Medicinrådet

Instructions for companies

This is the template for submitting evidence to the Danish Medicines Council (DMC) as part of the appraisal process for a new medicinal product or a new indication for an existing medicine. The template is not exhaustive.

Please note the following requirements:

- When preparing their application, companies must adhere to the current version of the DMC's methods guide.
- Always use the current (latest updated) version of this template downloadet from the DMC's website.
- Headings, subheadings and appendices must not be removed. Tables must not be deleted or edited, unless it is explicitly stated in the text.
- Text in grey and [in brackets] is only for example purposes and must be deleted.
- All sections in the template must be filled in. If a section or an appendix is not applicable, state "not applicable" (N/A) and explain why.
- The main body of the application must not be longer than 100 pages (including the title page, contact information and references – excluding appendices).
- The formatting is not to be altered and all cross-references must work.
- All applications must comply with the general data protection regulations, find more information on DMC's data policy here.
- Submissions in either Danish or English are accepted.

The assessment process cannot be initiated before all the requirements are met.

Documentation to be submitted

The following documentation must be sent to the DMC's email medicinraadet@medicinraadet.dk:

- Application in word format*
- Application in PDF format*
- Health economic model including budget impact model in one Excel file, with full access to the programming code. The model must include relevant sheets from the DMC Excel template 'Key figures including general mortality' available on the DMC's website.
- The European Public Assessment Report (EPAR) should be submitted. Send a draft version if the final one is not published at the time of submission, and send the final version as soon as possible.

Confidential information and blinding

The Danish Medicine Council publishes the application (including attachments) on the website together with the recommendation.

The applicant has the option to blind any confidential information in the application incl. appendices.

Medicinrådet

The application and paper/appendices

If there is confidential information in the application or note/appendices, the company must submit two versions of both the application and note/appendices:

- a version for the DMC's case processing, where the confidential information is marked with yellow marking.
- a version for publication on the DMC's website, where the confidential information is blinded with black marking. The DMC publishes this version.

It is the pharmaceutical companies that must ensure that the blinding is sufficient, so that the confidential information cannot be read when the document is edited.

Therefore, the applicant must ensure that the confidential information is sufficiently redacted blinded for publication on the DMC's website. This can be done, for example, by covering the text/information to be redacted with a black marker simultaneously replacing the underlying text with crosses ("XXX"), so that the text/information cannot be read when editing the document.

Read about redaction of confidential information on the DMC's website.

About macros in Excel

Due to IT security requirements, Excel files containing macros must be authorized and signed by the applicant before being submitted to the DMC. Find more information here.

Version log

Version log		
Version	**Date**	**Change**
2.5	10 September 2024	Section 3.4 and 3.4.1: new information regarding ATMP (Advanced Therapy Medicinal Products). Section 6.1.1 and 8.1: Updated text regarding data-cut. Section 4, 8, 10 and 12: Clarification regarding cost-minimization analysis.
2.4	5 July 2024	Section 11: Clarification in the text regarding costs and changes in the tables 26 and 30.
2.3	1 June 2024	Clarification regarding redaction of confidential information, clarification regarding EPAR, clarification regarding literature search and changes in the text regarding costs. New information about Joint Nordic assessments has been added.
2.2	3 November 2023	'Pharmaceutical' is exchanged with 'medicine'. Tabel 26 is new.
2.1	1 September 2023	Section 4.2: Updated information about discount rate (The DMC applies a discount rate of 3.5 % for all years) Section 10.1.3: Clarification regarding EQ-5D-5L and Danish preference weights Section 11.1: Updated information about Excel sheet 'Key Figures'
2.0	15 June 2023	New application template
1.3	6 December 2022	Clarification regarding new IT security requirements concerning macros in Excel files has been added, see page 1.
1.2	20 June 2022	Clarification of the introduction, including instructions on how to complete the form.
1.1	9 February 2022	Appendix K and onwards have been deleted (company-specific appendices) Color scheme for text highlighting table added after table of contents Section 6: Specific requirements for literature search Section 7: Stated it explicitly that statistical methods used need to be described Section 8.3.1: Listed the standard parametric models

Version log		
		Section 8.4.1: Added the need for description of quality of life mapping Appendix A: Specified that the literature search needs to be specific for the Danish context and the application Appendices B and D: Stated it explicitly that statistical methods need to be described in the tables in the appendices
1.0	27 November 2020	Application form for assessment made available on the website of the Danish Medicines Council.

Application for the assessment of <proprietary name of medicine> for <indication>

Color scheme for text highlighting	
Color of highlighted text	Definition of highlighted text
	Confidential information
[Other]	[Definition of color-code]

Contact information

Contact information	
Name	**[Name / company]**
Title	
Phone number	[Include country code]
E-mail	
Name (External representation)	**[Name / company]**
Title	
Phone number	[Include country code]
E-mail	

[If a company wishes to use external representation in relation to the application for evaluation of a new medicine / extension of indications, the following power of attorney must be completed and sent to medicinraadet@medicinraadet.dk.]

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Tables and Figures

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

Abbreviations

[Include a list of all abbreviations used in this application.]

1. Regulatory information on the medicine

Overview of the medicine	
Proprietary name	
Generic name	
Therapeutic indication as defined by EMA	[EMA indication]
Marketing authorization holder in Denmark	
ATC code	
Combination therapy and/or co-medication	
(Expected) Date of EC approval	
Has the medicine received a conditional marketing authorization?	[If yes, state the specific obligations to complete post-authorization measures for the conditional marketing authorization including due date]
Accelerated assessment in the European Medicines Agency (EMA)	
Orphan drug designation (include date)	
Other therapeutic indications approved by EMA	[In case of multiple indications these can be provided in table form in a separate appendix]
Other indications that have been evaluated by the DMC (yes/no)	[In case of multiple indications these can be provided in table form in a separate appendix]
Joint Nordic assessment (JNHB)	Are the current treatment practices similar across the Nordic countries (DK, FI, IS, NO, SE)? [yes/no] Is the product suitable for a joint Nordic assessment? [yes/no] If no, why not?
Dispensing group	BEGR/NBS
Packaging – types, sizes/number of units and concentrations	

2. Summary table

Provide the summary in the table below, maximum 2 pages.

Summary	
Indication relevant for the assessment	[Note if there are any deviations from the EMA indication and elaborate]
Dosage regiment and administration	
Choice of comparator	
Prognosis with current treatment (comparator)	[Briefly describe the expected course of the disease (progressive or stable disease). Does it lead to decreased life expectancy and or decreased health-related quality of life? State median survival or survival rate from the Danish population if applicable.]
Type of evidence for the clinical evaluation	[Head-to-head study or Indirect comparison (ITC, NMA, MAIC, other)]
Most important efficacy endpoints (Difference/gain compared to comparator)	[Insert results for maximum 3-4 endpoints with highest importance for the assessment]
Most important serious adverse events for the intervention and comparator	[State the most influential serious adverse events and their frequencies for both the intervention and the comparator(s)]
Impact on health-related quality of life	Clinical documentation: [List the tool and provide a data estimate with confidence interval] Health economic model: [Equal, better or worse than comparator]
Type of economic analysis that is submitted	Type of analysis (cost-utility, cost-minimizing etc.) Type of model (Markov model, partitioned survival model etc.)
Data sources used to model the clinical effects	
Data sources used to model the health-related quality of life	
Life years gained	XX years
QALYs gained	XX QALY

Summary	
Incremental costs	XX DKK
ICER (DKK/QALY)	XXX DKK/QALY
Uncertainty associated with the ICER estimate	[Describe the model assumptions with the largest overall impact on the incremental costs and QALY gain]
Number of eligible patients in Denmark	Incidence: Prevalence:
Budget impact (in year 5)	

3. The patient population, intervention, choice of comparator(s) and relevant outcomes

[Complete the following sections according to sections 2.1, 2.2, 2.3, and 2.4 of the methods guide.]

3.1 The medical condition

[Describe the medical condition including (1-3 pages including figures):

- The pathophysiology.
- The clinical presentation/symptoms of the condition.
- Patient prognosis, preferably for a Danish patient population. Provide the prognosis with the current treatment options.
- The influence of the condition on the patients' functioning and health-related quality of life.

The description of the disease should give the reader sufficient background information to understand the remainder of the application but must be kept short and concise.]

3.2 Patient population

[Describe the Danish patient population that is relevant for this application (1-3 pages including tables).

If certain patient characteristics affect the prognosis or the effectiveness of the treatment, describe the distribution of these factors within the Danish patient population.

Is the application aimed at a subgroup of patients within the indication? Describe the subgroup and provide a rationale for the subgroup selection.

Provide the incidence and prevalence in Denmark for the past 5 years in Table 1. Provide references for the data.]

Table 1 Incidence and prevalence in the past 5 years

Year	[Current year minus 5]	[Current year minus 4]	[Current year minus 3]	[Current year minus 2]	[Current year minus 1]
Incidence in Denmark					
Prevalence in Denmark					
Global prevalence *					

* For small patient groups, also describe the worldwide prevalence.

[State the patient populations that are included in this application, including any subgroups. Fill out Table 2 with expected number of patients. List the source(s) for the information provided.]

Table 2 Estimated number of patients eligible for treatment

Year	Year 1	Year 2	Year 3	Year 4	Year 5
Number of patients in Denmark who are eligible for treatment in the coming years					

3.3 Current treatment options

[Describe the current treatment algorithm and treatment options in Danish clinical practice, including potential subsequent treatments if relevant. Illustrate with a diagram if appropriate. Danish treatment guidelines should be referenced if available. Include a brief description of the expected prognosis with the current treatments.]

3.4 The intervention

[Provide the information in the table below and describe the intervention, including the mechanism of action. If the medicine has received a conditional approval, explain the conditions.]

Overview of intervention	
Indication relevant for the assessment	[Note if there are any deviations from the EMA indication and elaborate]
ATMP	[If it is an Advanced Therapy Medicinal Product, state the type and elaborate in section 3.4.1 after this table]
Method of administration	
Dosing	
Dosing in the health economic model (including relative dose intensity)	
Should the medicine be administered with other medicines?	
Treatment duration / criteria for end of treatment	
Necessary monitoring, both during administration and during the treatment period	
Need for diagnostics or other tests (e.g. companion diagnostics). How are these included in the model?	[Is the test currently applied in Danish clinical practice?]
Package size(s)	

3.4.1 Description of ATMP

[Describe the technology. For example vector type, knowledge of duration of effect, risk of immune reactions, cross-reactivity, integration into the host cell's DNA, risk of transferring vector to partner, fetus during pregnancy, special precautions, etc.

