot and cost-effectiveness acceptability curves (CEAC), the presentation of the PSA must also be supplemented with a description of the analysis. This involves a description of the form and location of incremental costs vs. the QALY gain cloud.
- In cases where there is considerable uncertainty about a single parameter, e.g. in cases where there is uncertainty about the effect on the OS, a univariate PSA may be performed and presented.
- It must be possible to change the number of simulations in the PSA in the Excel model.
- Include a convergence plot for the estimated mean. This is an iteration plot of ICERs as a function of the number of PSA simulations needed.
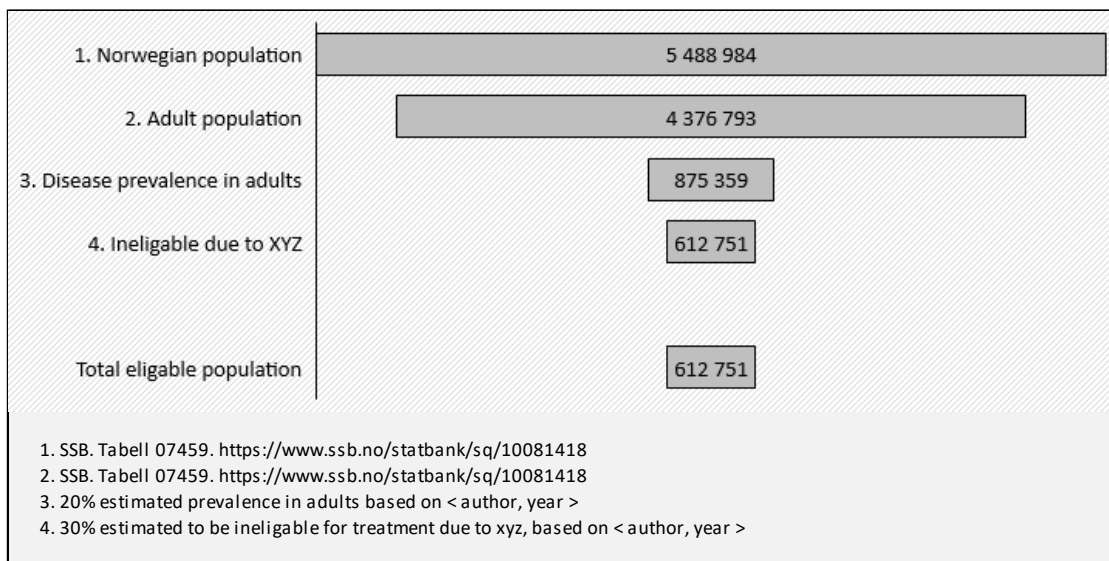
# 5. Patient numbers

## 5.1. Epidemiology of the disease in the Nordics
- Describe how the prevalence and incidence is expected to develop over the next 5 years, refer to background chapter.

## 5.2. Eligible patient population
- Describe the eligible patient population in each country. Use funnel charts (or equivalent) describing how the final eligible patient population has been calculated. There are multiple ways of estimating patient numbers and considerations that could be included (such as demographic development, age dependent prevalence, diagnostic developments, etc.). Adapt as necessary. Example chart below.

1. SSB. Tabell 07459. https://www.ssb.no/statbank/sq/10081418
2. SSB. Tabell 07459. https://www.ssb.no/statbank/sq/10081418
3. 20% estimated prevalence in adults based on < author, year >
4. 30% estimated to be ineligible for treatment due to xyz, based on < author, year >

## 5.3. Budgetary consequences and expected sales

- Budgetary consequences and expected sales should be performed according to national methods. Can be included in the JNHB dossier but can also be submitted separately.

## 5.4. Quantification of severity (Norway only)

Quantification of severity is relevant for Norway only. It can be included in the JNHB dossier but can also be submitted separately.

- Severity must be quantified according to NOMA guidelines Chapter 13 and Appendix.
- Provide a detailed description of how severity was calculated.
- Uncertainty in the severity calculation must also be presented.
- Describe sources of uncertainty in the assumptions.
- Present the consequences of the uncertainty, for example in table and/or diagram where the calculation of severity (absolute shortfall) as a function of age and/or prognosis is presented.
- Complete the table below. An excel tool is available here that can be used in most cases.

*Table 12. Severity calculations*

| Average age at treatment initiation | A | XX |
|---|---|---|
| Expected remaining QALYs (undiscounted) for the general population without the disease | QALYs$_A$ | |
| Expected remaining QALYs (undiscounted) for those with the disease and without the new treatment (that is, prognosis of patients treated with current standard treatment) | P$_A$ | |
| *If adjustments are made:* Expected remaining QALYs (undiscounted) for those with the disease without the new treatment (prognosis) - adjusted.  *If adjustments are not made, this row in the table can be deleted* | P*$_A$ | |
| Number of QALYs lost due to disease (absolute shortfall) | AS | |

# 6. References

- Provide a list of references.

# 7. Appendices