Medicinrådet

Instructions for Applicants

This is the dossier for submitting documentation to the Danish Medicines Council as part of the assessment process for a new drug or an extension of indication.

Please note the following requirements:

- The Danish Medicines Council's secretariat carries out a technical validation of all submissions. This means that the submission must comply with all requirements specified in *the checklist of formal requirements* available on the Danish Medicines Council's website before the assessment process can begin (day 0).
- The applicant must always use the current version of the checklist, dossier, standard sheets (Excel) and method guidelines.
- All submissions must comply with applicable data protection regulations. Find more information about the Danish Medical Council's data policy here .
- Text in gray and [in brackets] is provided for illustrative purposes only and must be deleted.
- All sections of the dossier must be completed. If a section or appendix is not relevant, "N/A" must be stated along with a brief explanation.
- If a Joint Clinical Assessment (JCA) has been conducted under the EU HTA Regulation, the applicant should not resubmit information already included in the JCA dossier. Instead, the applicant must refer in the relevant sections to the specific part of the JCA report where the information is provided. Please note that it may still be relevant to submit data from the same studies or updated analyses included in the JCA report, e.g. if data from a later data cut-off has become available, or if new comparator data affect the results of a relevant comparative analysis presented in the JCA report.

The assessment process will not begin until all requirements have been met.
The submission may be submitted in either Danish or English.

Documentation to be submitted

The following documentation must be submitted to the Danish Medicines Council by email to: ansogning@medicinraadet.dk.

- The submission dossier in Word format
- The submission dossier in PDF format
- One Excel file containing both the health economic analysis and the budget impact analysis. The analyses must be linked to the standard Excel sheets from the Danish Medicine Council's Excel template "Standard sheets (Excel)".
- The European Public Assessment Report (EPAR) must be attached. If the final version has not been published at the time of submission, please include a draft and submit the final version as soon as possible thereafter.

The applicant is also encouraged to submit an importable reference list in RIS format.

Medicinrådet

Confidential information in the submission and any appendices and notes

The Danish Medicines Council publishes the submission (including any appendices and notes) on its website together with the assessment report and recommendation.

The Danish Medicines Council must ensure the highest possible degree of transparency in the assessment of new drugs, in accordance with the Danish Medicines Council´s terms of reference and general principles of administrative law. Accordingly, the submission (including any appendices and notes) must be as transparent as possible. The Danish Medicines Council may redact (black out) specific information if it is considered confidential and of significant importance to the applicant. Any redactions must always be limited to specific words or values and must not include entire sentences or sections.

Confidential information must be marked in the initial version of the submission. If confidential information is included in the submission, appendices or any subsequent notes, the applicant must submit two versions:

- one version for the Danish Medicines Council's case processing, in which the confidential information is highlighted in turquoise (Hex: #00FFFF).
- one version for publication on the Danish Medicines Council's website, in which the confidential information is redacted using black marking. The Danish Medicines Council will publish this version.

The applicant is responsible for ensuring that redactions are sufficient to prevent disclosure of confidential information upon publication on the Danish Medicines Council's website. For example, the information to be redacted may be covered with black marking and the underlying text replaced with placeholder characters (e.g., “XXX”) to prevent the information from being recovered during document editing. Further information on confidential information and redaction is available on the Danish Medicines Council's website.

When redacting specific information, the applicant must provide concrete and specific justifications explaining why each redacted element is of significant importance to the applicant and why it should be withheld from the public. The justifications must be provided in 0. If the submission contains confidential information, completion of Appendix K is a requirement for technical validation.

Please note that if the applicant has redacted information on the grounds of confidentiality, this does not necessarily mean that a corresponding 1:1-redaction will apply in the event of a request for access to documents. The Danish Medicines Council may only withhold information or documents from public access to the extent permitted by the provisions of the Danish Access to Public Administration Files Act. Requests for access to documents are therefore assessed independently and on a case-by-case basis in accordance with the law. As a general rule, the Danish Medicines Council will obtain a statement from the applicant as part of this assessment.

Macros in Excel

Due to IT security requirements, Excel files containing macros must be signed with a certificate by the applicant before submission to the Danish Medicines Council. Find more information here.

Version Log

Version	Date	Revision
2.1	**March 10, 2026**	**Language and formatting changes**
2.0	February 20, 2026	English version approved and published.
1.0	September 1, 2023	Danish version of the submission dossier published on the Danish Medicines Council's website.

Language: English
Format: PDF
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Submission for the Assessment of <drug(s)> for <indication>

Contact Information

Contact information	
Company	**[Name of the applicant company]**
Name of contact person	
Title	
Telephone number (incl. country code)	
Email	
External representative	**[Name/applicant]**
Title	
Telephone number (incl. country code)	
Email	

[If an applicant wishes to appoint an external representative in connection with an submission for the assessment of a new drug or an extension of indication, this power of attorney must be completed and submitted to ansogning@medicinraadet.dk .]

Table of Contents

Tables and Figures

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

Abbreviations

[Insert a list of all abbreviations used in this submission].

1. Information on the Drug

Drug information	
Trade name	
Generic name	
Indication as formulated by the European Medicines Agency (EMA)	
Marketing Authorisation Holder in Denmark	
ATC code	
Combination therapy and/or concurrent treatment	[Yes/No. If yes, specify the drugs]
Expected date of EU approval (marketing authorisation)	[Yes/No]
Has the drug received a conditional marketing authorisation?	[Yes/No. If yes, specify the specific obligations associated with the conditional marketing authorisation, including expiry date]
Has the drug undergone 'accelerated assessment' at EMA?	[Yes/No]
Has the drug received orphan drug designation?	[Yes/No. If yes, provide the date of designation]
Other indications approved by EMA	[Yes/No]
Other indications assessed by the Danish Medicines Council	[Yes/No]
Joint Nordic Assessment (JNHB): **Is current treatment practice comparable across the Nordic countries (DK, FI, IS, NO, SE)?**	[Yes/No. Provide a brief explanation]
Joint Nordic Assessment (JNHB): **Is the drug suitable for a joint Nordic assessment?**	[Yes/No. Provide a brief explanation]
Has a Joint European Assessment (JCA) been conducted under EU HTA Regulation?	[Yes/No. If yes, specify the date of approval by the EU HTA Coordination Group and provide a link to the published JCA for the relevant indication, if available]

Dispensing	[BEGR/NBS]
Packaging – types, pack sizes/number of units, and strengths	

2. Summary Table

Complete the table below, maximum two pages.

Overview	
Indication relevant to the assessment	[Specify the indication as well as any deviations from the EMA indication and a brief justification]
Dosage regimen and route of administration	
Choice of comparator	
Prognosis with current standard treatment (comparator(s))	[Briefly describe the expected prognosis in terms of disease progression, mortality, and quality of life. Report median survival or survival rates from the Danish population, unless the disease has mortality comparable to the general population]
Type of documentation for the clinical evaluation	[E.g., *Head-to-head* study or indirect comparison (ITC, NMA, MAIC, other)]
Main outcomes including at least one outcome for health-related quality of life (difference/improvement compared with comparator(s))	[Insert results for a maximum of four outcomes that are most important to the assessment]
Serious adverse events for the intervention and comparator	[Specify the most frequent serious adverse events and the frequency for both intervention and comparator(s)]
Type of health economic analysis	[Specify cost-utility analysis or cost-minimisation analysis]
Health economic model	[Specify model type, e.g., Markov model or partitioned survival model]
Outcomes and data sources used to extrapolate patient transitions	[E.g., Outcome 1 (data source A), Outcome 2 (data source B)]
Instrument and data sources for health-related quality of life	[E.g., Instrument 1 (data source A), Instrument 2 (data source B)]

Life-years gained (discounted, half-cycle corrected, and adjusted for background mortality)	[X years]
QALYs gained (discounted, half-cycle corrected, and adjusted for background mortality)	[X QALYs]
ICER (DKK/QALY) (discounted, half-cycle corrected, and adjusted for background mortality)	[XX DKK/QALY]
Applicant's assessment of uncertainty	[Describe the most important uncertainties in the health economic analysis]

3. Patient Population, Intervention, Choice of Comparator(s) and Outcome(s)

The applicable documentation standards are set out in the Danish Medicines Council's methodological guideline and the supporting guideline on population, intervention, choice of comparator(s), and outcome(s). Section numbering and tables must not be modified. Rows in Table 6 and Table 7 may be deleted/added.

3.1 Patient Population

3.1.1 The Disease

[Describe the disease, including:

- The pathophysiology.
- The clinical presentation/symptoms of the disease.
- The impact of the disease on patients' functional ability and health-related quality of life.

Maximum 1-3 pages including figures.]

3.1.2 Selected patient population

[Table 1 must be completed. Describe and justify the following in maximum 1-3 pages (including figures and tables):

- The choice of patient population, including justification for any restriction to a subpopulation within the approved indication.
- How the expected number of patients reported in Table 1 has been calculated, including relevant references to Danish data sources. Supplement the description with a flowchart clearly illustrating which patients are included and excluded relative to the EMA indication, and the reason(s) for these inclusions/exclusions.
- Whether the incidence has been stable, increasing, or decreasing over the past five years. If the incidence has not been relatively stable, supplement with a table showing the trend over time.
- Whether diagnostic tests and examinations are used for patient selection.

For small patient populations, the applicant must also describe the global disease burden, including prevalence and incidence.]