Delete section if not applicable.]

3.4.2 The intervention in relation to Danish clinical practice

[Describe where in the treatment algorithm/course of treatment the intervention is expected to be used and describe how current clinical practice will be altered. Describe whether introduction of the intervention will replace medicine(s) or treatment(s) currently used in clinical practice, or if it will be an additional treatment option in the treatment algorithm.

In some cases, it may be relevant to compare different treatment sequences. This not only means that the new medicine and comparator differ in the overall course of treatment; it also means that introduction of the new medicine will result in changes to other treatment lines in an overall treatment pathway. In such cases, describe the treatment sequences in detail.

If the intervention is associated with diagnostic tests and methods used for patient selection that are not routinely applied in Danish clinical practice, please elaborate here.]

3.5 Choice of comparator(s)

[Comparator(s) is/are the treatment alternative(s) that the new medicine will be compared with. The choice of comparator should always be the medicine(s) or other treatment(s) (including preventive and palliative treatments) in Danish clinical practice that represent current standard treatment. The choice of comparator must be in accordance with sections 3.3 and 3.4.

State which comparators are included in the submission. Justify inclusion if the chosen comparator is not currently part of Danish clinical practice. If there is no existing treatment alternative for the disease, the comparator will be monitoring, placebo or no treatment. State if any of the comparators are used off-label.

In cases where there are several standard treatment alternatives in Danish clinical practice, include these as comparators in the application. In cases where the DMC has decided that several treatments are equivalent, only compare the intervention to one of the equivalent treatments.

Always include each comparator individually. This means that the applicant cannot combine data from two or more treatment alternatives and report it as the average effect or average costs in the health economic analysis.

In cases where the patient group used for comparison may have received one of several treatment alternatives, for example “investigator’s choice”, it will not always be possible to assess treatment alternatives individually. Describe and justify if such treatment alternatives are used as individual comparators.

Provide the following information for all the included comparators. If more than one comparator is included in the application, copy/paste the table for each comparator.]

Overview of comparator	
Generic name	
ATC code	
Mechanism of action	
Method of administration	
Dosing	
Dosing in the health economic model (including relative dose intensity)	
Should the medicine be administered with other medicines?	
Treatment duration/ criteria for end of treatment	
Need for diagnostics or other tests (i.e. companion diagnostics)	
Package size(s)	

3.6 Cost-effectiveness of the comparator(s)

[State whether the comparator has previously been evaluated and recommended by the DMC.

If the comparator has not been evaluated by the DMC, the applicant should include a supplementary analysis against a comparator that could reasonably be assumed to be cost-effective, for example a placebo comparator. For further information, see section 2.4.2 of the methods guide.]

3.7 Relevant efficacy outcomes

3.7.1 Definition of efficacy outcomes included in the application

[Define the efficacy outcomes considered relevant and necessary to evaluate the effect of the intervention vs. the comparator. Describe the rationale for the chosen efficacy outcomes.

All efficacy outcome measures included in the application must be defined in Table 3. For each efficacy outcome, describe the definition (operationalization), methods of data collection, time of data collection and method of analysis, including dealing with missing values. If a scale is used in the efficacy outcome, state how it was validated; if responder analyses is used, state and justify the responder definition. The level of detail needed depends on the efficacy outcome (see example text in Table 3).

For intermediate efficacy outcomes, surrogate efficacy outcomes, or if the efficacy outcomes are correlated, document how the outcomes relate to the direct endpoints. Explain how the relationship was estimated, what sources of evidence were used, and how the sources of evidence were identified (e.g. systematic literature review (SLR)).]

Table 3 Efficacy outcome measures relevant for the application

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
[Efficacy outcome measure 1] [Included study 1]		[Provide definition used in the studies]	
Overall survival (OS) [Included study 1]		OS is defined as the time from randomization to death from any cause. OS is defined as time from first treatment registered in registry X to date of death from any cause.	
ASAS40 [Included study 1]	Week 12	Proportion of patients achieving ASAS40. An ASAS40 response was defined as a ≥40% improvement and an absolute improvement from baseline of ≥2 units (range 0–10) in ≥3 of the following four domains: Patient Global Assessment of Disease Activity (0–10 cm VAS), pain (total back pain, 0–10 cm VAS), function (Bath Ankylosing Spondylitis Functional Index (BASFI), 0–10 cm VAS [source XX] and inflammation/morning stiffness (mean score of items 5 and 6 of the BASDAI (0–10 cm VAS)) without any	ASAS40 was evaluated by the investigator at every study visit.

Outcome measure	Time point*	Definition	How was the measure investigated/method of data collection
		worsening in the remaining domain [source YY].	

* Time point for data collection used in analysis (follow up time for time-to-event measures)

Validity of outcomes

[For all efficacy outcome measures, state whether the validity of the efficacy outcome measure has been investigated and how. Provide references - previous DMC assessments are accepted as references. If an instrument or scale is used, describe whether it has been validated for the relevant population, describe the scale and the minimal clinically relevant difference with the reference.

If composite efficacy outcomes are used, clearly describe the rationale for grouping efficacy outcomes, whether the composite efficacy outcome has international consensus and whether information about individual efficacy outcomes is available.]

4. Health economic analysis

[Complete this section according to section 6 of the methods guide. Describe and justify the choice of health economic analysis (cost-utility analysis or cost-minimization analysis). All input data sources used in the health economic model must be described in the application.]

4.1 Model structure

[Describe the model used in the health economic analysis (see section 6 of the methods guide.)

Depict the structure of the model clearly, showing the different stages and the main features of how it works. Explain the structure based on the clinical pathway of care and describe how the model structure and its health states capture the disease for the patient population (described in section 3.2).]

4.2 Model features

[In Table 4 describe the model features with regards to the population, perspective, half-cycle correction, cycle length (see section 6.9 of the methods guide), discount rate, model structure, comparator, and cost, and provide a justification. The text in column 1 should be customized for each individual assessment.]

Table 4 Features of the economic model

Model features	Description	Justification
Patient population	Adult patients with NSCLC	[Note if there are any deviations from section 3.2 and elaborate]
Perspective	Limited societal perspective	According to DMC guidelines
Time horizon	Lifetime (40 years)	To capture all health benefits and costs in line with DMC guidelines. Based on mean age at diagnosis in the Danish population (40 years). Validated by Danish clinical expert
Cycle length	14 days	Consistent with length of treatment cycle (day 1 every 14 days)
Half-cycle correction	Yes	
Discount rate	3.5 %	The DMC applies a discount rate of 3.5 % for all years
Intervention	XX	
Comparator(s)	XX	According to national treatment guideline. Validated by Danish clinical expert
Outcomes	[List the outcomes used for efficacy in the model] OS, PFS	

5. Overview of literature

[All essential literature applied in this application must be presented in the tables below, i.e. internal and published literature used in the clinical assessment, health-related quality of life, and (as input to) the economic model. This also includes evidence generated from real-world data, i.e. real-world evidence (RWE). Please read the DMC's guidelines for RWE in the document 'Real-world evidence in applications to the Danish Medicines Council' available on the DMC's website.

If using literature from NICE or other HTA bodies, original citations must be provided, i.e. it is not sufficient to solely refer to the appraisal document. If the data is not sourced from a published article (citation), please indicate where to find the referenced data, such as the appraisal document or committee papers with page number(s).

As a rule, a systematic literature search must be conducted to identify all evidence relevant for this application (efficacy and safety, health-related quality of life and key model inputs). Detailed information on which databases/sources were used for the searches (e.g. MEDLINE and CENTRAL), the number of publications screened on title and abstract, the number of publications selected for full text screening, and the number of publications that were identified as relevant for the current application must be provided in Appendix H, Appendix I or Appendix J in accordance with section 3 of the methods guide. If the clinical assessment and health economic analysis are exclusively informed by a head-to-head study with the most relevant comparator in Danish clinical practice, the literature search for efficacy and safety studies can be omitted.

In cases where no systematic literature search has been performed, please justify the rationale for lack of systematic literature search. For literature input found by non-systematic/targeted searches, the searches must be documented in the relevant Appendix (Appendix H, Appendix I or Appendix J), Further specifications are available in the appendices.

If existing systematic literature review(s) (SLR) are used, these must be adapted to the current application. See Appendix H for the requirements.]

5.1 Literature used for the clinical assessment

[State whether a literature search was conducted, or whether the application is based on a head-to-head study with a comparator relevant to Danish clinical practice.

The literature search must be described in Appendix H. In Table 5, please list the literature used in the clinical assessment.]

Table 5 Relevant literature included in the assessment of efficacy and safety [sample text in table for full paper, data on file and conference abstract]

Reference (Full citation incl. reference number)*	Trial name*	NCT identifier	Dates of study (Start and expected completion date, data cut-off and expected data cut-offs)	Used in comparison of*
Full paper James ND, Sydes MR, Clarke NW, et al. Systemic therapy for advancing or metastatic prostate cancer (STAMPEDE): a multi-arm, multistage randomized controlled trial. BJU Int. 2009 Feb;103(4):464-9. [5]	STAMPEDE	NCT00268476	Start: DD/MM/YY Completion: DD/MM/YY Data cut-off DD/MM/YY Future data cut-offs DD/MM/YY	<intervention> vs. <comparator> for <population>
Data on file Unpublished data 2023.: DRUG-Z Clinical Study Report. [2]	DRUG-Z 123	NCT12345678	Start: DD/MM/YY Completion: DD/MM/YY	<intervention> vs. <comparator> for <population>

* If there are several publications connected to a trial, include all publications used.

5.2 Literature used for the assessment of health-related quality of life

[State whether a literature search was conducted, or whether health-related quality of life data, including health state utility values, was solely obtained from a head-to-head study with a comparator relevant to Danish clinical practice. In cases where no systematic literature search has been performed, please justify the inclusion of literature input and the rationale for lack of systematic literature search.

The literature searches (systematic and/or targeted) must be described in Appendix I. Please list the literature used for health-related quality of life in Table 6.]

Table 6 Relevant literature included for (documentation of) health-related quality of life (See section 10)

Reference (Full citation incl. reference number)	Health state/Disutility	Reference to where in the application the data is described/applied
Authors. Article title. Journal. Year; volume(issue): pp [reference number]	E.g. First line metastatic recurrence	

5.3 Literature used for inputs for the health economic model

[State whether a literature search was conducted to identify literature used for input to the health economic model. In cases where no systematic literature search has been performed, please justify the inclusion of literature-input and the rationale for lack of systematic literature search.