Table 1. Expected number of patients and patient uptake of the intervention

	Year 1	Year 2	Year 3	Year 4	Year 5
Expected number of patients*	[E.g., 100]	[E.g., 60]	[E.g., 60]	[E.g., 60]	[E.g., 60]
Patient uptake**	*[Enter %]*	*[Enter %]*	*[Enter %]*	*[Enter %]*	100%

*The number of patients in Denmark eligible for the new treatment in accordance with the EMA indication, minus the number of patients who are not considered suitable for treatment (e.g., due to age or comorbidity), and minus those who are expected to decline treatment. As a general rule, the number of new (incident) patients per year should be used. However, if prevalent patients are expected to be offered treatment, these should be included in year 1. **Patient uptake is defined relative to the expected number of eligible patients. If full patient uptake (100%) is not expected from year 1 due to a gradual implementation, the relevant percentage uptake must be specified for each year. Once the new treatment is expected to be fully implemented, patient uptake must reach 100% (no later than year 5). For definitions of patient numbers and patient uptake, see the Danish Medicines Council's guideline on budget impact analysis.

3.2 Intervention

- [Table 2 and Table 3 must be completed.
- If the drug has received a conditional marketing authorisation, describe the associated conditions.
- Briefly describe the intervention, including its mechanism of action.
- Insert a table showing the dose distribution based on the most recent pre-specified data cut from the clinical study or studies. The dose distribution must also be included in the health economic model, as it forms the basis for the calculation of drug costs. See the Danish Medicines Council's guideline for calculating costs.
- Briefly describe whether there may be differences between the dose distribution observed in the clinical study(ies) and the dose expected to be used in Danish clinical practice, and the expected implications for effectiveness, safety, and costs.]

Table 2. Overview of the intervention

Therapeutic indication relevant to the assessment	
Generic name	
ATC code	
Mechanism of action	
Route of administration	
Packaging type, pack sizes, shelf life, and strengths	
Package size(s)	
If vials: Can these be shared?	
Pre-medication: Is premedication required? If yes, specify which	
Co-administration: Is the drug to be administered with other drugs? If yes, specify which	
Need for diagnostics, monitoring, or other tests (e.g., *companion diagnostics*)	

Table 3. The intervention in the clinical study and in the health economic model

	Clinical study	Health economic model
Dosage and frequency **[if weight-based, specify body weight in parenthesis and any criteria for switching to a flat dose]**	E.g., 5 mg/kg on day 1 and 8 every 3 weeks	E.g., 5 mg/kg on day 1 and 8 every 3 weeks. Max 400 mg (flat dose from 80 kg)
Average dose	E.g., 400 mg	E.g., 350 mg
Criteria for treatment discontinuation	E.g., max 6 series	E.g., max 6 series
Treatment duration	[Report median and, if possible, mean]	[Report modelled mean used in the health economic model]

	Clinical study	Health economic model
Dose adjustment: Specify whether/how dose adjustments are applied*	E.g., the treatment can be dose adjusted down to 3 mg/kg in case of toxicity.	E.g., the dose distribution from [study name] forms the basis for calculating drug costs.
Treatment interruption: Specify whether/how treatment interruptions (pause) are applied*	E.g., the treatment cannot be interrupted	E.g., interruptions are not included in the cost calculations

*If Relative Dose Intensity (RDI) is used to account for dose adjustments and/or treatment interruptions, include a definition of RDI. See the Danish Medicines Council's guideline for calculating costs.

3.2.1 The Intervention in the Context of Danish clinical practice

[Describe the current treatment algorithm and where the intervention is expected to be used within it, as well as any changes to the overall treatment algorithm.

If the intervention requires diagnostic tests or methods for patient selection that are not routinely used in Danish clinical practice, provide an explanation here.]

3.2.2 Advanced Therapy Medical Products

[For Advanced Therapy Medical Products (ATMPs): Describe the technology, e.g., vector type, expected duration of effect, risk of immune reactions, cross-reactivity, integration into the host cell DNA, risk of vector transmission to a partner or fetus during pregnancy, and any special precautions.

If a JCA has been prepared for the drug, refer instead to the relevant section(s) of the JCA in which the technology is described.]

3.3 Choice of Comparator(s)

- [Table 4 and Table 5 must be completed. If more than one comparator is included in the submission, copy and complete the tables separately for each comparator.
- Provide a justification for the choice of comparator(s).
- Report whether the comparator is used without an EMA indication for the relevant disease (i.e. off-label use).
- Insert a table showing the dose distribution based on the most recent pre-specified data cut from the clinical study or studies. The dose distribution must also be included in the health economic model, as it forms the basis for the calculation of drug costs. See the Danish Medicines Council's guideline for calculating costs.
- Briefly describe whether there may be differences between the dose distribution observed in the clinical study or studies and the dose expected to be used in Danish clinical practice, and the expected implications for effectiveness, safety, and costs.]

Table 4. Overview of the comparator

Overview	
Therapeutic indication relevant to the assessment	
Generic name	
ATC code	
Mechanism of action	
Route of administration	
Packaging type, pack sizes, shelf life, and strengths	
Package size(s)	
If vials: Can these be shared?	
Pre-medication: Is premedication required? If yes, specify which	
Co-administration: Is the drug to be administered with other drugs? If yes, specify which	
Need for diagnostics, monitoring, or other tests (e.g., *companion diagnostics*)	

Table 5. Comparator in the clinical study and in the health economic model

	Clinical study	Health economic model
Dosage and frequency **[if weight-based, specify body weight in parenthesis and any criteria for switching to a flat dose]**	E.g., 5 mg/kg on day 1 and 8 every 3 weeks	E.g., 5 mg/kg on day 1 and 8 every 3 weeks. Max 400 mg (flat dose from 80 kg)
Average dose	E.g., 400 mg	E.g., 350 mg
Criteria for treatment discontinuation	E.g., max 6 series	E.g., max 6 series
Treatment duration	[Specify median and, if possible, mean]	[Report modelled mean used in the health economic model]

	Clinical study	Health economic model
Dose adjustment: Specify whether/how dose adjustments are applied*	E.g., the treatment can be dose adjusted down to 3 mg/kg in case of toxicity.	E.g., the dose distribution from [study name] forms the basis for calculating drug costs.
Treatment interruption (pause): Specify whether/how treatment interruptions are applied*	E.g., the treatment cannot be interrupted	E.g., interruptions are not included in the cost calculations
Dosage and frequency **[if weight-based, specify body weight in parenthesis and any criteria for switching to a flat dose]**	E.g., 5 mg/kg on day 1 and 8 every 3 weeks	E.g., 5 mg/kg on day 1 and 8 every 3 weeks. Max 400 mg (flat dose from 80 kg)

*If Relative Dose Intensity (RDI) is used to account for dose adjustments and/or treatment interruptions, include a definition of RDI. See the Danish Medicines Council's guideline for calculating costs.

3.4 Subsequent Treatment

[Describe whether patients in Danish clinical practice are expected to be treated with one or more subsequent lines of treatment after the intervention and/or comparator, including the proportion of patients in each treatment arm (e.g., 80% of patients with progressed disease). Describe differences and similarities between the subsequent treatments given in the clinical study or studies and those used in Danish clinical practice, and any implications for the transferability of the clinical study results.

If one or more subsequent lines of treatment may be given after the intervention and/or comparator:

- Insert a table in Appendix C showing the distribution of subsequent treatments in the clinical study.
- Complete Table 6 **Fejl! Henvisningskilde ikke fundet.**regarding assumptions applied in the health economic analysis.]

Table 6. Assumptions regarding subsequent treatment in the health economic analysis

	[Intervention] %	[Comparator] %	Mean treatment duration (incl. source)	Dosage (dose, frequency and route of administration, incl. source)	Any assumptions regarding dose adjustments and treatment interruptions, incl. source)
Proportion of patients receiving a subsequent line of treatment	[x% of e.g., patients with progressed disease]	…			
[Name of subsequent treatment 1]	[% of patients receiving subsequent treatment]	..			
[Name of subsequent treatment 2]	..	..			
…					

3.5 Relevant Outcomes

[If a JCA has been prepared, refer instead to the relevant section(s) of the JCA report in which the outcomes are defined and described. The rest of this section, including tables, should be filled in with “N/A”.]

3.5.1 Definition of Outcomes

[Table 7 must be completed. Define the outcomes considered relevant and necessary to evaluate the effect of the intervention compared with the comparator. Describe the rationale for the selected outcomes.

All outcomes included in the submission must be defined in Table 7.

For indirect comparisons, clearly state any differences in outcome definitions across studies. Describe how such differences are addressed in the comparison and the implications for the interpretation of the results.]

Table 7. Outcomes

Outcome	Follow-up time point	Definition
Overall survival (OS) [Included study 1]		OS is defined as the time from randomization to death from any cause. OS is defined as the time from first treatment recorded in registry X to the date of death from any cause.
ASAS40 [Included study 1]	Week 12	Proportion of patients achieving ASAS40 response. An ASAS40 response was defined as a ≥ 40% improvement and an absolute improvement from baseline of ≥ 2 units (scale 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 (BASFI (Bath Ankylosing Spondylitis Index), Spondylitis Functional Index), 0-10 cm VAS [source XX], and inflammation/morning stiffness (mean score for items 5 and 6 in BASDAI) (0-10 cm VAS)) without worsening in the remaining domain [source YY].

3.5.2 Relevance of Outcomes

When intermediate or surrogate outcomes are used, it must be documented how these outcomes relate to health-related quality of life and/or survival. Describe the evidence supporting the association between the surrogate outcome and the patient-relevant outcome, including the sources used and how they were identified (e.g., through a systematic literature review (SLR)).]

3.5.3 Validity of Outcomes

[As a general rule (exceptions include overall survival and progression-free survival), it must be stated whether the validity of the outcome has been assessed and how this was done. References must be provided. Previous assessments conducted by the Danish Medicines Council may be cited as a reference. If an instrument or scale is used, it must be described whether it has been validated for the relevant population. The scale and the minimal clinically relevant difference must be described with reference to the relevant source.

If composite outcomes are used, the rationale for grouping these measures must be clearly described, including whether there is international consensus regarding the composite outcomes and whether information on the individual outcome are available.]