The literature searches (systematic and/or targeted) must be described in Appendix J. In Table 7, please list the literature used for input to the economic model, regardless of whether the studies have been listed in the previous tables.]

Table 7 Relevant literature used for input to the health economic model

Reference (Full citation incl. reference number)	Input/estimate	Method of identification	Reference to where in the application the data is described/applied
Authors. Article title. Journal. Year; volume (issue): pp [reference number]	Overall survival	Targeted literature review	Section 9.2. Table X

6. Efficacy

[Complete this section according to sections 4 and 5 of the methods guide for each comparison. If more than one comparison is included in the application, i.e. due to more than one comparator or more than one population, copy/paste sections 6 to 9 for each comparison.]

6.1 Efficacy of [intervention] compared to [comparator] for [patient population]

6.1.1 Relevant studies

[Present all studies used in the comparison in Table 8 including real-world evidence studies. State if the population in the application is a subpopulation in the study, and if so, whether the subpopulation was pre-defined in the study protocol. State which data cut(s) from the study are used in the application, what the median follow-up time is and whether the data cut was predefined. All clinical data used in the application must, as a starting point, come from the latest available predefined data cut. All studies must be described in detail in Appendix A.]

Table 8 Overview of study design for studies included in the comparison

Trial name, NCT-number (reference)	Study design	Study duration	Patient population	Intervention	Comparator	Outcomes and follow-up time
Study 1	Randomized phase III / open-label / placebo-control/ active comparator-control			Treatment, administration, dosing	Treatment, administration, dosing	[All primary and secondary outcomes in the study must be listed. Specify follow-up periods for each outcome measure or median follow-up time for time-to-event outcome measures. State whether the follow-up period was predefined]
Trial name, NCTxxxx (reference for publication(s))	Randomized, double blinded, placebo controlled, phase III study of drug X versus placebo.	12 weeks double blinded period follow by 40 weeks open label (52 weeks in total). Patients that were randomized to placebo switched to open label drug X after week 12.	Treatment naive patients with active disease and incomplete response to conventional treatment.	Drug X (subcutaneous administration), 90 mg week 0, 4, 8, 12 hereafter every 12 weeks.	Drug X matching placebo (s.c.) week 0, 4, 8, 12 hereafter every 12 weeks.	ACR20-response (week 24), ACR50-response (week 24), ACR70-response (week 24), PASI75-response (week 24), PASI90-response (week 24), PASI100 response (week 24), body surface area affected by psoriasis (week 24), HAQ-DI-score (week 24), SF-36 PCS-score (week 24), mTSS-score (week 24), Leeds Enthesistis Index (LEI)-score (week 24), Leeds Dactylitis Index-Basic (LDI_B)-score (week 24), Nail Psoriasis Severity Index (NAPSI) (week 24).

6.1.2 Comparability of studies

[Address any differences between the included studies and describe how differences are addressed in the comparison between studies (not relevant for comparisons based on head-to-head studies).]

6.1.2.1 Comparability of patients across studies

[Add all relevant information in Table 9 with baseline characteristics of patients included in the studies used in the comparative analysis. Add more rows if necessary. One table for each comparison in the application must be provided. If a network meta-analysis is conducted, the baseline characteristics must be presented in a separate table. The table should make it possible to compare baseline characteristics across studies included for each comparison. Information about all relevant prognostic factors and effect modification factors must be included. If real-world data is used provide baseline characteristics before and after weighting/matching.

Adjust the number of columns in the table to match the number of studies included and study-arms (turn the page horizontal to include more studies). Adjust the number of rows to include all relevant baseline characteristics.

Address any differences in baseline characteristics between different study-arms and between studies and describe how differences are addressed in the comparison between studies below the table.]

Table 9 Baseline characteristics of patients in studies included for the comparative analysis of efficacy and safety

	[Study name]		[Study name]		[Study name]	
	[int./ comp.]	[int./ comp.]	[int./ comp.]	[int./ comp.]	[int./ comp.]	[int./ comp.]
Age						
Gender						
[characteristic]						
[characteristic]						
[characteristic]						

6.1.3 Comparability of the study population(s) with Danish patients eligible for treatment

[Address comparability of the study population with Danish patients eligible for treatment. Fill out Table 10 with information of characteristics in the relevant population in Danish clinical practice and the values used in the health economic model. Add rows to fit the relevant characteristics.]

Table 10 Characteristics in the relevant Danish population and in the health economic model

	Value in Danish population (reference)	Value used in health economic model (reference if relevant)
Age		
Gender		
Patient weight		
[characteristic]		
[characteristic]		

6.1.4 Efficacy – results per [study name 1]

[Provide a summary of the key efficacy findings for each study included in the comparative analysis (intervention and comparator studies). This does not apply to the effect on health-related quality of life, which must be reported in section 10. A short summary is sufficient for studies that have been published, whereas a more thorough description of the data and how they were obtained must be included if results have not yet been published. In addition, provide detailed information about the results of all outcomes included in the comparative analysis in Appendix B. Clearly explain any inconsistencies between published data and the EMA's scientific discussion.

Data should be presented according to the intention-to-treat principle whenever possible. Additional, alternative presentations of the data should be justified. The proportion of patients that discontinued the study in each study arm and the reason for discontinuation should be presented.

All effect estimates must be presented with confidence intervals (or other measures of uncertainty if confidence intervals cannot be computed) and the method for each analysis should be clearly described. This includes the type of model, adjustment variables, weights, stratification factors, correlation structure (repeated measures),

transformations of outcome and/or adjustment variables, handling of missing values and exclusions.

Whenever possible, both absolute and relative difference must be presented along with incidence rates for intervention and comparator(s) in each study.

Survival analyses without competing risks should provide Kaplan–Meier curves that include the number of patients at risk at various time points. In addition, the estimated median survival as well as the estimated hazard ratio (HR) and the estimated survival rates at relevant and appropriate time points should be presented. For hazard ratios, a graphical check of the proportional hazards assumption must be included, e.g. Schoenfeld residuals. In the event of competing risks, appropriate methods should be used, e.g. Aalen-Johansen estimator for estimating the cumulative incidence.

Include references for all data. All outcomes included in the application must be presented in Appendix B.

Data for health-related quality of life should be reported in section 10.]

6.1.5 Efficacy – results per [study name 2]

[Complete a section for each study in the comparison according to the description in 6.1.4.]

7. Comparative analyses of efficacy

[If a head-to-head study comparing the intervention and comparator directly is included as evidence of efficacy, the following section describing comparative analysis is not of relevance. Please state "not applicable". Table 11 should still be completed with results from the head-to-head study.]

7.1.1 Differences in definitions of outcomes between studies

[All efficacy outcomes included in the comparative analysis must be described in section 3.7. If there are discrepancies in the definition of outcomes between studies, list them here. Explain how differences were addressed in the comparative analysis.]

7.1.2 Method of synthesis

[Clearly describe the method used for the comparative analysis, e.g. meta-analysis, network meta-analysis, indirect analysis or narrative synthesis. Choice of method must be justified and specific analytical decisions in relation to the method chosen should be clearly specified.

If head-to-head studies are combined in a meta-analysis, provide the details of the analysis in this section.

If the efficacy and safety documentation is based on an indirect comparison, e.g. network meta-analysis, provide a brief description of the methodology here and a detailed description of the methodology in Appendix C. Tables and figures may be used for clarification.

If weighting techniques are used, e.g. matching adjusted indirect comparisons, summary statistics of the weights (or a histogram) should be provided and the effective sample size given. For inverse probability weighting describe the model for obtaining the probabilities and the choice of weights (e.g. average treatment effect among persons treated).

If composite outcomes are used, state whether information about individual outcomes is available.

If any studies or subpopulations have been excluded from the comparative analyses, provide a justification for the exclusion.

If the statistical analysis has been performed using methods that adjust for potential confounders, difference in effect modifier, prognostic factors and/or design features (e.g. by regression modeling, matching or weighting techniques), the variables used for the adjustment must be clearly described and specified. Methods applied to check assumptions in the statistical analyses must be clearly stated and described.

Survival analyses should provide Kaplan–Meier curves that include the number of patients at risk at various time points. In addition, the estimated median survival as well as the estimated hazard ratio (HR) and the estimated survival rates at relevant and appropriate time points should be presented. For hazard ratios a graphical check of the proportional hazards assumption must be included. If weighting techniques have been used, Kaplan-Meier curves and HR for the weighted population must be presented. In the event of competing risks, appropriate methods should be used, e.g. Aalen-Johansen estimator for estimating the cumulative incidence.

Insert references for all data.]

7.1.3 Results from the comparative analysis

[Provide the results from the comparative analyses in the Table 11 below. Whenever possible, both absolute and relative results must be presented. Incidence rates for intervention and comparator must be presented as well, where applicable. All results must be presented with confidence intervals or other measure of uncertainty. The timepoint for the outcome must be provided.

Data should be presented according to the intention-to-treat principle. Additional, alternative presentations of the data should be justified.

Survival analyses should include a presentation of the estimated median survival as well as the estimated hazard ratio (HR) and the estimated survival rates at relevant and appropriate time points.

The table can be adjusted to suit the data, and additional columns may be added.]

Table 11 Results from the comparative analysis of [intervention] vs. [comparator] for [patient population]

Outcome measure	[Intervention] (N=x)	[Comparator] (N=x)	Result
[Outcome measure 1], time point	[xx]	[xx]	[xx]
[Outcome measure 2], time point	[xx]	[xx]	[xx]
[Outcome measure 3], time point			
OS	Median: X months (95 % CI: X;Y)	Median: X months (95 % CI: X;Y)	X months HR: X;X (95 % CI: X;X)
Proportion of patients achieving ASAS40 (week 12)	**n/N, %** (95 % CI: X;Y)	**n/N, %** (95 % CI: X;Y)	**Absolute risk: X %** **Relative risk: X %**

7.1.4 Efficacy – results per [outcome measure]

[Complete a section for each outcome measure.]

8. Modelling of efficacy in the health economic analysis

If a cost-minimization analysis is performed, there may be parts of this section that are not relevant to complete. Please write 'Not applicable' in this case.