4. Health Economic Analysis

[The applicable documentation standards are specified in the Danish Medicines Council's methodological guideline and the supporting guideline on health economic analysis and extrapolation. Section numbering and tables must not be modified. Rows and/or columns must not be added.]

4.1 Reference-case Assumptions

[Table 8 must be completed.]

Table 8. Reference-case assumptions in the health economic analysis

	Assumption	Justification
Patient population	[Specify the patient population in the health economic analysis]	[Describe any deviations from the section on relative effectiveness, e.g., subgroups]
Intervention	[Specify the intervention in the health economic analysis]	[Describe any deviations from the section on relative effectiveness]
Comparator(s)	[Specify the comparator in the health economic analysis]	[Describe any deviations from the section on relative effectiveness]
Clinical outcomes	[List all outcomes used in the health economic analysis]	[Provide justification, e.g., if surrogate outcomes are used]
Type of analysis	[E.g., cost-utility analysis]	[Provide justification]
Type of model	[E.g., partitioned survival model]	[Provide justification]
Mean age at model entry	[E.g., 60 years]	[Provide justification]
Time horizon	[E.g., 40 years]	[Provide justification, e.g., lifetime perspective]
Cycle length	[E.g., 1 month]	[Provide justification]
Half-cycle correction	[Yes/No + elaborate if some costs are not half-cycle corrected]	[If no: Provide justification, e.g., if administration or dispensing of drug occurs on day 1 of the cycle]

4.2 Model Type and Model Structure

[Table 9 must be completed. Justify the choice of analysis (cost-utility analysis or cost-minimisation analysis) and the choice of model type (e.g., partitioned survival model, semi-Markov model, or Markov model).

Describe the model structure and include a graphical illustration of the health states and possible patient transitions between health states. For each treatment arm, explain how the model structure reflects the disease and treatment pathway in Danish clinical practice. In the column "Assumptions", briefly state whether the model contains other relevant assumptions related to the patient transitions in the model.]

Table 9. Choice of health economic analysis, model, and model structure

Type of health economic analysis	Type of model	Model structure	Assumptions
[E.g., cost-utility analysis]	[E.g., partitioned survival model]	[E.g., 3 health states (state A, state B, and state C)]	[E.g., assumptions regarding cure, waning effect, or use of surrogate outcomes]

5. Literature Review

[*Applicable documentation standards are specified in the Danish Medicines Council's methodological guideline and the supporting guideline on literature. Section numbering and tables must not be modified. Rows may be added to the tables.]*

5.1 Literature Used to Assess Clinical Effectiveness and Safety

All references used in the assessment of clinical effectiveness and safety must be listed in Table 10. The source of each effectiveness outcome and safety measure must be clearly stated in the table.

If a JCA has been prepared, the table must refer to the relevant section of the JCA report, if this is comprehensive. If additional literature is included that is not part of the JCA report, references to these specific sources must also be provided.]

Table 10. Relevant literature included in the assessment of effectiveness and safety

Reference	Study name	NCT number	Study dates (start date and expected end date, data cut-off, and expected data cut-offs)	Used for comparison of*
Author. Title of the article. Journal. Year; volume (edition): pp. [ref. no.] … Data on file: Title etc. [ref. no.] EMA EPAR [ref. no.]			Start: DD/MM/YY End: DD/MM/YY Data *cut-off* DD/MM/YY Future *data cut-offs* DD/MM/YY	<effectiveness/ safety outcome > for <intervention> vs. <comparator> for <population>

*List all study publications used and specify, for each, which comparison they are used for.

5.2 Literature Used to Assess Health-Related Quality of Life

[All references used in the assessment of health-related quality of life must be listed in Table 11.

If a JCA has been prepared, the table must refer to the relevant section of the JCA report, if this is comprehensive. If additional literature is included that is not part of the JCA report, references to these specific sources must also be provided.]

Table 11. Relevant literature included in the assessment of health-related quality of life

Reference	Instrument and purpose	Identification method (documented in appendix)	Used in section
Author. Title of the article. Journal. Year; volume (edition): pp. [ref.nr]	E.g., EQ-5D-5L for estimating utility values in health state "C"	E.g., Systematic literature search (Appendix I) Focused literature search (Appendix I) Head-to-head study	E.g., 10.3
Data on file: Title etc. [ref. no.]		Head-to-head study	

5.3 Literature Used as Input in the Health Economic Model

[All literature used in the health economic model must be listed in Table 12.

If a JCA has been prepared, the table must refer to the relevant section of the JCA report, if this is comprehensive. If additional literature is included that is not part of the JCA report, references to these specific sources must also be provided.]

Table 12. Relevant literature used in the health economic model

Reference (Full citation including reference number)	Input/estimate	Identification method (documented in appendix)	Used in section
Author. Title of the article. Journal. Year; volume (edition): pp. [ref. no.]		E.g., Systematic literature search (Appendix J) Focused literature search (Appendix J) Head-to-head study	

Reference (Full citation including reference number)	Input/estimate	Identification method (documented in appendix)	Used in section
Data on file: Title etc. [ref. no.]		Head-to-head study	

6. Clinical Studies

[*Applicable documentation standards are specified in the Danish Medicines Council's methodological guideline and the supporting guideline on clinical effectiveness and safety. Section numbering and tables must not be modified. Rows and/or columns may be deleted/added in Table 14, and rows may be deleted/added in Table 13 and Table 15.*

If more than one comparison is included in the submission (i.e. due to more than one comparator or more than one population), Section 6.1 must be copied and completed separately for each comparison/population.]

6.1 [Intervention] Compared with [Comparator] in [Patient Population]

6.1.1 Relevant Studies

- [Present in Table 13 all studies used in the comparison. This includes studies of the applicant's drug and of the comparator, including real-world evidence (RWE) studies. All studies must be described in detail in Appendix A, and the corresponding study protocols must be submitted as supplementary appendices.
- Indicate whether the population in the submission is a subpopulation of the study and, if so, whether the subpopulation was predefined in the study protocol.
- All clinical data used in the submission must be from the latest available predefined data cut. State the date of the latest available predefined data cut used and the median follow-up time. Also state when data from the next planned data cut is expected to be available.
- Report the proportion of patients who discontinued the study in each study arm and the reasons for discontinuation.
- Report the proportion of patients in each study arm who did not receive the treatment to which they were randomised.
- For each included study, the internal and external validity must be discussed.

If a JCA has been prepared, refer instead to the section in the JCA report where the relevant clinical studies are described. If data are available from a later data cut from the included studies than those used in the JCA, this must be described.]

Table 13. Overview of study characteristics for all studies included in the comparison

Study name, NCT number (reference)	Studio design	Duration of study	Patient population	Intervention	Comparator	Outcomes and follow-up time
Study 1	Randomized phase III/unblinded/placebo-controlled/active comparator			Treatment, administration, dosage	Treatment, administration, dosage	[All primary and secondary outcomes in the study must be reported. Specify the follow-up periods for each outcome or median follow-up time for time-to-event outcomes. State whether the follow-up period was predefined.]
Study name, NCTxxxx (reference to publication(s))	Randomized, double-blind, placebo-controlled, phase III study of drug X vs. placebo	12-week double-blind period followed by 40-week unblinded period (total 52 weeks). Patients randomised to placebo crossed over to drug X without blinding after week 12	Treatment-naïve patients with active disease and incomplete response to conventional therapy	Drug X (subcutaneous administration), 90 mg weeks 0, 4, 8, 12, then every 12 weeks	Drug X matching placebo (subcutaneous) weeks 0, 4, 8, 12, then 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 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 these differences are handled in the comparison between the studies (not relevant for RCTs with direct comparison between intervention and comparator). If a JCA has been prepared, refer instead to the relevant section in the JCA report where the comparability of the relevant studies is described.]

6.1.2.1 Comparability of Patients Across Studies

[Complete Table 14 with baseline characteristics of patients included in all studies for the population used in the comparative and health economic analysis, including all prognostic and effect-modifying variables. Adjust the number of columns in the table to match the number of included studies and study arms (change the page orientation to landscape if necessary to include more studies). Briefly describe the most important differences in baseline characteristics.

If a JCA has been prepared, refer instead to the relevant section in the JCA report where comparability of patients across studies is described. In that case, Table 14 should not be completed with baseline characteristics. Instead, enter "N/A", and provide a reference to the relevant table(s) with baseline characteristics in the JCA report.

Table 14. Patients' baseline characteristics in included studies used in the comparative analysis of effectiveness and safety

	[Study name]		[Study name]		[Study name]	
	[int./comp.]	[int./comp.]	[int./comp.]	[int./comp.]	[int./comp.]	[int./comp.]
Age						
Sex						
[Characteristics]						
…						

6.1.3 Comparability of Study Population(s) with Danish Patients Eligible for Treatment

[Address the comparability of both the study population and the population used in the health economic model with Danish patients eligible for treatment. Complete Table 15 with information on the characteristics of the relevant population in Danish clinical practice and the corresponding values used as input parameters in the health economic model. Adjust the number of rows to include all relevant baseline characteristics.]

Table 15. Characteristics of the relevant Danish population and input parameters in the health economic model

	Danish population (source)	Study population	Health economic model (source)
Age			
Sex			
Body weight			
[Characteristics]			
…			

6.1.4 Analysis Method

[Data must be presented according to the intention-to-treat principle whenever possible. Any supplementary presentations (e.g., subgroup and sensitivity analyses) must be justified, for example if such analyses improve the comparability between the study and Danish clinical practice.

The method used for each analysis must be clearly described (or referenced if described elsewhere). This includes model type, adjustment variables, weighting, stratification factors, correlation structure (repeated measures), transformations of outcomes and/or adjustment variables, handling of missing values, handling of intercurrent events, censoring rules, and exceptions. The proportion of patients with missing measurement(s) in each study arm must be reported for each outcome.