8.1 Presentation of efficacy data from the clinical documentation used in the model

[In this section, please describe how efficacy has been modelled in the health economic analysis. This includes extrapolation of efficacy data and calculation of transition probabilities (for a Markov model) and a description of any other model assumptions related to efficacy. The clinical data, which is the basis for modeling of the effect in the health economic analysis, must basically come from the same data cut as the clinical data and results presented in sections 6 and 7. If the efficacy data is considered mature,

and extrapolation was deemed unnecessary, please state how the efficacy data was applied in the model.]

8.1.1 Extrapolation of efficacy data

[In this section, the main assumptions and methods used for extrapolating data must be presented. The full method description and results must be presented in Appendix D. If extrapolations are not of relevance for this application, please write "not applicable" under the subtitle.]

Please follow section 6.4.2 of the methods guide and the online appendix "Anvendelse af forløbsdata i sundhedsøkonomiske analyser".

8.1.1.1 Extrapolation of [effect measure 1]

[Please fill out the table below. The table is not to be altered. If a row is not of relevance, please state "Not applicable".]

Table 12 Summary of assumptions associated with extrapolation of [effect measure]

Method/approach	Description/assumption
Data input	[Name of registrational study, name of studies from indirect comparison]
Model	[Describe which/how many models have been applied in extrapolating efficacy e.g. full parametrization vs. piecewise]
Assumption of proportional hazards between intervention and comparator	[Yes/No/Not applicable]
Function with best AIC fit	[Intervention: X function] [Comparator: X function]
Function with best BIC fit	[Intervention: X function] [Comparator: X function]
Function with best visual fit	[Intervention: X function] [Comparator: X function]
Function with best fit according to evaluation of smoothed hazard assumptions	[Intervention: X function] [Comparator: X function]
Validation of selected extrapolated curves (external evidence)	[E.g. studies, databases, RWE, clinical experts' opinions on clinical plausibility]
Function with the best fit according to external evidence	[Intervention: X function] [Comparator: X function]

Method/approach	Description/assumption
Selected parametric function in base case analysis	[Intervention: X function] [Comparator: X function]
Adjustment of background mortality with data from Statistics Denmark	[Yes/No] If 'No': briefly describe why the data has not been adjusted for background mortality
Adjustment for treatment switching/cross-over	[Yes/No] If 'Yes': briefly describe the assumption/method
Assumptions of waning effect	[Yes/No] If 'Yes': briefly describe the assumption/method
Assumptions of cure point	[Yes/No] If 'Yes': briefly describe the assumption/method

[Please present a figure that includes both:

- Observed time-to-event data for both intervention and comparator (if applicable).
- All investigated extrapolation functions that have been applied in the base case analysis for both intervention and comparator. The figure must display the entire time horizon of the model.]

8.1.1.2 Extrapolation of [effect measure 2]

[Please use the same template as stated in section 8.1.1.1.]

8.1.2 Calculation of transition probabilities

[If transition probabilities that were calculated from clinical data have been used, they must also be presented. Demonstrate how the transition probabilities were calculated from the clinical data. If appropriate, provide the transition matrix and describe how the clinical outcomes have been transformed as well as any other relevant details here.]

Table 13 Transitions in the health economic model

Health state (from)	Health state (to)	Description of method	Reference
Disease-free survival	Recurrence		
	Death		
Recurrence	Death		

Health
state/Transition

[Include a figure showing the proportion of patients in each health state per cycle in a stacked plot if a Markov model has been used. Additionally, present the transition probabilities.

If there is evidence suggesting that transition probabilities may change over time, the level of integration of this change must be clearly stated in the analysis. If there is evidence that this is the case, but it has not been included, provide an explanation of why it has not been included.

Describe the relevance of the selected estimates for Danish clinical practice.]

8.2 Presentation of efficacy data from [additional documentation]

[If efficacy data from additional documentation is applied in the health economic model, please fill in this section using the same template as stated in section 8.1.]

8.3 Modelling effects of subsequent treatments

[Describe how the clinical effects of potential subsequent treatments are modelled, if subsequent treatment lines differ between intervention and comparator. This includes a description of which references have been used to justify the assumptions e.g. data from registrational trial, external studies, clinical databases or RWE.]

8.4 Other assumptions regarding efficacy in the model

[All assumptions regarding efficacy not previously described in the model should be stated and justified.]

8.5 Overview of modelled average treatment length and time in model health state

[Please present estimates for the modelled average and modelled median of the effect measures predicted by the extrapolation model. The estimates must not have been modified with discounting and half-cycle correction. However, the estimate must be adjusted for background mortality of the Danish population (if relevant). In this context, the DMC Excel sheet '*General Mortality*' must be applied. The template can be found in the Excel file 'Key figures including general mortality' on the DMC's website. (The observed median from the registrational (or other relevant study) must also be

presented in the table. If the median has not been reached yet, please state "not reached".]

Table 14 Estimates in the model

	Modelled average [effect measure] (reference in Excel)	Modelled median [effect measure] (reference in Excel)	Observed median from relevant study
[Name of intervention]	[X months/years]	[X months/years]	[X months/years]
[Name of comparator]	[X months/years]	[X months/years]	[X months/years]

In Table 15 please provide the modelled average treatment length and time in model health state and describe any assumptions used to derive these.]

Table 15 Overview of modelled average treatment length and time in model health state, undiscounted and not adjusted for half cycle correction (adjust the table according to the model)

Treatment	Treatment length [months]	Health state 1 [months]	Health state 2 [months]
[Intervention]	[xx]	[xx]	[xx]
[Comparator]	[xx]	[xx]	[xx]

9. Safety

[The application must contain safety data from the same studies and reports used to document the efficacy of the intervention and the comparator. In cases where safety data is available for a population that is considerably larger than the population in the studies of clinical efficacy, this data must also be submitted (in separate tables).

The terms used to describe safety must be clearly defined e.g. adverse events (all causes / regardless of attribution) and adverse reactions (treatment-related adverse events).

In cases where safety data is not available for the intervention and/or comparator, the applicant should instead submit data that is as far as possible equivalent to the data requested below.]

9.1 Safety data from the clinical documentation

[State the definition of the safety population.

The tables in the following section must be filled out. Clearly state the source of the data and the time period the data covers/median treatment duration for all tables. Additional rows and columns can be added to the tables (e.g. for indirect comparisons, data for the comparator arm in each study must be provided). Provide a comparative analysis of the results.]

Table 16 Overview of safety events. State the time period the table covers.

	Intervention (N=x) (source)	Comparator (N=x) (source)	Difference, % (95 % CI)
Number of adverse events, n			
Number and proportion of patients with ≥1 adverse events, n (%)			
Number of serious adverse events*, n			
Number and proportion of patients with ≥ 1 serious adverse events*, n (%)			
Number of CTCAE grade ≥ 3 events, n			
Number and proportion of patients with ≥ 1 CTCAE grade ≥ 3 events§, n (%)			
Number of adverse reactions, n			
Number and proportion of patients with ≥ 1 adverse reactions, n (%)			
Number and proportion of patients who had a dose reduction, n (%)			
Number and proportion of			

	Intervention (N=x) (source)	Comparator (N=x) (source)	Difference, % (95 % CI)
patients who discontinue treatment regardless of reason, n (%)			
Number and proportion of patients who discontinue treatment due to adverse events, n (%)			

* A serious adverse event is an event or reaction that at any dose results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or results in a congenital anomaly or birth defect (see the ICH's complete definition).

§ CTCAE v. 5.0 must be used if available.

[List the frequency of all serious adverse events with frequency of ≥ 5% recorded in the study/studies in the table below. Additional rows and columns can be added to the tables (e.g. for indirect comparisons, data for the comparator arm in each study must be provided). If more than two studies are included in the comparison, the results can be presented in separate tables. A list of all serious adverse events observed in the study must be reported in Appendix E. Clearly state the source of the data and the time period the data covers/median treatment duration.]

Table 17 Serious adverse events (time point)

Adverse events	Intervention (N=x)		Comparator (N=x)	
	Number of patients with adverse events	Number of adverse events	Number of patients with adverse events	Number of adverse events
Adverse event, n (%)				
…				

* A serious adverse event is an event or reaction that at any dose results in death, is life-threatening, requires hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or results in a congenital anomaly or birth defect (see the ICH's complete definition).

[Describe how safety data is used in the health economic model. The applicant must justify any exclusion of relevant safety data in the health economic analysis.]

Table 18 Adverse events used in the health economic model

Adverse events	Intervention	Comparator		
	Frequency used in economic	Frequency used in economic	Source	Justification

Adverse events	Intervention	Comparator
	model for intervention	**model for comparator**
Adverse event, n (%)		
[Add a new row for each adverse event included in the model]		

9.2 Safety data from external literature applied in the health economic model

[If safety data from external literature was used in the health economic analysis, please describe how it was applied in the model. Please list the adverse events applied in the model in Table 19.]

Table 19 Adverse events that appear in more than X % of patients

Adverse events	Intervention (N=x)			Comparator (N=x)			Difference, % (95 % CI)	
	Number of patients with adverse events	Number of adverse events	Frequency used in economic model for intervention	Number of patients with adverse events	Number of adverse events	Frequency used in economic model for comparator	Number of patients with adverse events	Number of adverse events
Adverse event, n								

10. Documentation of health-related quality of life (HRQoL)

If a cost-minimization analysis is performed, the focus must be on comparing the intervention and the comparator's effect on health-related quality of life measured in the clinical studies. If a cost-minimization analysis is carried out, sections 10.2 and 10.3 are not relevant to complete. Please write 'Not applicable' in this case.

[Section 7 of the methods guide must be followed. In general, health-related quality of life must be based on the generic measuring instrument EQ-5D-5L in order to make comparison between different DMC assessments possible. In cases where health-related quality of life based on EQ-5D-5L is not available, other generic or disease-specific instruments must be included and mapped to EQ-5D-5L with validated mapping algorithms if possible (see details in section 10.2.1). If the studies included have collected health-related quality of life with disease-specific instruments in addition to EQ-5D-5L or other generic measuring instruments, these can be reported as supplementary information. The reason for their inclusion in the assessment must be well-argued. Summarize in Table 20 all measuring instruments included.]