For hazard ratios, a graphical assessment of the proportional hazards assumption must be provided (e.g., Schoenfeld residuals). In the presence of competing risks, appropriate methods (e.g., the Aalen-Johansen estimator) must be used to estimate cumulative incidence.]

6.1.5 Effect – Results per Study [Study name 1]

[Provide a summary of the most important effectiveness results for each study included in the comparative analysis, excluding effects on health-related quality of life, which should be reported in Section 10.

Clearly explain any discrepancies between published data and EMA's scientific discussion (EPAR).

Report the event rates for both intervention and comparator(s) from each study, and present both the absolute (e.g., difference in median OS or OS rate) and relative differences (e.g., HR or RR) for the outcomes. All effect estimates must be presented with confidence intervals. For composite outcomes, the frequency (and missing

measurements) of each individual components/events must be reported for all treatment arms, when possible.

For time-to-event outcomes, survival curves must be presented, including censoring and the number of patients at risk at relevant time points. In addition, the estimated median survival, hazard ratio (HR), and survival at relevant time points must be reported.

Effect estimates must always be presented for the outcomes included in the health economic model.

If a JCA has been prepared, refer instead to the relevant section in the JCA report where the results for each individual outcome for the relevant PICO(s) have been reviewed. In this case, separate subsections for each outcome should not be created. If data are available from a later data cut-off than used in the JCA report, the applicant must refer to the relevant section in the JCA report and additionally present updated data from the same analyses with the new data cut.]

6.1.6 Effect – Results per [Study name 2]

[Complete a separate subsection for each study included in the comparison as described in Section 6.1.5.]

7. Comparative Analyses

[*Applicable documentation standards are specified in the Danish Medicines Council's methodological guideline and the supporting guideline on clinical effectiveness and safety. Section numbering and tables must not be modified. Rows may be added/deleted in Table 16.*

The subsections should be marked as "N/A" if the relative effectiveness is based on a single head-to-head study directly comparing the intervention and the comparator.

If a JCA has been prepared with a comparative analysis of the intervention vs. the comparator, refer to the relevant sections of the JCA in the subsections. Table 16 must still be completed with the relevant outcomes. Instead of entering data, references to the relevant sections of the JCA report should be provided. As a general rule, the comparative analysis from the JCA must be used. If new data for the intervention and/or comparator are available, the analysis from the JCA must be updated accordingly, but based on the same patients and adjustments as used in the JCA.]

7.1 Analysis Method

[Describe and justify the choice of method used for the comparative analysis. The instructions for reporting analysis methods described in Section 6.1.4 also apply to comparative analyses.

If the evidence on effectiveness and safety is based on an indirect comparison, provide a brief description of the method here, and include a detailed description in Appendix D.

Tables and figures may be used where appropriate. Always report effect data for the raw study data (naive comparison) as well as for any adjusted analyses.

If weighting techniques are used, e.g., matching-adjusted indirect comparisons (MAIC), the applied weights (e.g., in the form of a histogram), and the effective sample size must be reported. For inverse probability weighting, the model for estimating probability of treatment with the intervention (propensity scores) must be described, as well as the choice of weights (e.g., *average treatment effect among treated* (ATT), corresponding to the population in the intervention study). Baseline characteristics before and after weighting must be presented, and standardised mean differences (SMDs) before and after weighting must be reported.]

7.2 Results of the Comparative Analysis

[The instructions for reporting effect estimates described in Section 6.1.4 also apply to comparative analyses. Data must be presented in accordance with the intention-to-treat principle whenever possible. Any supplementary analyses (e.g., subgroup or sensitivity analyses) of data must be justified, e.g., if such analyses increase the comparability between the study and Danish clinical practice.

Table 16 must be completed with absolute and relative results. If weighting techniques have been used, a figure must be presented showing survival curves for both the unweighted and the weighted population, as well as corresponding hazard ratios. Effect estimates must always be presented for all outcomes included in the health economic model.]

Table 16. Results from the comparative analysis of [intervention] vs. [comparator] in [patient population]

Outcome	[Intervention] (N = x)	[Comparator] (N = x)	Result
OS	Median: X months (95% CI: X;Y)	Median: X months (95% CI: X;Y)	X months HR: X (95% CI: X;X)
Proportion achieving ASAS40 (week 12)	n/N, % (95% CI: X;Y)	n/N, % (95% CI: X;Y)	Absolute risk difference: X %-points (95% CI: X;Y) Relative risk: X (95% CI: X;Y)

7.3 Effect – Results per [Outcome]

[Complete one subsection for each outcome as described in Section 6.1.5]

8. Safety

[*Applicable documentation standards are specified in the Danish Medicines Council's methodological guidelines and the supporting guideline on clinical effectiveness and safety.*

Section numbering and tables must not be modified. Rows/columns may be deleted/added in the tables.]

[Table 17 must be completed with estimates of overall safety, e.g., the proportion of serious adverse events, for both the intervention and the comparator, including the absolute and relative differences. The data source and the time period covered by the data and/or median follow-up time must be reported. It must be clearly specified how the safety population is defined. For indirect comparisons, the tables must include data for the intervention and comparator arms in each study.

If a JCA has been prepared, refer instead to the relevant section of the JCA report where the data are described. If data from a later data cut-off than used in the JCA report are available, the applicant must refer to the relevant section of the JCA report and additionally present data from the new data cut-off.]

Table 17. Overview of adverse events [specify data source and time period]

	[Intervention] (N = [x])	[Comparator] (N = [x])	Difference, %-points	Difference, RR (95% CI)
All adverse events (AE), n (%)				
Serious AE (SAE), n (%)[1]				
AE grade ≥ 3, n (%)[2]				
Dose reduction due to AE, n (%)				
Treatment discontinuation due to AE, n (%)				

AE = adverse event; CI = confidence interval; RR = risk ratio; SAE = serious adverse event. [1]See ICH definition. [2]CTCAE v. 5.0 is preferred.

[Complete Table 18 for all adverse events with a frequency of ≥ 10%, regardless of grade/severity reported in the study or studies, as well as all adverse events grade ≥ 3 that occurred in ≥ 3% in at least one treatment arm (if the events are not graded according to common terminology criteria for adverse events (CTCAE), report serious adverse events (SAE)). The applicant may use *lower* frequency thresholds if necessary to adequately illustrate the comparative safety profile. A lower threshold value may, for

example, be relevant to highlight the occurrence of rare adverse events of particular importance.

If more than two studies are included in the comparison, the results may be presented in separate tables. A list of all serious adverse events occurring in ≥ 1% of patients must be provided in 0.]

Table 18. Proportion of patients with adverse events [specify data source and time period]

	[Intervention] (N = [x])		[Comparator] (N = [x])	
	All[1]	Grade ≥ 3 or SAE[2]	All[1]	Grade ≥ 3 or SAE[2]
[Adverse Event A], n (%)				
[Adverse Event B], n (%)				
…				

SAE = serious adverse event; [1]List all adverse events with a frequency of ≥ 10%. [2]Report SAEs if adverse events are not graded according to CTCAE, and report events with a frequency of ≥ 3% in at least one treatment arm.

9. Extrapolation of patient transitions

[Applicable documentation standards are specified in the Danish Medicines Council's methodological guideline and the supporting guideline on health economic analysis and extrapolation.

Section numbering and tables must not be modified. Rows may be deleted/added in Table 20 and Table 22, and rows and/or columns may be deleted/added in Table 21.]

9.1 Clinical Data Used for Extrapolation of Patient Transitions

[Briefly describe which clinical outcome (including sources) are used for extrapolation and which types of extrapolation are applied for the individual patient transitions (parametric extrapolation models and/or transition probabilities). Provide a table that clearly shows which clinical outcome and data sources inform the individual transitions in the model. When surrogate outcomes are used, include a description of the underlying structural assumptions about the relationship between the surrogate outcomes and the clinical outcome(s) of primary interest, including a review of the evidence supporting the clinical plausibility of this relationship.

The individual extrapolations must be described in Section 9.2 and Appendix E.1 for parametric extrapolation models, and in Section 9.3 and Appendix E.2 for extrapolations with transition probabilities.]

9.2 Extrapolation Using Parametric Extrapolation Models

9.2.1 Extrapolation of [Clinical Outcomes 1]

[Table 19 must be completed. Detailed justification for the choice of parametric extrapolation model, including supporting figures and tables, must be provided in Appendix E.1. In this section, present:

- A figure for each treatment arm showing the extrapolated data for all examined models together with the observed data (including confidence intervals for the Kaplan-Meier data), adjusted for background mortality and any other assumptions (e.g., cure assumption).
- A figure including both treatment arms, in which only the selected extrapolation models for the intervention and comparator are shown together with the observed data (including confidence intervals for the Kaplan-Meier data), adjusted for background mortality and any other assumptions (e.g., cure assumption).

If a joint extrapolation model estimated using data from both treatment arms is applied, for example based on an assumption of proportional hazards, Appendix E.1 must also be completed for the same outcome using separate (independent) extrapolation models based on the observed data for each treatment arm. This also applies if these models are not included in the applicant's primary analysis. The corresponding figures and data must also be available in the submitted model, and it must be possible to apply separate (independent) extrapolation models in the model.

The model must include, for each treatment arm and each extrapolated outcome, tables reporting relevant annual rates (e.g., 1-, 3-, 5-, and 10-year rates) for alle examined models. All rates must be adjusted for background mortality and any other assumptions (e.g., cure assumption).]

Table 19. Overview of assumptions related to extrapolation of [clinical outcome]

Method/approach	Description/assumption
Data	[Study name, source]
Selected distribution	[Intervention: X distribution] [Comparator: X distribution]
Models examined	[Describe which parametric extrapolation models were examined]
Assumptions	

Method/approach	Description/assumption
Proportional hazards between intervention and comparator	[Yes/No] If 'Yes': Briefly describe modelling (joint vs. separate)
Flexible parametric models	[Yes/No] If 'Yes': Briefly describe the model
Cure point and/or share	[Yes/No] If 'Yes': Briefly describe the assumption/method
Treatment waning	[Yes/No] If 'Yes': Briefly describe the assumption/method
Other assumptions	[Yes/No] If 'Yes': Briefly describe the assumption/method
Internal validity	
Distribution with best AIC fit	[Intervention: X distribution] [Comparator: X distribution]
Distribution with best BIC fit	[Intervention: X distribution] [Comparator: X distribution]
Distribution(s) with best visual fit on probability scale (e.g., Kaplan-Meier data)	[Intervention: X distribution] [Comparator: X distribution]
Distribution(s) with best visual fit according to evaluation of smoothed hazards	[Intervention: X distribution] [Comparator: X distribution]
External validity	
Sources for validating external validity	[Specify sources]
Distribution with highest external validity	[Intervention: X distribution] [Comparator: X distribution]

9.2.2 Extrapolation of [Clinical Outcome 2]

[Complete as Section 9.2.1.]

9.3 Extrapolation Using Transition Probabilities

[Table 20 and Table 21 must be completed. Provide an assessment of the internal validity of the selected transition probabilities. This includes a description of the relevance,

representativeness, and clinical plausibility of the individual transition probabilities, including differences between health states and treatment arms. Supporting tables and figures must be included in Appendix E.2, e.g., comparisons of observed data and modelled data during the study period. Results from the literature search must be provided in 0.

Provide an assessment of the external validity focusing on clinical plausibility in relation to evidence from external sources. Include supporting tables and figures in Appendix E.2, e.g., comparisons of external data and modelled data.]

Table 20. Transition probabilities in the health economic model

From health state	To health state	Transition probability, incl. calculation	Assumption	Source
A	*A*	*E.g., S(t+Δt)/S(t)*	*E.g., time-dependent, and different between arms as…*	*[Study name]*
	B	*E.g., 1 − S(t+Δt)/S(t)*	*…*	
	C	*…*		
B	*B*	*E.g., 0.05* $1 - e^{-\lambda t}$*, where λ is the hazard rate and* t *is the cycle length*	*E.g., constant over time and identical in both arms*	
	…	*…*		

Table 21. Transition matrix for [intervention/comparator]

Off/On	State A	State B	State C	…
State A	*S(t+Δt)/S(t)*	*1 − S(t+Δt)/S(t)*	*…*	
State B	*…*	*0.05*	*…*	
State C				
…				

9.4 Summary and Validity of Extrapolated Patient Transitions

[Table 22 must be completed. Provide a Markov trace for each treatment arm, i.e. a stacked chart showing the proportion of patients in each health state over time.

Describe the table and figures, and explain whether the overall set of assumptions regarding extrapolation of patient transitions yields logical and clinically plausible transitions over time and across health states and treatment arms, both during and after the observation period.

If the primary outcome (e.g., OS) is modelled indirectly through other patient transitions in the model, including the use of a surrogate outcomes (e.g., PFS), this section must include a figure comparing observed and modelled data for the primary outcome during the observation period.]

Table 22. Modelled means in years, undiscounted estimates, half-cycle corrected and adjusted for background mortality

	[Intervention]	[Comparator]	Difference
Total life years			
Life years in [health state A]			
Life years in [health state B]			

Duration of treatment [Drug A]			
Duration of treatment [Drug B]			
...			

10. Health-Related Quality of Life

[*Applicable documentation standards are specified in the Danish Medicines Council's methodological guideline and the supporting guideline on health-related quality of life.*

Section numbering and tables must not be modified. Rows may be deleted/added in the tables.

If a JCA has been prepared, refer to the relevant sections of the JCA report. See details in the individual subsections.

All included instruments must be reviewed individually in Section 10.2, and the same documentation standards apply to all included instruments. This also applies to instruments whose main purpose is to be used in the calculation of utility values. It does not apply to instruments used solely to estimate disutilities associated with adverse events.

If mapping is applied, the mapping study must be described in 0, while the justification for using mapping and the choice of mapping algorithm must be described under the relevant instrument in Section 10.2 (for indirect mapping) or under the relevant utility calculation in Section 10.3 (for direct mapping).

If a cost-minimisation analysis is performed, Section 10.3 should not be completed. Section 10.2 must still be completed, as a cost-minimisation analysis assumes that the drugs are equivalent with respect to health-related quality of life.

If the evidence for an instrument and/or the calculated utility values is too limited to complete parts of Sections 10.2 and 10.3, this must be explicitly stated and justified in the relevant sections.]

10.1 Overview

[Complete Table 23 with all included instruments, including instruments used solely to calculate utility values and any instruments based on external sources. Complete Table 24, including utility values based on external sources. Indicate whether additional data are expected from later data-cuts.]

Table 23. Overview of included instruments for measuring health-related quality of life

Instrument	Median follow-up time and data-cut	Use	Source	Reference to description
Instrument 1 (e.g. EQ-5D-5L)	16 months (June 22, 2023)	E.g., effect, utility values	Study x	E.g., Section 10.1.1
Instrument 2				E.g., Section 10.1.2
...				

Table 24. Basis for estimating utility values

Instrument	Preference weights	Source	Short description
E.g., EQ-5D-5L	DK		E.g., from the same study informing clinical

Instrument	Preference weights	Source	Short description
			effectiveness and safety
..	..		E.g., identified in a focused literature search
..	..		E.g., mapping from [instrument] to [instrument]

10.2 Instruments

[Complete section 10.2.1 for each instrument in Table 23. The first instrument should be presented in a subsection corresponding to Section 10.2.1, the second instrument in Section 10.2.2, and so on. Additional sections should be created after Section 10.2.2 if more than two instruments are included.]

10.2.1 ["Instrument 1"]

10.2.1.1 Study Design and Instrument ["Instrument 1"]

[If a JCA has been prepared, refer instead to the relevant sections of the JCA report. The applicant must ensure that all the questions below can be answered through reference to the JCA. If not, the applicant must provide the additional information needed to address the relevant questions.

Describe and justify the choice and use of instrument and study design. If results are reported from an instrument that does not originate from the study informing clinical effectiveness and safety, any differences in study populations (inclusion and exclusion criteria) must be described. The applicant must also justify why the external sources are appropriate despite these differences.]

10.2.1.2 Data Collection ["Instrument 1"]

[If a JCA has been prepared, refer instead to the relevant sections of the JCA report. The applicant must ensure that all the questions below can be answered through reference to the JCA. If not, the applicant must provide the additional information needed to address the relevant questions.

Table 25 must be completed for all measurement time points and must be accompanied by a description of the data collection, including any reasons for differences in response rates across treatment arms (e.g., differences in adverse event profiles) and the implications of these differences. If Table 25 is very long, it may be included in Appendix G.1 rather than in this section. If the instrument forms the basis for calculating utility

values, Table 26 must also be completed. Note that the number of responses must be based on the number of complete questionnaire responses.]

Table 25. Overview of responses [create a table for both intervention and comparator]

Time	Number of patients "at risk "* at time point *t* (expected number of responses) N	Number of responses at time point *t* N	Proportion of responses among patients "at risk " at time point *t*** %	Proportion of responses among patients at randomisation*** %
Measurement time point 1	99	90	91% (i.e., 90/99)	90% (i.e., 90/100 if 100 patients at randomisation)
Measurement time point 2	85	80	94% (i.e., 80/85)	80% (i.e., 80/100)
Measurement time point 3	80	60	75% (i.e., 60/80)	60% (i.e., 60/100)
…	…	…	…	…

* Number of patients "at risk": Patients who have not died or been censored before time point *t*, and are therefore expected to complete the questionnaire. Patients who discontinued treatment must be included.

**Proportion of responses among patients "at risk" at time point *t* = number of responses at time *t* / number of patients "at risk" at time *t*.

***Proportion of responses since randomisation = number of responses at time *t* / number of patients at randomisation.

Table 26. Overview of responses by health states [create a table for both intervention and comparator]

Health state	Number of responses in the health state N	Number of patients who provided at least one response in the health state N
Health state 1	500	99
Health state 2	100	60
Etc.	…	…

10.2.1.3 Results ["Instrument 1"]

[If a JCA has been prepared, refer instead to the relevant sections of the JCA report. Note that for preference-based instruments (e.g., EQ-5D-5L), the Danish Medicines Council

requires results calculated using Danish preference weights. These results must be reported in this section if they are not provided in the JCA report.

Complete Table 27 for all measurement time points and include a graph showing the mean change (with 95% confidence intervals) since baseline for both the intervention and the comparator (see example in figure below). When reporting results for the instrument that forms the basis for the calculation of utility values, the development in index score (with preference weights) must also be reported. For EQ-5D-5L, for example, both index score results using Danish preference weights and EQ-VAS must be reported. Results for all individual domains must be reported in Appendix G.]

Example of a figure showing mean change over time in a given measure of health-related quality of life:

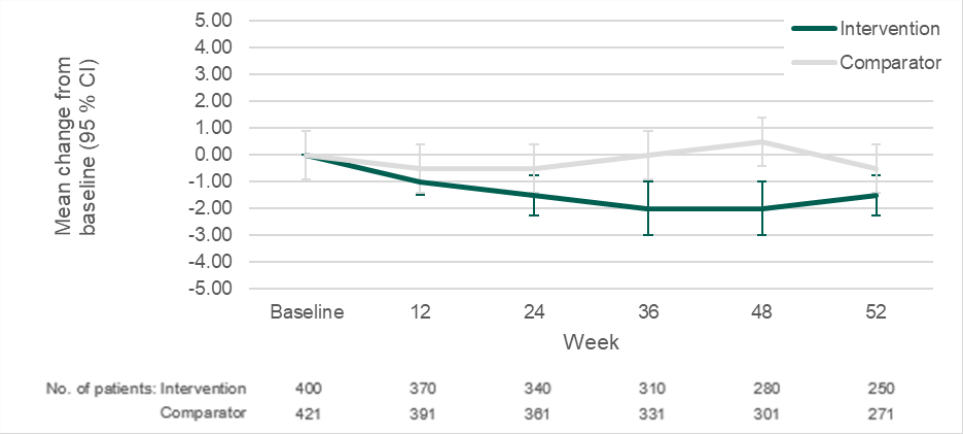

Table 27. Results for [instrument 1]

	Intervention	Comparator	Difference
	Mean (SE)	Mean (SE)	Difference (95% CI)
Baseline			
Time point 1			
Time point 2			
Etc.			