Table 20 Overview of included HRQoL instruments

Measuring instrument	Source	Utilization
Instrument 1 (e.g. EQ-5D-5L)	Trial x	Describe purpose of HRQoL instrument (clinical effectiveness, utilities, disutilities etc.)
Instrument 2		
…		

[Information on all HRQoL instruments included from the studies informing clinical effectiveness must be described in section 10.1. Corresponding health state utilities based on the studies described in section 10.1 must be described in section 10.2. If health state utilities are obtained from other sources than those informing clinical effectiveness, these must be described in section 10.3.]

10.1 Presentation of the health-related quality of life [make a subsection for each of the applied HRQoL instruments]

[If data from multiple HRQoL instruments is included, please fill out section 10.1.1 - 10.1.3 for each instrument.]

10.1.1 Study design and measuring instrument

[Describe and justify the choice of study design, including, but not limited to:

- The a priori expectations of changes in HRQoL and the clinical rationale for the changes
- Reasons for choosing the instrument used to measure HRQoL (validity, reliability, and sensitivity with regards to patient population)
- Was the instrument used in the manner it is validated for?
- Did the study design or chosen instrument cause a risk of bias?
- If the population contributing to HRQoL data differs from the population contributing to other clinical outcome data, describe the differences and their consequences for the assessment.

For further information, see the CONSORT-PRO guideline.]

10.1.2 Data collection

[Describe and justify the data collection in terms of:

- How and at which time points the HRQoL data was collected.
- Report relevant data collection time points in Table 21.
- Report missing observations.
- Report for each time point the number and percentage missing since randomization.
- Report for each time point the number and percentage completed. Completion rate must be defined as percentage completed from patients "at risk" at time point "x".
- Describe how missing observations were handled and what assumptions were taken.
- Describe the characteristics of patients who have missing values and compare their characteristics with the population who do not have missing values.]

Table 21 Pattern of missing data and completion

Time point	HRQoL population N	Missing N (%)	Expected to complete N	Completion N (%)
	Number of patients at randomization	Number of patients for whom data is missing (% of patients at randomization)	Number of patients "at risk" at time point X	Number of patients who completed (% of patients expected to complete)
Baseline	E.g. 100	10 (10%)	99	90 (91%)
Time point 1	100	12 (12%)	85	80 (94%)
Time point 2	100	20 (20%)	80	…

Time point	HRQoL population N	Missing N (%)	Expected to complete N	Completion N (%)
Etc.	…	…	…	…

10.1.3 HRQoL results

- [In Table 22, provide results at baseline and at all relevant data collection timepoints, in the HRQoL instrument. Argue for the relevance of the selected data collection time points.
- Include a graph displaying the mean change (with error bars showing the 95 % confidence intervals) from baseline through the different data collection time points for both the intervention and comparator. See an example of the graph below.
    - If EQ-5D-5L data is available, please provide both results on index-score (with Danish preference weights) and EQ-VAS.
- If specific domains from the assessment instrument need to be highlighted, data should be provided in Appendix F. Argue for the relevance of the domain-specific data.]

Example of figure displaying the mean change from baseline through the different data collection time points for both the intervention and comparator:

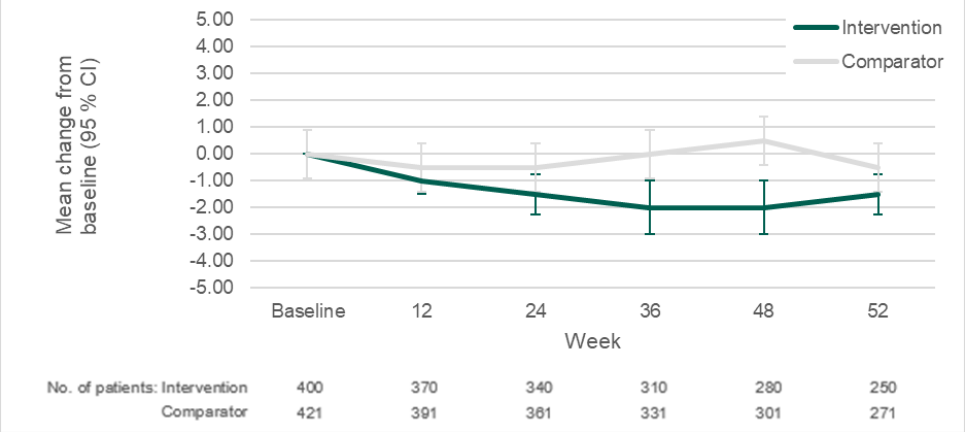


Table 22 HRQoL [instrument 1] summary statistics

	Intervention		Comparator		Intervention vs. comparator
	N	Mean (SE)	N	Mean (SE)	Difference (95% CI) p-value

	Intervention	Comparator	Intervention vs. comparator
Baseline			
Time point 1			
Time point 2			
…			
Follow-up			

10.2 Health state utility values (HSUVs) used in the health economic model

[If other studies than the study forming the basis for clinical effectiveness have been applied for health state utility values, complete section 10.3.]

10.2.1 HSUV calculation

- If EQ-5D-5L and Danish preference weights have not been used, this must be described and justified according to sections 7.1.3 and 7.2 of the methods guide.
- Describe whether HSUVs have been age-adjusted according to section 7.3 of the methods guide.
- Regression-based utility values: If the utility values have been calculated from a regression model (for example state specific utility values or for specific subgroups), please provide regression equations and necessary formulas to calculate the final utility values.

10.2.1.1 Mapping

[Describe mapping methods if applied:

- Describe the purpose of the original mapping study, thoroughly describe the study and patient characteristics on which the mapping is based, and compare it to the patient population included in the application.
- Shortly describe the methods for choosing the patient population, recruiting patients and data collection in the mapping study, including the number of patients and, if any, censored patients.
- Describe the statistical methods used for estimating the overlap between the two questionnaires in the mapping study, including choice for statistical tests and statistical models for the mapping algorithm.
- Present the performance of the statistical models tested, and the reasoning for choosing the model used to estimate the final mapping algorithm. In particular focus

on precision, i.e., the use of root mean square error (RMSE), mean square error (MSE) or mean absolute error (MAE).

- The Danish Medicines Council prefers mappings for which a validation has been carried out. Describe the patient population used for the validation in the same way, as for the patient population under bullet 1.
- Present uncertainty of the utility-values estimated through the mapping, and how said uncertainty was calculated.
- Describe the preference weights relevant to the mapping, and how they were applied in the actual mapping.]

10.2.2 Disutility calculation

[If disutilities associated with adverse events are applied in the health economic model, complete the following and list the disutilities in Table 23:

- Justify why disutilities are relevant to include and to what extent the inclusion captures relevant adverse events.
- Describe how disutilities are calculated and include a formula presenting the calculation.]

10.2.3 HSUV results

[The following steps must be completed:

- Present results in Table 23 and describe:
- Regression based utility values: If regression-based utility values have been used, please present a column with the number of patients and observations that each utility value is based on.
- If sensitivity analyses with different HSUVs have been conducted, these must be described and justified.]

Table 23 Overview of health state utility values [and disutilities]

	Results [95% CI]	Instrument	Tariff (value set) used	Comments
HSUVs				
HSUV A	0.761 [0.700-0.810]	EQ-5D-5L	DK	For example: Estimate is based on mean of both trial arms.
HSUV B	0.761 [0.700-0.810]	EQ-5D-5L	DK	For example: Estimate is based on mean of both trial arms.

	Results [95% CI]	Instrument	Tariff (value set) used	Comments
…				
[Disutilities]				
…				

10.3 Health state utility values measured in other trials than the clinical trials forming the basis for relative efficacy

[If other studies than the study forming the basis for relative efficacy have been used for health state utility values, complete the subsections below. All other studies must be identified in a systematic literature review and described in Appendix I.]

10.3.1 Study design

[See description in 10.1.1.]

10.3.2 Data collection

[See description in 10.1.2.]

10.3.3 HRQoL Results

[See description in 10.1.3.]

10.3.4 HSUV and disutility results

[See description in 10.2 and fill out relevant tables below.]

Table 24 Overview of health state utility values [and disutilities]

	Results [95% CI]	Instrument	Tariff (value set) used	Comments
HSUVs				
HSUV A	0.761 [0.700-0.810]	EQ-5D-5L	DK	Estimate is based on mean of both trial arms.
HSUV B	0.761 [0.700-0.810]	EQ-5D-5L	DK	Estimate is based on mean of both trial arms.

	Results [95% CI]	Instrument	Tariff (value set) used	Comments
…				
[Disutilities]				
…				

Table 25 Overview of literature-based health state utility values

	Results [95% CI]	Instrument	Tariff (value set) used	Comments
HSUV A				
Study 1	0.761 [0.700-0.810]	EQ-5D-5L	DK	EQ-5D-5L data was collected in X trial. Estimate is based on mean of both trial arms.
Study 2				
Study 3				
HSUV B				
…				
[Disutility A]				
…				

11. Resource use and associated costs

[Overall guide for completing the section concerning resource use and associated costs:

- Please find guidance in section 8 in the methods guide and the DMC's catalogue of unit costs on how to describe the resource use and associated costs.
- If unit costs have been included in the model using DRG tariffs, provide a description of the diagnosis- and procedure code that have been used to find the DRG code on the Danish Health Data Authority's website Interactive DRG.
- State the basis for all assumed costs along with a reference.]

11.1 Medicines - intervention and comparator

[Guide for completing this section:

- Include medicines (intervention and comparator), included in the health economic analysis, in the table below. The table can be customized in accordance with the number of comparators; other than this, the table format must *not* be changed.
- All medicines included in the health economic analysis must be provided in the Excel file 'Key figures including general mortality' on the DMC's website.
- If more packages of the medicine are available, justify the relevance of the packages quantities applied in the model.
- Considerations of medicine waste must be described. Justify how the wastage has been modelled in Excel. The same applies for assumptions concerning vial sharing.
- Describe assumptions concerning the treatment duration for the intervention and the comparator. If time-on-treatment data is used to extrapolate the treatment duration, describe the method used in Appendix D.
- Model assumptions, that concern topics such as dosage (e.g. weight-based/body surface area (BSA) dose vs. fixed dose) and relative dose intensity (RDI), must be described in section 3.4 and 3.5 for the intervention and comparator, respectively, and *not* in this section.]

Table 26 Medicines used in the model

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
[Name of the intervention]	[E.g. 5 mg]	[E.g. 97 %]	[E.g. every second week]	[Yes/no]
[Name of the comparator]	[E.g. 5 mg]	[E.g. 97 %]	[E.g. every second week]	[Yes/no]

11.2 Medicines– co-administration

[Guide for completing this section:

- Some treatments require co-administration of e.g. prophylactics to minimize the risk of experiencing adverse events. If this is the case for the comparator and/or the new intervention, the medicine costs of the co-administrations must be included in the analysis.
- If co-administrations are not of relevance for this application, please write "not applicable" under the subtitle.]