10.2.2 ["Instrument 2"]

10.2.2.1 Study Design and Instrument ["Instrument 2"]

[See Section 10.2.1.1]

10.2.2.2 Data Collection ["Instrument 2"]

[See Section 10.2.1.2]

10.2.2.3 Results ["Instrument 2"]

[See Section 10.2.1.3]

10.2.3 Summary when reporting multiple instruments

[If several different instruments are used, a summary of the advantages and disadvantages of the individual instruments must be provided here, as well as any explanations for differences in reported health-related quality of life between the instruments. Any differences in populations (inclusion and exclusion criteria and patient characteristics) and differences between instruments must also be briefly summarized.]

10.3 Utility Values

10.3.1 Data Sources

[Describe the data sources, including which of the instruments reported in Section 10.2 forms the basis for calculating utility values. Indicate whether age adjustment has been performed in accordance with the Danish Medicines Council's methodological guideline. If there are factors that limit the validity of comparing utility values across states, e.g., different sources, instruments or preference weights, these must be described in this section.]

10.3.2 Calculation of Utility Values

[Describe the choice of regression model, including underlying assumptions regarding, for example, correlation between observations of the same individual and the handling of missing data. Justify the relationship between the model structure in the health economic model and the regression equation used, including how the explanatory variables reflect the mechanisms (treatment and disease progression) behind changes in health-related quality of life for each treatment arm.

All information required to calculate the final utility values, including statistical details on the choice of regression model, the exact specification of regression equations, and the resulting estimates, must be provided in Appendix G.4.]

10.3.3 Adverse Events, Comorbidity and Other State-Specific Adjustments to Utility Values

[If utility values are adjusted in certain health states or model cycles due to, for example, comorbidity or adverse events, this must be justified and presented in tabular form in this section. Relevant formulas used for the adjustment must also be provided.]

10.3.4 Results for Utility Values

[Complete Table 28. Present and describe any sensitivity analyses performed using alternative utility values.]

Table 28. Utility values used in the health economic model

	Utility value [95% CI]	Instrument, preference weight	Source and reference
Main analysis			
State A	0.761 [0.700-0.810]	EQ-5D-5L, UK	Study 1, Section 10.3.2
State B			
...			
Decrease in health-related quality of life			
...			
State A			
...			

11. Calculations of Costs

[Applicable documentation standards are specified in the Danish Medicines Council's methodological guideline and the supporting guideline on the calculation of costs. Section numbering and tables must not be modified. Rows may be deleted/added in the tables.]

11.1 Drug Costs

11.1.1 Drug Costs for Intervention and Comparator

[All information regarding dosing must be described in Sections 3.2 and 3.2.2. The respective dose distributions must form the basis for calculating the distribution across packages. All available packages must be included in the health economic model. Briefly describe how the drug costs have been calculated.]

11.1.2 Drug Costs for Subsequent Treatment

[All information regarding subsequent treatment and dosing must be described in Section 3.4. The respective dose distributions must form the basis for calculating the distribution across packages. All available packages must be included in the health economic model. Briefly describe how the drug costs for subsequent treatment have been calculated and implemented in the patient pathway in the health economic model.]

11.2 Hospital Costs

11.2.1 Administration

[Complete Table 29.]

Table 29. Assumptions regarding administration costs

Route of administration	Diagnosis and procedure codes*	DRG group	Unit cost, DKK
[E.g., IV administration of drug X)]	[E.g., DC679M (A)]	[E.g., 11MA98: 1-dagsgruppe, pat. mindst 7 år]	[DRG tariff in DKK]

*Include other patient information if relevant for the choice of DRG group; A = action diagnosis

11.2.2 Disease Management

[Complete Table 30.]

Table 30. Assumptions regarding disease management costs

Activity/pathway	Frequency	Duration	Diagnosis and procedure codes*	DRG group	Unit cost
[E.g., visit to oncologist]	[E.g., every 3 weeks]	[E.g., until progression]	[E.g., DC679M (A)]	[E.g., 11MA98: 1-dagsgruppe, pat. mindst 7 år]	[DRG tariff in DKK]
[E.g., CT scan + outpatient visit]	[E.g., every 2 months]	[E.g., first 12 months]	[E.g., DC679M (A) UXCD75 (P)]	[E.g., 30PR06: CT-scanning, kompliceret]	[DRG tariff in DKK]
[E.g., CT scan + outpatient visit]	[E.g., every 6 months]	[E.g., from 12 to 36 months after treatment initiation]	[E.g., DC679M (A) UXCD75 (P)]	[E.g., 30PR06: CT-scanning, kompliceret]	[DRG tariff in DKK]

*Include other patient information if relevant for the choice of DRG group; A = action diagnosis; P = procedure.

11.2.3 Treatment Monitoring

[Complete Table 31.]

Table 31. Assumptions regarding costs for treatment monitoring

Activity/Pathway	Frequency	Duration	Diagnosis and procedure codes*	DRG group	Unit cost
[E.g., visit to oncologist]	[E.g., every 3 weeks]	[E.g., until progression]	[E.g., DC679M (A)]	[E.g., 11MA98: 1-dagsgruppe, pat. mindst 7 år]	[DRG tariff in DKK]
[E.g., CT scan + outpatient visit]	[E.g., every 2 months]	[E.g., first 12 months]	[E.g., DC679M (A) UXCD75 (P)]	[E.g., 30PR06: CT-scanning, kompliceret]	[DRG tariff in DKK]
[E.g., CT scan + outpatient visit]	[E.g., every 6 months]	[E.g., from 12 to 36 months after treatment initiation]	[E.g., DC679M (A) UXCD75 (P)]	[E.g., 30PR06: CT-scanning, kompliceret]	[DRG tariff in DKK]

*Include other patient information if relevant for the choice of DRG group; A = action diagnosis; P = procedure.

11.2.4 Management of adverse events

[Complete Table 32. As a general rule, only costs for the management of adverse events of grade ≥ 3 should be included, and only if the difference between the intervention and comparator is ≥ 3%-points. If the events are not CTCAE-graded, SAEs may be used instead. Any deviations must be justified. Briefly describe how costs are incorporated into the health economic model.]

Table 32. Assumptions regarding costs for the management of adverse events

Adverse event	Proportion		Diagnosis codes*	DRG group	Unit cost
	[Intervention]	[Comparator]			
[Hospitalisation due to adverse event A, %]	[18%]	[10%]	[E.g., DN179 (A) and DC679M (B), duration ≥ 12 hours (long)]	[11MA01: Akutte medicinske nyresygdomme uden dialyse og uden plasmaferese]	[DRG tariff in DKK]

Adverse event	Proportion		Diagnosis codes*	DRG group	Unit cost
	[Intervention]	[Comparator]			
[Outpatient visit due to adverse event B, %]					

*Include relevant procedure codes and other patient information if relevant for the choice of DRG group; A = action diagnosis; B = secondary diagnosis.

11.2.5 Other Hospital Costs

[Briefly describe all assumptions and sources used if other hospital costs are included.]

11.3 Patient Costs

[Complete Table 33. Briefly explain if some activities occur during the same visit to avoid double-counting.]

Table 33. Assumptions regarding patient time

Activity	Frequency of activity	Time spent on activity	Transport time	Note
[E.g., IV administration of drug X]	[E.g., every 2 weeks]	[E.g., 1 hour]	[90 minutes]	
[E.g., visit to oncologist]	[E.g., every 3 weeks]	[E.g., 1 hour]	[0]	E.g., no additional transport time, as it occurs on the same day as IV administration

11.4 Other Costs

[Briefly describe all assumptions and sources used if other costs are included.]

12. Results

[Applicable documentation standards are specified in the Danish Medicines Council's methodological guideline and the supporting guideline on uncertainties and sensitivity

analyses. Section numbering and tables may not be modified. Rows may be deleted/added in the tables, but the cost categories in Table 34 must not be changed.

Table 34 and Table 35 must be completed. If scenarios are presented instead of one base case, duplicate the tables below for each scenario.]

Table 34. Results, discounted estimates, half-cycle corrected (where relevant), and adjusted for background mortality

	[Intervention]	[Comparator]	Difference
Drug costs			
Drug costs for subsequent treatment			
Administration			
Disease management			
Treatment monitoring			
Management of adverse events			
Patient costs			
Other costs, e.g., co-medication			
...			
Total costs			
Life years in health state A			
Life years in health state B			
...			
Total life years			
QALYs in health state A			
QALYs in health state B			
...			
Total QALYs			

	[Intervention]	[Comparator]	Difference
Incremental costs per life year gained			
Incremental costs per QALY gained (ICER)			

Table 35. Results per drug in combination treatments

	Drug costs
Intervention: Drug A	
Intervention: Drug B	
…	
Comparator: Drug C	
Comparator: Drug D	
...	

12.1 Sensitivity Analyses

12.1.1 Deterministic Sensitivity Analyses

[Complete Table 36].

Table 36. Results of deterministic sensitivity analyses

Deterministic sensitivity analysis	Incremental costs	Incremental QALYs	ICER
[Sensitivity analysis 1			
[Sensitivity analysis 2]			
…			

12.1.2 Probabilistic Sensitivity Analyses (PSA)

[The PSA presentation must include:

- A scatter plot of incremental costs vs. incremental QALYs with the mean PSA estimate marked in the plot. For cost-minimisation analyses, present the PSA as a histogram of incremental costs.