11.3 Administration costs

[Guide for completing this section:

- Describe the rationale for including or not including administration costs associated with the intervention and comparator.
- Describe assumptions concerning resource use, frequency, and unit costs. The frequency must be presented non-numerically (e.g. every 3rd week).
- If the unit cost for administration has been included in the model using DRG tariffs, please fill out the table below.

Table 27 Administration costs used in the model

Administration type	Frequency	Unit cost [DKK]	DRG code	Reference
[E.g. i.v. infusion, subcutaneous infusion]	[E.g. every 3rd week]			DRG 202[X]

11.4 Disease management costs

[Guide for completing this section:

- Describe the rationale for including or not including disease management costs associated with the intervention and comparator.
- Describe assumptions concerning resource use, frequency, and unit costs. The frequency must be presented non-numerically (e.g. every 3rd week).
- If the unit cost for disease management has been included in the model using DRG tariffs, please fill out the table below.

Table 28 Disease management costs used in the model

Activity	Frequency	Unit cost [DKK]	DRG code	Reference
[Activity]	[E.g. every 3rd week]			DRG 202[X]

11.5 Costs associated with management of adverse events

[Guide for completing this section:

- The frequencies of the adverse events included as input in the model, must be presented in section 9.
- Briefly describe the management of adverse events in clinical practice, including monitoring, follow-up, use of resources, costs, and other relevant information.
- Describe how the costs of adverse events have been modelled (e.g. one-time cost).
- Please avoid including unit costs for adverse events that would not be associated with any resource use in Danish clinical practice. Additionally, in order to avoid

double-counting, only include unit costs for adverse events for which the clinical definitions are overlapping e.g. neutropenia and decreased lymphocytes, one time.

- Please use the following approach if DRG tariffs are applied: on the Danish Health Data Authority's website Interactive DRG, select the patient's reason for admission (the adverse event) under "diagnosis and supplementary information", and select the patient's general illness in the same cell. Subsequently, note the adverse event with an "A" for action diagnosis, and the disease with a "B" for secondary diagnosis.]

Table 29 Cost associated with management of adverse events

	DRG code	Unit cost/DRG tariff
[Adverse event]		
[Adverse event]		

11.6 Subsequent treatment costs

[Guide for completing this section:

- Describe assumptions concerning the topics listed below:
  - The proportion of patients estimated to be treated with subsequent treatment.
  - If relevant, outline the distribution/share of subsequent therapies in cases where more than one subsequent treatment is available for the patient population.
  - Dosing schedule description and route of administration.
  - Relative dose intensity (RDI).
  - Medicine waste.
  - If relevant, resource use and costs associated with administration, monitoring, and management of adverse events.
  - Average duration of treatment.
- Include the subsequent treatments in the table below. The table can be customized in accordance with the number of comparators; other than that, the table format must *not* be changed.]

Table 30 Medicines of subsequent treatments

Medicine	Dose	Relative dose intensity	Frequency	Vial sharing
[Name of the intervention]	[E.g. 5 mg]	[E.g. 97 %]	[E.g. every second week]	[Yes/no]
[Name of the comparator]	[E.g. 5 mg]	[E.g. 97 %]	[E.g. every second week]	[Yes/no]

11.7 Patient costs

[Guide for completing this section:

- The costs incurred by patients and their families as a consequence of the medicine treatment (transport costs and time spent) must be included, if relevant. The time spent for patients and relatives and the transport costs must be valued in accordance with the DMC's catalogue of unit costs.
- Check that the number of visits to the hospital is aligned with the patient resource use (e.g. due to administration, monitoring and management of adverse events).]

Table 31 Patient costs used in the model

Activity	Time spent [minutes, hours, days]
Activity	

11.8 Other costs (e.g. costs for home care nurses, out-patient rehabilitation and palliative care cost)

If palliative care costs are included, a description of the assumptions of resource use and unit costs must be provided including whether the resource use is at regional or municipality level. If the palliative care costs associated with the intervention and comparator are thought to be roughly the same, these should not be included in the Excel model.

12. Results

If a cost minimization analysis is performed, there may be parts of this section that are not relevant to complete. Please write 'Not applicable' in this case.

12.1 Base case overview

[Provide an overview of the base case including the central aspects in Table 32. The text in column 1 should be customized for each individual assessment.]

Table 32 Base case overview

Feature	Description
Comparator	
Type of model	Markov model
Time horizon	30 years (life time)

Feature	Description
Treatment line	1st line. Subsequent treatment lines not included.
Measurement and valuation of health effects	Health-related quality of life measured with EQ-5D-5L in study x (reference). Danish population weights were used to estimate health-state utility values
Costs included	Medicine costs Hospital costs Costs of adverse events Patient costs
Dosage of medicine	Based on weight
Average time on treatment	Intervention: X Comparator: Y
Parametric function for PFS	Intervention: X Comparator: Y
Parametric function for OS	Intervention: X Comparator: Y
Inclusion of waste	
Average time in model health state Health state 1 Health state 2 Health state 3 Death	

12.1.1 Base case results

[Complete Table 33. The results for the intervention and comparator as well as the difference must always be presented.]

Table 33 Base case results, discounted estimates

	[Intervention]	[Comparator]	Difference
Medicine costs			

	[Intervention]	[Comparator]	Difference
Medicine costs – co-administration			
Administration			
Disease management costs			
Costs associated with management of adverse events			
Subsequent treatment costs			
Patient costs			
Palliative care costs			
Total costs			
Life years gained (health state A)			
Life years gained (health state B)			
Total life years			
QALYs (state A)			
QALYs (state B)			
QALYs (adverse reactions)			
Total QALYs			
Incremental costs per life year gained **Incremental cost per QALY gained (ICER)**			

12.2 Sensitivity analyses

[Section 9 of the methods guide must be followed.]

12.2.1 Deterministic sensitivity analyses

[Present the results obtained from deterministic one-way sensitivity analyses in Table 34.]

Table 34 One-way sensitivity analyses results

	Change	Reason / Rational / Source	Incremental cost (DKK)	Incremental benefit (QALYs)	ICER (DKK/QALY)
Base case					
[relevant analysis]					
[relevant analysis]					

[If there is a need for longer justifications/descriptions, provide them in text form. Present tornado diagram.

If conducted, describe two-way, multi-way and/or scenario analyses and present their results when appropriate in a table.]

12.2.2 Probabilistic sensitivity analyses

[Guide for completing the section concerning the probabilistic sensitivity analysis (PSA):

- Please find supplemental guidance in section 9.2.2 in the methods guide and fill in Table 40 in Appendix G.
- A PSA must contain all parameters from the model that are uncertain. Choice of parameters and the associated probability distributions must be justified.
- It must be easy to change the choice of distributions, e.g. via a drop-down list in the Excel model.
- It must 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 must be described, and correlation must be taken into account in the PSA. Describe the method used to account for correlated parameters.

- In cases where a parameter has not been estimated empirically, an account must be given of how the uncertainty surrounding the estimate is determined.
- 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.

13. Budget impact analysis

[Guide for completing the section concerning budget consequences:

- Please find supplemental guidance in section 10 in the methods guide.
- The assumptions of expected *number of patients* both given a recommendation and given a non-recommendation of the medicine must be described in the section. If the number of patients does not match with 3.2, it must be discussed.
- The assumptions of expected *market share*, both given a recommendation and given a non-recommendation of the medicine, must be described in the section.
- The cost input in the budget impact analysis must originate from the cost-analysis described in section 11 of this application, but discounting and patient costs must be excluded.
- The tables below demonstrate how to present the budget consequences for the regional hospital budgets. The tables must *not* be changed other than inserting additional comparators when relevant.]

Number of patients (including assumptions of market share)

Table 35 Number of new patients expected to be treated over the next five-year period if the medicine is introduced (adjusted for market share)

	Year 1	Year 2	Year 3	Year 4	Year 5
			Recommendation		

	Year 1	Year 2	Year 3	Year 4	Year 5
[Name of intervention]					
[Name of comparator]					
			Non-recommendation		
[Name of intervention]					
[Name of comparator]					

Budget impact

Table 36 Expected budget impact of recommending the medicine for the indication

	Year 1	Year 2	Year 3	Year 4	Year 5
The medicine under consideration is recommended	DKK X	DKK X	DKK X	DKK X	DKK X
The medicine under consideration is NOT recommended	DKK X	DKK X	DKK X	DKK X	DKK X
Budget impact of the recommendation	DKK X	DKK X	DKK X	DKK X	DKK X

14. List of experts

[Provide names, job function and workplace of any clinicians consulted during this application submission. Input from clinicians, who do not want their name and function to appear in the public assessment report will not be considered valid. The applicant can highlight the clinician's name and function in yellow to signal that only the Danish Medicines Council (including the secretariat and the expert committee) may be familiar with the name and function of the clinician. The clinician's name and function will then be marked as confidential information in the public assessment report.]

15. References

[Insert the reference list.]

Appendix A. Main characteristics of studies included

[Complete Table 37 for each study included. Comply with section 3 of the methods guide.]

Table 37 Main characteristic of studies included

Trial name:	**NCT number:**
Objective	[Briefly state the overall objective of the study]
Publications – title, author, journal, year	[State all publications related to the trial.]
Study type and design	[State the phase of the trial and describe the method of randomization, degree of blinding, extent of crossover, status (ongoing or completed), etc. E.g.: Double-blinded randomized placebo-controlled phase 3 study. Enrolled patients were randomly assigned 1:1 using a stratified permuted block randomization scheme via an interactive response system. No crossover was allowed. The investigators, patients, and sponsor were masked during treatment assignment.]
Sample size (n)	
Main inclusion criteria	
Main exclusion criteria	
Intervention	[State the intervention including dose, dosing schedule, and number of patients receiving the intervention]
Comparator(s)	[State the comparator(s) including dose, dosing schedule, and number of patients receiving the comparator]
Follow-up time	[E.g.: Median follow-up of 7.3 months (range 0.5–16.5)]
Is the study used in the health economic model?	[Yes/No. For studies not included in the economic model, but considered relevant to the submission, please provide the rationale]
Primary, secondary and exploratory endpoints	[State all primary, secondary and exploratory endpoints of the study, regardless of whether results are provided in this application. Definition of included outcomes and results must be provided in Appendix D.] **Endpoints included in this application:**

Trial name:	NCT number:
	[E.g.: The primary endpoint was progression-free survival as assessed by the investigator, according to RECIST version 1.1. Secondary endpoints were overall survival, confirmed objective response according to RECIST version 1.1, response duration, progression-free survival assessed by an independent review facility, health-related quality of life (HRQoL) as assessed by QLQ-C30, and safety. **Other endpoints:** E.g.: Time-to-next-treatment and objective response rate were included as secondary endpoints in the study, but results are not included in this application.]
Method of analysis	[State the method of analysis, i.e. intention-to-treat or per-protocol. E.g.: All efficacy analyses were intention-to-treat analyses. We used the Kaplan–Meier method to estimate rates of progression-free survival and overall survival, and a stratified log-rank test for treatment comparisons. Hazard ratios adjusted for XX and YY were estimated with Cox proportional hazards regression. The proportional hazards assumption was assessed by looking for trends in the scaled Schoenfeld residuals.]
Subgroup analyses	[For each analysis, provide the following information: - characteristics of included population - method of analysis - was it pre-specified or post hoc? - assessment of validity, including statistical power for pre-specified analyses.]
Other relevant information	

Appendix B. Efficacy results per study

Results per study

[Complete the table for all studies included, regardless of whether they have been used in the health economic model. Explain how all estimates, such as CIs and p-values, have been estimated, this includes the method used, adjustment variables, stratification variables, weights, corrections (in cases with 0 counts), correlation structure (mixed effects model for repeated measurements) and methods used for imputation. Specify how assumptions were checked. Survival rates: state at which time point these are reported for.]

Table 38 Results per study

Results of [trial name (NCT number)]											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
Example: median overall survival (time point)	XXX	247	22.3 (20.3–24.3) months	4.9	1.79–8.01	0.002	HR: 0.70	0.55–0.90	0.005	The median survival is based on the Kaplan-Meier estimator. The HR is based on a Cox proportional hazards model with adjustment for the variables used for stratification for randomization, and study arm.	
	ZZZ	248	17.4 (15.0–19.8) months								
Example: 1-year survival	XXX	247	74.5% (68.9–80.2)	10.7	2.39–19.01	0.01	HR: 0.70	0.55–0.90	0.005	The survival rates are based on the Kaplan–Meier estimator. The HR is based on a Cox proportional hazards model	
	ZZZ	248	63.8% (57.6–70.0)								

Results of [trial name (NCT number)]											
				Estimated absolute difference in effect			Estimated relative difference in effect			Description of methods used for estimation	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***P* value**	**Difference**	**95% CI**	***P* value**		
										with adjustment for stratification, and study arm.	
Example: HRQoL (time point)	XXX	211	−1.5 (-3.1 to 0.1)	4.5	−8.97 to −0.03	0.04	NA	NA	NA	The absolute difference in effect is estimated using a two-sided t-test.	
	ZZZ	209	−6.0 (−10.2 to −1.8)								
Insert outcome 4	Intervention										
	Comparator										

Appendix C. Comparative analysis of efficacy

[For meta-analyses, the table below can be used. For any type of comparative analysis (i.e. paired indirect comparison, network meta-analysis or MAIC analysis), describe the methodology and the results here in an appropriate format (text, tables and/or figures).]

Table 39 Comparative analysis of studies comparing [intervention] to [comparator] for patients with [indication]

Outcome		Absolute difference in effect			Relative difference in effect			Method used for quantitative synthesis	Result used in the health economic analysis?
	Studies included in the analysis	Difference	CI	P value	Difference	CI	P value		
Example: median overall survival		NA	NA	NA	HR: 0.70	0.55–0.90	0.005	The HRs for the studies included were synthesized using random effects meta-analysis (DerSimonian–Laird).	Yes/No
Example: 1-year survival		10.7	2.39–19.01	0.01	HR: 0.70	0.55–0.90	0.005	The HRs for the studies included were synthesized using random effects meta-analysis (DerSimonian–Laird). The absolute difference was estimated by applying the resulting HR to an assumed 1-year survival rate of 64.33% in the comparator group.	
Example: HRQoL		**–4.5**	−8.97 to −0.03	0.04	NA	NA	NA	HRQoL results for the studies included were synthesized using the standardized mean	

Outcome		Absolute difference in effect			Relative difference in effect			Method used for quantitative synthesis	Result used in the health economic analysis?
	Studies included in the analysis	Difference	CI	P value	Difference	CI	P value		
								difference (SMD). The estimated meta-analytical SMD of −0.3 (95% CI −2.99 to −0.01) was transformed to the scale of ZZZ* assuming a population standard deviation of 15 on the ZZZ* scale. *Fill in the name of an appropriate measure of HRQoL.	
Insert outcome 4									

Appendix D. Extrapolation

[Describe in detail how extrapolation is performed in accordance with sections 6.4.2 and 6.4.3 of the methods guide and the online appendix "Anvendelse af forløbsdata i sundhedsøkonomiske analyser".

- Specify which parametric function was selected for the intervention and comparator, respectively. All standard parametric models (exponential, Weibull, Gompertz, gamma, log normal, log logistic and generalized gamma) and other considered extrapolations must be available in the Excel model.
- Specify if the extrapolation models for the intervention and comparator are fitted in a joint model or independently.
- The section must include a discussion about using the same or different parametric function to extrapolate data for the intervention and comparator.
- A graphical representation of the time-to-event data curves where both the Kaplan-Meier (KM) estimate and the parametric distributions are shown in the same figure must be presented in this section (for both intervention and comparator). The figure must include a graph with the general population's mortality rate and must display the entire time horizon of the model.
- Describe whether (and how) adjustments have been made for treatment switching/cross-over (intervention and/or comparator).
- Describe and explain how the extrapolations have been validated and present the results. When relevant, present a graphical representation of the validation.]

D.1 Extrapolation of [effect measure 1]

D.1.1 Data input

D.1.2 Model

D.1.3 Proportional hazards

[If the extrapolation model relies on proportional hazards, provide a plot with Schoenfeld residuals and a log-cumulative hazard plot.]

D.1.4 Evaluation of statistical fit (AIC and BIC)

[Provide a table with the AIC and BIC and discuss the statistical fit.]

D.1.5 Evaluation of visual fit

D.1.6 Evaluation of hazard functions

[Provide a plot of the hazard function of the effect measure. The plots must be presented in separate figures for the intervention and comparator, respectively, and must include the estimated hazard for the observed data (if applicable). The plot must be discussed in the context of chosen the distribution for extrapolating the data of the effect measure.]

D.1.7 Validation and discussion of extrapolated curves

D.1.8 Adjustment of background mortality

D.1.9 Adjustment for treatment switching/cross-over

D.1.10 Waning effect

D.1.11 Cure-point

D.2 Extrapolation of [effect measure 2]

[For each effect measure please, fill in this section using the same template as stated in section D.1]

Appendix E. Serious adverse events

[Please list all serious adverse events observed in the study.]

Appendix F. Health-related quality of life

[If specific domains from the assessment instrument need to be highlighted, data should be presented here. Argue for the relevance of the domain-specific data.]

Appendix G. Probabilistic sensitivity analyses

[Show in Table 40 which data/assumptions (point estimate, and lower and upper bound) form the basis for the selected probability distributions used in the probabilistic analysis.]

Table 40. Overview of parameters in the PSA

Input parameter	Point estimate	Lower bound	Upper bound	Probability distribution
Probabilities				
Efficacy Outcome A	0.72			Beta
HSUV				
State A	0.79			Beta
Costs				
Hospitalization	20000			Gamma

Appendix H. Literature searches for the clinical assessment

H.1 Efficacy and safety of the intervention and comparator(s)

[Follow section 3 of the methods guide. Describe how the literature search was performed. Explain the selection of the search criteria and terms used, search filters, and the inclusion and exclusion criteria. Sufficient details should be provided so that the results may be reproduced.
Literature searches that are more than one year old are generally not accepted. If this is the case, a new search (e.g. in PubMed) should be carried out for more recent literature on the intervention and chosen comparator(s).

If an existing/global systematic literature review (SLR) is (re)used the appendix must be filled out with data/information from such SLR and it must be clear how the SLR has been adapted to the current application. The inclusion and exclusion criteria, PRISMA flowchart, and list of excluded full text references should reflect the purpose of the application. Thus, unedited technical reports or SLRs will not be accepted in/as the appendix. Please find an editable PRISMA flowchart at the end of this document. This diagram is to be used when existing SLRs are (re)used, so it is clear how it has been locally adapted, i.e. how many references are included and excluded from the original SLR. As mentioned above, if the literature search is more than a year old, a new search (e.g. in PubMed) should be carried out for more recent literature on the intervention and chosen comparator(s).

Objective of the literature search: What questions is the literature search expected to answer?

Databases/other sources: Fill in the databases and other sources, e.g. conference material used in the literature search.]

Table 41 Bibliographic databases included in the literature search

Database	Platform/source	Relevant period for the search	Date of search completion
Embase	e.g. Embase.com	E.g. 1970 until today	dd.mm.yyyy
Medline			dd.mm.yyyy
CENTRAL	Wiley platform		dd.mm.yyyy

Abbreviations:

Table 42 Other sources included in the literature search

Source name	Location/source	Search strategy	Date of search
e.g. NICE	www.nice.org.uk		dd.mm.yyyy
e.g. EMA website			dd.mm.yyyy

Abbreviations:

Table 43 Conference material included in the literature search

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search
Conference name	e.g. conference website	Manual search	List individual terms used to search in the conference material:	dd.mm.yyyy
	Journal supplement [insert reference]	Skimming through abstract collection		dd.mm.yyyy

H.1.1 Search strategies

[Describe the development of the search strategy and search string. Specify the inclusion and exclusion criteria for the search and justify (e.g. patient population, intervention, comparator, outcomes, study design, language, time limits, etc.).]

[The search must be documented with exact search strings line by line as run, incl. results, for each database.]

Table 44 of search strategy table for [name of database]

No.	Query	Results
#1		88244
#2		85778
#3		115048
#4		7011
#5		10053
#6		12332
#7		206348

No.	Query	Results
#8		211070
#9	#7 OR #8	272517
#10	#3 AND #6 AND #9	37

H.1.2 Systematic selection of studies

[Describe the selection process, incl. number of reviewers and how conflicts were resolved. Provide a table with criteria for inclusion or exclusion. If the table relates to an existing SLR broader in scope, please indicate which criteria are relevant for the current application.]