- A brief description of the scatter plot, including the overall pattern and distribution of points (e.g., whether all points lie in the northeast quadrant, or 20% of the points lie in the northwest quadrant, while the remaining points lie in the northeast quadrant).
- A cost-effectiveness acceptability curve (CEAC).
- A convergence plot showing the cumulative mean ICER as a function of the number of PSA simulations.

13. Budget Impact Analysis

[Applicable documentation standards are specified in the Danish Medicines Council's methodological guidelines and the supporting guideline on budget impact analysis. Section numbering and tables must not be modified.

Table 37 must be completed if the health economic analysis is a cost-utility analysis. Please note that the budget impact must be calculated based on the expected number of patients and patient uptake provided in Section 3.1.2.]

Table 37. Budget impact (undiscounted estimates), DKK

	Year 1	Year 2	Year 3	Year 4	Year 5
Regional costs with recommendation					
Drug costs	[x]	[x]	[x]	[x]	[x]
Other regional hospital costs	[x]	[x]	[x]	[x]	[x]
Total with recommendation	[x]	[x]	[x]	[x]	[x]
Regional costs without recommendation					
Drug costs	[x]	[x]	[x]	[x]	[x]
Other regional hospital costs	[x]	[x]	[x]	[x]	[x]
Total without recommendation	[x]	[x]	[x]	[x]	[x]
Total budget impact	[x]	[x]	[x]	[x]	[x]

14. List of Experts

[Provide the name, job title, and workplace of clinicians consulted during the preparation of this submission.]

15. References

[Insert the reference list.]

Appendix A. Study Characteristics

[Table 38 must be completed for each included study. If a JCA has been prepared, provide instead a reference to the relevant section in the JCA report where the clinical study is described, without providing additional information about the study.]

Table 38. Main characteristics of included studies

Study name	NCT number:
Objective	[Briefly describe the overall objective of the study]
Publications – title, author(s), journal, year	[Provide all publications related to the study (including upcoming publications).]
Study type and design	[Specify the study type and phase and describe the randomisation method, degree of blinding, crossover design (if applicable), and study status (ongoing/completed), etc.] [Example: Double-blind randomized placebo-controlled phase 3 study. Eligible patients were randomly assigned 1:1 using a stratified permuted block randomisation system via an interactive response system. Crossover was not permitted. Investigators, patients, and the sponsor were blinded during treatment allocation.]
Number of trial participants (N)	
Primary inclusion criteria	
Primary exclusion criteria	
Intervention	[Specify the intervention, including dose, dosing schedule, and the number of patients receiving the intervention.]
Comparator(s)	[Specify the comparator(s), including dose, dosing schedule, and the number of patients receiving the comparator.]
Follow-up time	[Provide follow-up time for primary and secondary outcomes included in the submission, as well as for safety and HRQoL outcomes.] Example: Median follow-up for OS was 7.3 months (range 0.5-16.5).]
Is the study used in the health economic model?	[Yes/No. For studies that are not included in the health economic model but are considered relevant to the submission, provide the reason.]

Study name	NCT number:
Primary, secondary, and exploratory outcomes	[Provide all primary, secondary and exploratory outcomes of the study, regardless of whether the results are reported in this submission. Definitions of included outcomes and results must be provided in Appendix E.1.] **Outcomes included in this submission:** [Example: The primary outcome was progression-free survival assessed by the study investigator according to RECIST, version 1.1. Secondary outcomes were overall survival, confirmed objective response rate according to RECIST, version 1.1, duration of response, progression-free survival assessed by an independent review committee, health-related quality of life (HRQoL) assessed using the QLQ-C30 instrument, and safety.] **Other Outcomes:** [Example: Time to next treatment and objective response rate were included as secondary outcomes in the study, but results are not included in this submission.]
Analysis method	[Describe the analysis method.] Example: All effectiveness analyses were conducted according to the *intention-to-treat* principle. Kaplan-Meier methods were used to estimate progression-free survival and overall survival, and a stratified log-rank test was used for treatment comparisons. Hazard ratios adjusted for XX and YY were estimated using a Cox proportional hazards regression model. The proportional hazards assumption was evaluated by assessing trends in scaled Schoenfeld residuals.]
Subgroup analyses	[Provide the following information for each analysis: - characteristics of the included population - analysis method - was it pre-specified or post hoc? - validity assessment, including statistical power for pre-specified analyses.]
Other relevant information	

Appendix B. Results for Clinical effectivness per Study

[Table 39must be completed for all included studies, regardless of whether they are used in the health economic model. Describe how all estimates, e.g. CIs and p-values, have been estimated, including the method used, adjustment variables, stratification variables, weights, corrections (in cases with zero counts), correlation structure (mixed-effects models for repeated measures), and methods used for imputation in cases of missing data. Specify how assumptions were assessed. For survival rates, indicate the time point at which they were estimated. Relevant subgroup and sensitivity analyses for the individual studies must also be reported. If a JCA has been prepared, refer instead to the relevant section in the JCA report where data from the individual clinical studies are described. If more recent data cuts from the studies are available than those included in the JCA report, the results from the newer data cuts must be presented here, while the "References" column must contain the reference to the relevant section in the JCA report. Table 39 must also be completed for studies that are not included in the JCA report.]

Table 39. Results per study

Results from [study name (NCT number)]											
				Estimated absolute difference in effect			**Estimated relative difference in effect**			**Analysis method**	**References**
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***p*-value**	**Difference**	**95% CI**	***p*-value**		
Example: overall median 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	Median survival was estimated using the Kaplan-Meier method. HRs were estimated using a Cox proportional hazards model adjusted for the	
	ZZZ	248	17.4 (15.0-19.8) months								

Results from [study name (NCT number)]											
				Estimated absolute difference in effect			Estimated relative difference in effect			Analysis method	References
Outcome	**Study arm**	**N**	**Result (CI)**	**Difference**	**95% CI**	***p*-value**	**Difference**	**95% CI**	***p*-value**		
										stratification variables used in randomisation and study arm.	
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	Survival rates are based on the Kaplan-Meier estimator. HR is based on a Cox proportional hazards model adjusting for stratification and study arm.	
	ZZZ	248	63.8% (57.6-70.0)								
Insert outcome 3	Intervention										
	Comparator										

Appendix C. Subsequent Treatment

[Insert a table with the distribution of subsequent treatments from the clinical study or studies. For each treatment arm, the table should include the proportion of patients who received a subsequent line of treatment and the distribution of subsequent treatments. For example, 80% of patients with disease progression received a subsequent line of treatment, with 50% receiving drug A and 50% receiving drug B.]

Appendix D. Comparative Analyses

[The table below must be used for comparative analyses when a direct comparison is not available. For each type of comparative analysis (e.g., paired indirect comparison, network meta-analysis, or MAIC analysis), the method, assumptions, and results must be described in an appropriate format (text, tables and/or figures, e.g. network diagram for network meta-analysis). Relevant subgroup and sensitivity analyses for the comparative analyses must also be presented. If a JCA has been prepared, refer instead to the relevant section in the JCA report where the results of the comparative analysis are described. Table 40 should only be completed if the analysis has been updated in relation to the JCA, (e.g., due to a more recent data cut-off.]

Table 40. Comparative analysis of studies comparing [intervention] with [comparator] for patients with [indication]

Outcome		Absolute difference			Relative difference			Analysis method	Are results used in the health economic analysis?
	Studies included in the analysis	Difference	CI	p-value	Difference	CI	p-value		
Example: Median overall survival		REACH	REACH	REACH	HR: 0.70	0.55-0.90	0.005	HRs for the included studies were synthesised using a 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	HRs for the included studies were synthesised using a random-effects meta-analysis (DerSimonian-Laird). The absolute difference was estimated using the corresponding HR assuming a 1-	

Outcome		Absolute difference			Relative difference			Analysis method	Are results used in the health economic analysis?
	Studies included in the analysis	Difference	CI	p-value	Difference	CI	p-value		
								year survival rate of 64.33% in the comparator group.	
Outcome 3									

Appendix E. Extrapolation of Patient Transitions

E.1 Parametric Extrapolation Models

[When extrapolating multiple clinical outcomes, present the outcomes in the same order as as in Section **Fejl! Henvisningskilde ikke fundet.**]

E.1.1 Extrapolation of [Clinical Outcome 1]

[The justifications for the choice of extrapolation model must be done systematically, which includes:

- An assessment of log-cumulative hazard plots and (Schoenfeld) residual plots to support the argument for whether treatment arms should be modelled separately (independently) or jointly, and to assess whether structural changes indicate that the use of more flexible models may be appropriate (Section E.1.1.1).
- an assessment of both internal and external validity by comparing several different models (Sections E.1.1.2 and E.1.1.3).]

E.1.1.1 Log-Cumulative Hazard Plots and Residual Plots

[Include log-cumulative hazard plots and (Schoenfeld) residual plots, and describe what these show and what conclusions are drawn from them.]

E.1.1.2 Internal validity

E.1.1.2.1 Assessment of Statistical and Visual Fit (AIC and BIC)

[Include a table with AIC and BIC values for each treatment arm and discuss the statistical and visual fit within the observation period.]

E.1.1.2.2 Assessment of Smoothed Hazard Functions

[Include a plot of the hazard function for the outcome. The plots must be presented in separate figures for the intervention and comparator and must include the estimated hazard for the observed data. The plot must be discussed in relation to the selected distribution.]

E.1.1.3 External Validity

[Describe the external validity with a focus on clinical plausibility and consistency with evidence from external sources. Include figures and tables that support the assessment of external validity, including comparisons between modelled data and external data.]

E.1.1.4 Other Assumptions

[This section should be used if assumptions require a more detailed and extensive description related to the extrapolation of the relevant outcome.]