Table 45 Inclusion and exclusion criteria used for assessment of studies

Clinical effectiveness	Inclusion criteria	Exclusion criteria	Changes, local adaption
Population			
Intervention			
Comparators			
Outcomes			
Study design/publication type			
Language restrictions			

[Insert the PRISMA flow diagram(s) here (see example here) or use the editable diagram at the end of this document. If an existing SLR is used, the editable diagram is to be used, so it is clear how many references have been included and excluded from the original SLR.]

Table 46 Overview of study design for studies included in the analyses

Study/ID	Aim	Study design	Patient population	Intervention and comparator (sample size (n))	Primary outcome and follow-up period	Secondary outcome and follow-up period
Study 1						
Study 2						

H.1.3 Excluded fulltext references

[Please provide in a list or table the references that were excluded during fulltext screening along with a short reason. If using an existing, locally adapted SLR, please fill in the references originally included in the SLR but excluded in the current application.]

H.1.4 Quality assessment

[Describe strengths and weaknesses of the literature search performed.]

H.1.5 Unpublished data

[The quality of any unpublished data must be specifically addressed and a publication plan for unpublished data must be submitted].

Appendix I. Literature searches for health-related quality of life

I.1 Health-related quality-of-life search

[Follow sections 3 and 7.1.2 of the methods guide.
Describe how the literature search for the health-related quality of life data was performed. Explain the selection of the search criteria and terms used, search filters, and the inclusion and exclusion criteria. Sufficient details should be provided so that the results may be reproduced. Literature searches that are more than one year old are generally not accepted. If this is the case, a new search (e.g. in PubMed) should be carried out for more recent literature.

If existing/global systematic literature review (SLR) is (re)used, Appendix I must be filled out with data/information from such SLR and it must be clear how the SLR has been adapted to the current application. The inclusion and exclusion criteria, PRISMA flowchart, and list of excluded full text references should reflect the purpose of the application. Thus, unedited technical reports or SLRs will not be accepted in/as the appendix. Please find an editable PRISMA flowchart at the end of this document. This diagram is to be used when existing SLRs are (re)used, so it is clear how it has been locally adapted, i.e. how many references are included and excluded from the original SLR. As mentioned above, if the literature search is more than a year old, a new search (e.g. in PubMed) should be carried out for more recent literature.

If targeted literature searches have been carried out, e.g. to identify reduction of health related quality of life associated with adverse events (disutilities), these should be documented. In separate sections (for each individual search), account for the sources used, the choice of search criteria and terms, and explain the process of inclusion and exclusion. Sufficient information must be provided to enable the results to be reproduced where possible.

Objective of literature search: What questions is the literature search expected to answer?

Sources: Describe briefly which databases, and other sources were used in the literature search.]

Table 47 Bibliographic databases included in the literature search

Database	Platform	Relevant period for the search	Date of search completion
Embase	Embase.com		dd.mm.yyyy
Medline	Ovid		dd.mm.yyyy

Database	Platform	Relevant period for the search	Date of search completion
Specific health economics databases[1]			dd.mm.yyyy

Abbreviations:

Table 48 Other sources included in the literature search

Source name	Location/source	Search strategy	Date of search
e.g. NICE	www.nice.org.uk		dd.mm.yyyy
CEA Registry	Tufts CEA - Tufts CEA		dd.mm.yyyy

Table 49 Conference material included in the literature search

Conference	Source of abstracts	Search strategy	Words/terms searched	Date of search
Conference name	e.g. conference website	Electronic search	List individual terms used to search in the congress material:	dd.mm.yyyy
	Journal supplement [insert reference]	Skimming through abstract collection		dd.mm.yyyy

I.1.1 Search strategies

[Describe the development of the search strategy and search string. Enter the inclusion and exclusion criteria for the search and justify (e.g. patient population, outcomes, study design, language, time frame, etc.).

The search must be documented for each database or resource incl. terms and syntax used, number of results retrieved in the table below.

Describe which criteria have been used to reject irrelevant studies (for example of a table to record exclusions, see Table 5 in NICE DSU Technical Support Document 9) and

[1] Papaioannou D, Brazier J, Paisley S. Systematic searching and selection of health state utility values from the literature. Value Health. 2013;16(4):686-95.

how the final selection has been made. Use PRISMA charts if appropriate (see example here) or use the editable table at the end of this document].

Table 50 Search strategy for [name of database]

No.	Query	Results
#1		88244
#2		85778
#3		115048
#4		7011
#5		10053
#6		12332
#7		206348
#8		211070
#9	#7 OR #8	272517
#10	#3 AND #6 AND #9	37

Literature search results included in the model/analysis:

[Insert results in a table]

I.1.2 Quality assessment and generalizability of estimates

[Provide a complete quality assessment for each relevant study identified. When non-Danish estimates are used, generalizability must be addressed.]

I.1.3 Unpublished data

[The quality of any unpublished data must be specifically addressed and a publication plan for unpublished data must be submitted.]

Appendix J. Literature searches for input to the health economic model

J.1 External literature for input to the health economic model

[Describe and document how the literature for the model was identified and selected. This may be a combination of systematic database searches, targeted searches etc. Explain in separate sections (for each type of search) the sources used, the selection of the search criteria and terms used, and explain the process for inclusion and exclusion. Sufficient details should be provided so that the results may be reproduced where possible.]

J.1.1 Example: Systematic search for […]

[Objective of the literature search: What questions is the literature search expected to answer?]

Table 51 Sources included in the search

Database	Platform/source	Relevant period for the search	Date of search completion
Embase	e.g. Embase.com	e.g. 1970 until today	dd.mm.yyyy
Medline			dd.mm. yyyy
CENTRAL	Wiley platform		dd.mm. yyyy

Abbreviations:

[Describe the selection process and criteria for inclusion or exclusion. For systematic searches, the requirements from the literature search for clinical evidence apply, see Appendix H].

J.1.2 Example: Targeted literature search for [estimates]

[Objective of the literature search: What questions is the literature search expected to answer?]

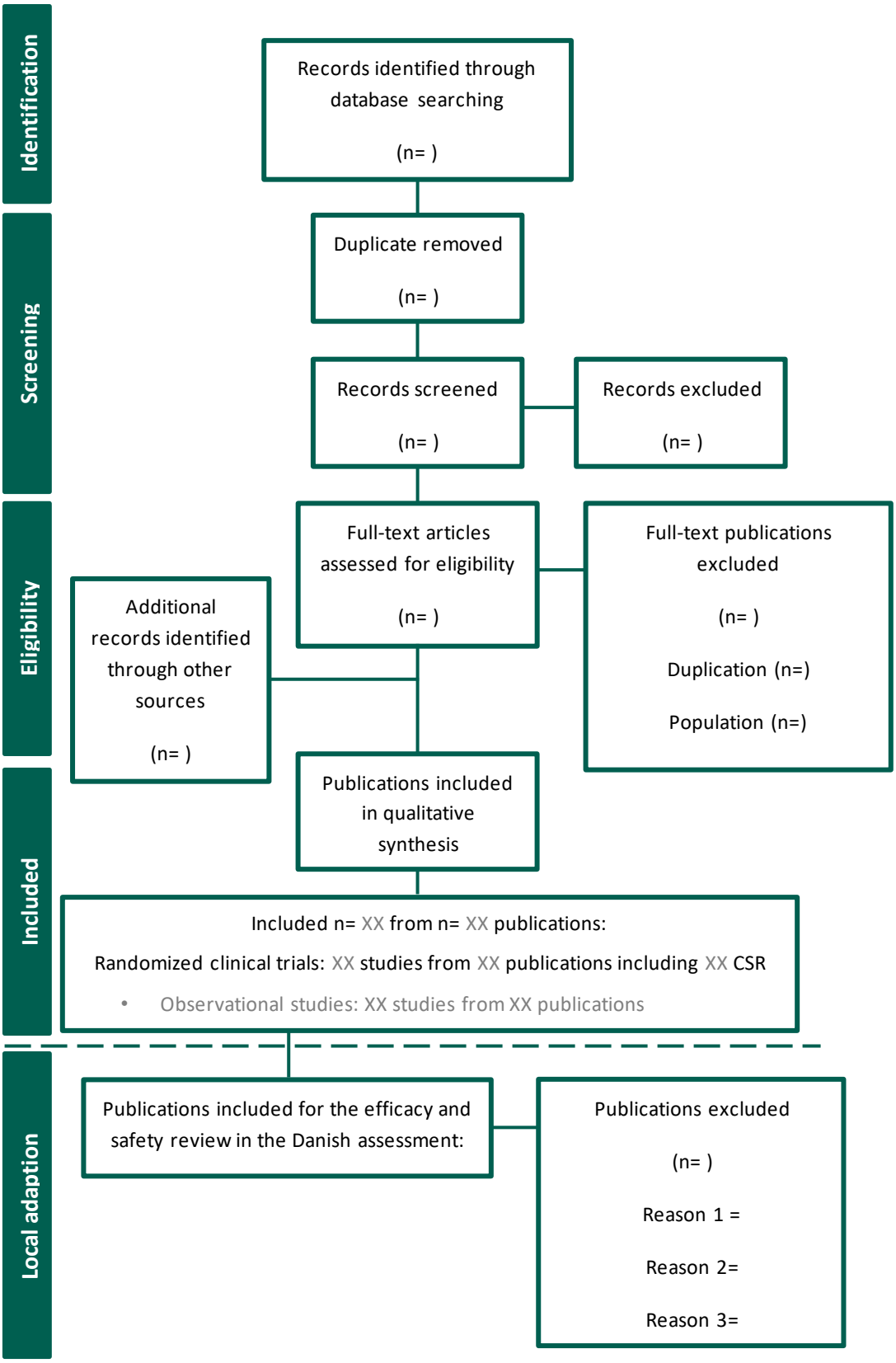
Table 52 Sources included in the targeted literature search

Source name/ database	Location/source	Search strategy	Date of search
e.g. NICE	www.nice.org.uk		dd.mm.yyyy
			dd.mm.yyyy

Abbreviations:

[Describe the selection process and criteria for inclusion or exclusion.]

Example of PRISMA diagram. The diagram is editable and may be used for recording the records flow for the literature searches and for the adaptation of existing SLRs.



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