E.1.2 Extrapolation of [Clinical Outcome 2]

[To be completed as Section E.1.1]

E.2 Transition Probabilities

E.2.1 Internal Validity

[Supporting tables and figures may be included here.]

E.2.2 External Validity

[Supporting tables and figures may be included here.]

E.2.3 Other Assumptions

[This section should be used if assumptions require a more detailed and extensive description.]

Appendix F. Serious Adverse Events

[List all serious adverse events with a frequency of ≥ 1% that were observed in the study or studies included in the assessment. If a JCA has been prepared, refer instead to the relevant section of the JCA report where the serious adverse events are described.]

Appendix G. Health-Related Quality of Life

G.1 Data Collection – Overview of Responses

[If a JCA has been performed, refer instead to the relevant sections of the JCA report.]

G.2 Reporting of Domains

[For each measurement, present frequencies and proportions for each domain and each response level. The development over time (and possibly across treatment arms) must be presented in figures. If a JCA has been performed, refer instead to the relevant sections of the JCA report.]

G.3 Mapping

[Description of the mapping study.]

G.4 Calculation of Utility Values

[The applicant must describe and justify how the utility values for the individual health states were estimated, including all necessary formulas used to calculate the final utility values. The description should cover the choice of regression model, choice of explanatory variables, presentation of the final model and regression results (parameter estimates, standard errors, and confidence intervals), validation of the final model, uncertainties, and sensitivity analyses.]

Appendix H. Literature Searches for the Clinical Assessment

H.1 Effect and Safety of the Intervention and Comparators

[Describe the literature search, including the objective and search strategy. Describe the search terms used, as well as any search filters and limitations applied.

Insert tables listing the databases and other sources used. The name of the database, platform/website, and the date(s) of the searches must be reported. Examples of tables are provided below.]

Example of table. Bibliographic databases

Database	Platform/Website	Date of search
PubMed/Medline	Ovid/https://pubmed.ncbi.nlm.nih.gov	dd.mm.yyyy
Embase	Ovid/www.embase.com	dd.mm.yyyy

Example of table. Other sources

Source	Website	Search strategy/ keywords used	Date of search
NICE	www.nice.org.uk	'non-small cell lung cancer'	dd.mm.yyyy

[The searches must be documented with search strings reported line by line, including the number of hits. These may be inserted as tables in this section or submitted as supplementary materials in any format (e.g. Word or PDF).]

H.2 Systematic Selection of Studies and References

[Describe the selection process, including number of reviewers involved and how disagreements were resolved.

Complete Table 41 with inclusion and exclusion criteria (PICOS) or replace it with an equivalent table. If the analysis is based on a broader SLR, it must be stated whether the criteria were modified for the Danish context, e.g. with regard to a (smaller) population or (fewer) comparators.

Complete Table 42 with the studies/references that are included in the assessment and Table 43 with the studies/references that are excluded. These may also be submitted as supplementary materials.]

Table 41. Inclusion and exclusion criteria [may be deleted/replaced]

Clinical effectiveness	Inclusion criteria	Exclusion criteria	Modification, local adaptation
Population			
Intervention			
Comparators			
Outcome			
Study design/ publication type			
Limitations, e.g. language			

[Complete the PRISMA diagram below or replace with an equivalent one. If the analysis is based on a broader SLR, the boxes for 'Local adaptation' must indicate how many studies/publications are transferred to and excluded from the Danish assessment.]

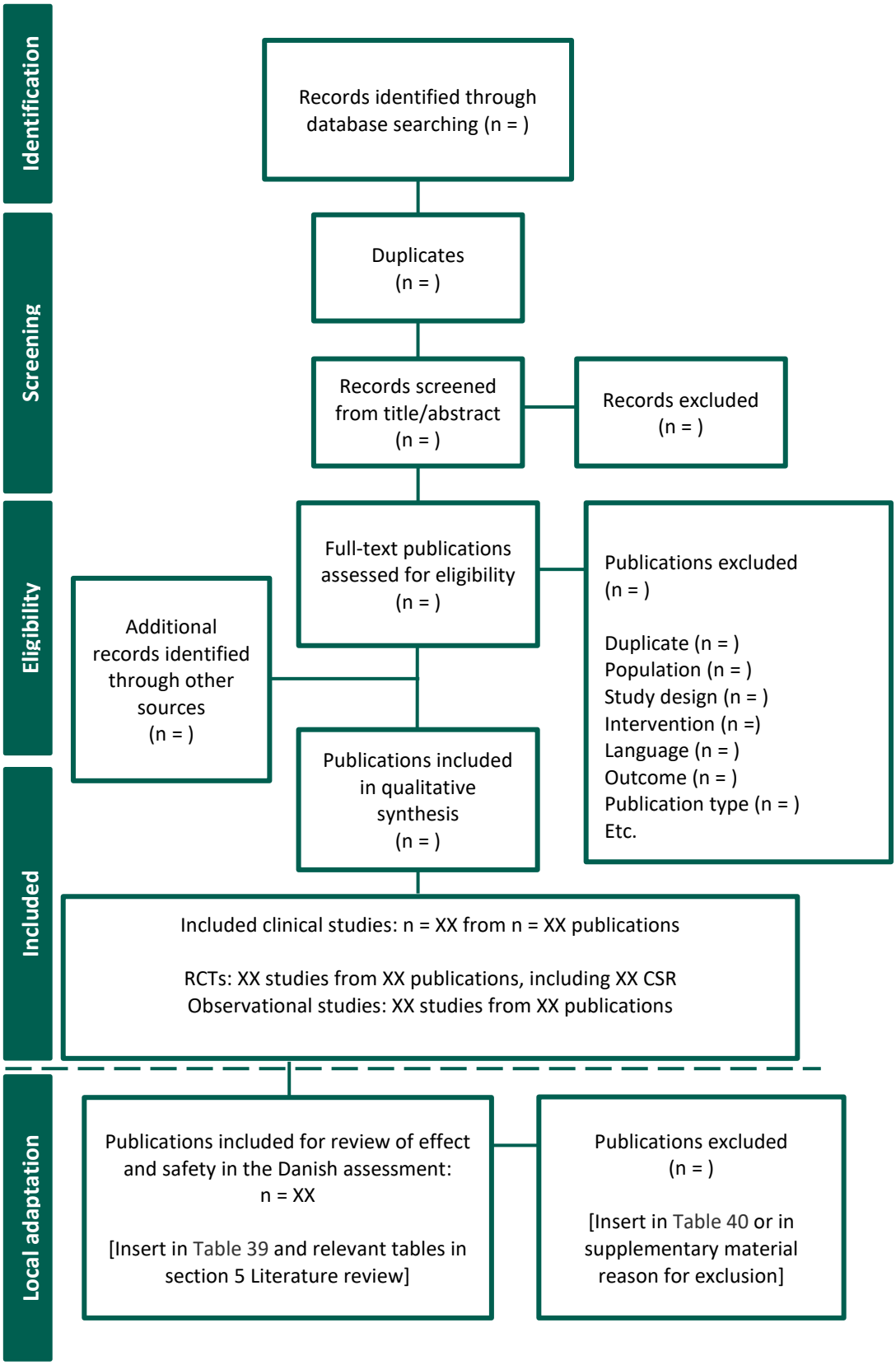
Identification
Screening
Eligibility
Included
Local adaptation
Records identified through database searching (n =)
Duplicates (n =)
Records screened from title/abstract (n =)
Records excluded (n =)
Full-text publications assessed for eligibility (n =)
Publications excluded (n =)
Duplicate (n =)
Population (n =)
Study design (n =)
Intervention (n =)
Language (n =)
Outcome (n =)
Publication type (n =)
Etc.
Additional records identified through other sources (n =)
Publications included in qualitative synthesis (n =)
Included clinical studies: n = XX from n = XX publications
RCTs: XX studies from XX publications, including XX CSR
Observational studies: XX studies from XX publications
Publications included for review of effect and safety in the Danish assessment: n = XX
[Insert in Table 39 and relevant tables in section 5 Literature review]
Publications excluded (n =)
[Insert in Table 40 or in supplementary material reason for exclusion]

Table 42. Studies/references included in the Danish assessment

Reference(s)
Study 1
Study 2

Table 43. Excluded studies/references [may alternatively be submitted as supplementary material]

Reference(s)
Study 1
Study 2

Appendix I. Literature Searches for Health-Related Quality of Life

I.1 Systematic Search

[Follow the instructions/structure described in Appendix H. The tables may be copied and inserted as needed.]

I.2 Focused Search

[Describe the objective of the search and the sources used, as well as the date the search was conducted. The search must be documented/described in as much detail as possible, including the search techniques and search terms used, as well as the criteria 5used to assess relevance.

Insert a table with identified references and transfer the references included in the assessment to the relevant table in Section 5.]

Appendix J. Literature Searches for Additional Inputs to the Health Economic Model

J.1 Systematic Search

[Follow the instructions/structure described in Appendix H. The tables may be copied and inserted as needed.]

J.2 Focused Search

[Describe the objective of the search and the sources used, as well as the date the search was conducted. The search must be documented/described in as much detail as possible, including the search techniques and search terms used, as well as the criteria used to assess relevance.

Insert a table with identified references and transfer the references included in the assessment to the relevant table in Section 5.]

Appendix K. Justification for Confidential Information

[The applicant must provide a specific and detailed justification explaining why particular information is of significant importance to the applicant and therefore should remain confidential. This includes, among other things, unpublished study data, estimated health gains (life years and QALYs), utility values, treatment duration, expected patient numbers, the use of non-confidential data for extrapolating patient transitions, and name, job title, and workplace of clinical experts. The justifications for confidential information must be provided in Table 44].

Table 44. Justification for confidential information

Parameter	Justification
[Confidential information 1]	[Specific and detailed justification]
[Confidential information 2]	[Specific and detailed justification]
….	

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