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 pharmaceutical or a new indication for an existing pharmaceutical, which will be assessed by updating an existing treatment guideline. The template is not exhaustive, companies must adhere to the current version of the relevant guideline alongside using this template when preparing their submission.

Please note the following requirements:

- Headings, subheadings and appendices must not be removed. Tables must not be 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.
- 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 will be initiated when all the requirements are met.

Documentation to be submitted

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

- Application in word format*
- Application in PDF format*
- The European Public Assessment Report (EPAR) should be submitted as soon as possible (draft versions will be accepted).

* Later in the appraisal process, once the application has received Day 0, the application must be assembled and sent to the DMC in one blinded version and one highlighted version (both in word and pdf).

Confidential information

- Please refer to DMC´s principles for use of unpublished data.

Version log

Version log		
Version	**Date**	**Change**
1.1	1 April 2025	New e-mail address ansogning@medicinraadet.dk is added.
1.0	29 June 2023	Application form for pharmaceutical, which will be assessed by updating an existing treatment guideline, made available on the website of the Danish Medicines Council.

Application for the assessment of <proprietary name of pharmaceutical> by updating the <name of guideline>

Contact information

Contact information	
Name	**[Name]**
Title	
Phone number	[Include country code]
E-mail	
Name (External representation)	**[Name]**
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 pharmaceutical / extension of indications, the following power of attorney must be completed and sent to ansogning@medicinraadet.dk.]

Table of contents

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 pharmaceutical

Overview of the pharmaceutical	
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 pharmaceutical 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]
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	
Therapeutic indication relevant for the assessment	[Note if there are any deviations from the EMA indication and elaborate]
Dosage regiment and administration:	
Choice of comparator [if any]	
Most important efficacy endpoints (Difference/gain compared to comparator)	[Insert results for the efficacy endpoints included in the current treatment guideline]
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)]

3. The patient population, intervention and relevant outcomes

3.1 The medical condition, patient population, current treatment options and choice of comparator(s)

[Please refer to the relevant treatment guideline. Information relevant for the assessment, that are not addressed in the treatment guideline, can be described here.]

3.2 The intervention

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

Overview of intervention	
Therapeutic indication relevant for the assessment	[Note if there are any deviations from the EMA indication and elaborate]
Method of administration	
Dosing	
Should the pharmaceutical 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)	

3.2.1 The intervention in relation to Danish clinical practice

[Describe where in the treatment algorithm/course of treatment the intervention is expected to be used.

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.]

4. Overview of literature

[If the treatment guideline includes a network meta-analysis (NMA) for the PICO relevant for the application, a systematic literature search can be omitted.

If the application includes an indirect comparison, as a rule, a systematic literature search must be conducted for the new intervention (and relevant indication) as well as the relevant comparator to identify all evidence relevant for this application (efficacy and safety). 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 D in accordance with section 3 of the methods guide for assessing new pharmaceuticals.

All essential literature/studies applied in this application must be presented in the table below. All studies must be described in detail in Appendix A.]

Table 1 Relevant literature included in the assessment of efficacy and safety [sample text in table for full paper and conference abstract]

Trial name, NCT identifier and reference (Full citation incl. reference number)*	Study design	Study duration	Dates of study (Start and expected completion date, data cut-off and expected data cut-offs)	Patient population (specify if a subpopulation in the relevant study)	Intervention	Comparator	Relevant for PICO nr. in treatment guideline	Outcomes and follow-up period
Trial name, NCTxxxx (reference for publication(s))	Randomized phase III / open-label / placebo-control/ active comparator-control	E.g.: 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.	Start: DD/MM/YY Completion: DD/MM/YY Data cut-off DD/MM/YY Future data cut-offs DD/MM/YY	E.g.: Treatment naive patients with active disease and incomplete response to conventional treatment.	Treatment, administration, dosing	Treatment, administration, dosing	1	[All primary and secondary outcomes in the study and included in the treatment guideline must be listed with timepoints.]

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

5. Clinical question(s) [number in treatment guideline]

[If more than one comparison is included in the application, i.e., due to multiple clinical questions in the treatment guideline, copy/paste section 5 for each question.

If an NMA is used to answer the clinical question(s) in the treatment guideline, section 5.2.3 and 5.2.4 can be omitted.]

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

5.1.1 Relevant studies

[All relevant studies should be listed in Table 1. 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.]

5.1.2 Comparability of studies

[In case of an indirect comparison:

- Address any differences between the studies used for indirect comparison and describe how these differences are addressed in the analysis.

In case of an NMA in treatment guideline:

- Address any differences between the study/ies for the new intervention and the studies included in the treatment guideline.]

5.1.3 Comparability of patients across studies and with Danish patients eligible for treatment

[Add all relevant information in Table 2 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. 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.

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).

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.

Address comparability of the study population with Danish patients eligible for treatment.]

Table 2 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]						

5.2 Comparative analyses of efficacy and safety

5.2.1 Efficacy and safety – results per study

[Please provide key efficacy and safety findings for each study included in the comparative analysis (intervention and comparator studies) in Appendix B. Only data for outcomes included in the treatment guideline should be provided. If no data are available for a specific outcome, please explain. 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 outcome 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.

Include references for all data.

5.2.2 Please provide a qualitative description of safety data. Differences in definitions of outcomes between studies

[If there are discrepancies in the definition of outcomes between studies, list them here. Explain how differences were addressed in the comparative analysis.]

5.2.3 Method of synthesis

[If the treatment guideline includes an NMA, this section can be omitted.

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. 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.]

5.2.4 Results from the comparative analysis

[If the treatment guideline includes an NMA, this section can be omitted.

Provide the results from the comparative analyses in the Table 3 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 3 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			

Outcome measure	[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;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 %**
Proportion of patients with AE ≥ grade 3	**n/N, %** (95 % CI: X;Y)	**n/N, %** (95 % CI: X;Y)	**Absolute risk: X %** **Relative risk: X %**

6. References

[Insert the reference list.]

Appendix A. Main characteristics of studies included

[Complete Table 4 for each study included. Comply with section 3 of the methods guide.]

Table 4 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	[Insert the inclusion criteria related to NCT number from www.clinicaltrials.gov]
Main exclusion criteria	[Insert the exclusion criteria related to NCT number from www.clinicaltrials.gov]
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)]
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 **Fejl! Henvisningskilde ikke fundet.**.] **Endpoints included in this application:** [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

Trial name:	NCT number:
	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. 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 5 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)								
	ZZZ	248									
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 6 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 difference (SMD). The	

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		
								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. Literature searches for the clinical assessment

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

[Please refer to the treatment guideline for instructions as well as 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.

If an existing/global systematic literature review (SLR) is (re)used, Appendix D 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 as Appendix D. Please find an editable PRISMA flowchart at the end of this document.

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 7 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 8 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 9 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

Abbreviations:

D.1.2 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 10 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
#8		211070
#9	#7 OR #8	272517
#10	#3 AND #6 AND #9	37

D.1.3 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.]

Table 11 Inclusion and exclusion criteria used for assessment of studies

Clinical effectiveness	Inclusion criteria	Exclusion criteria
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.]

Table 12 Overview of study design for studies included in the technology assessment

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						

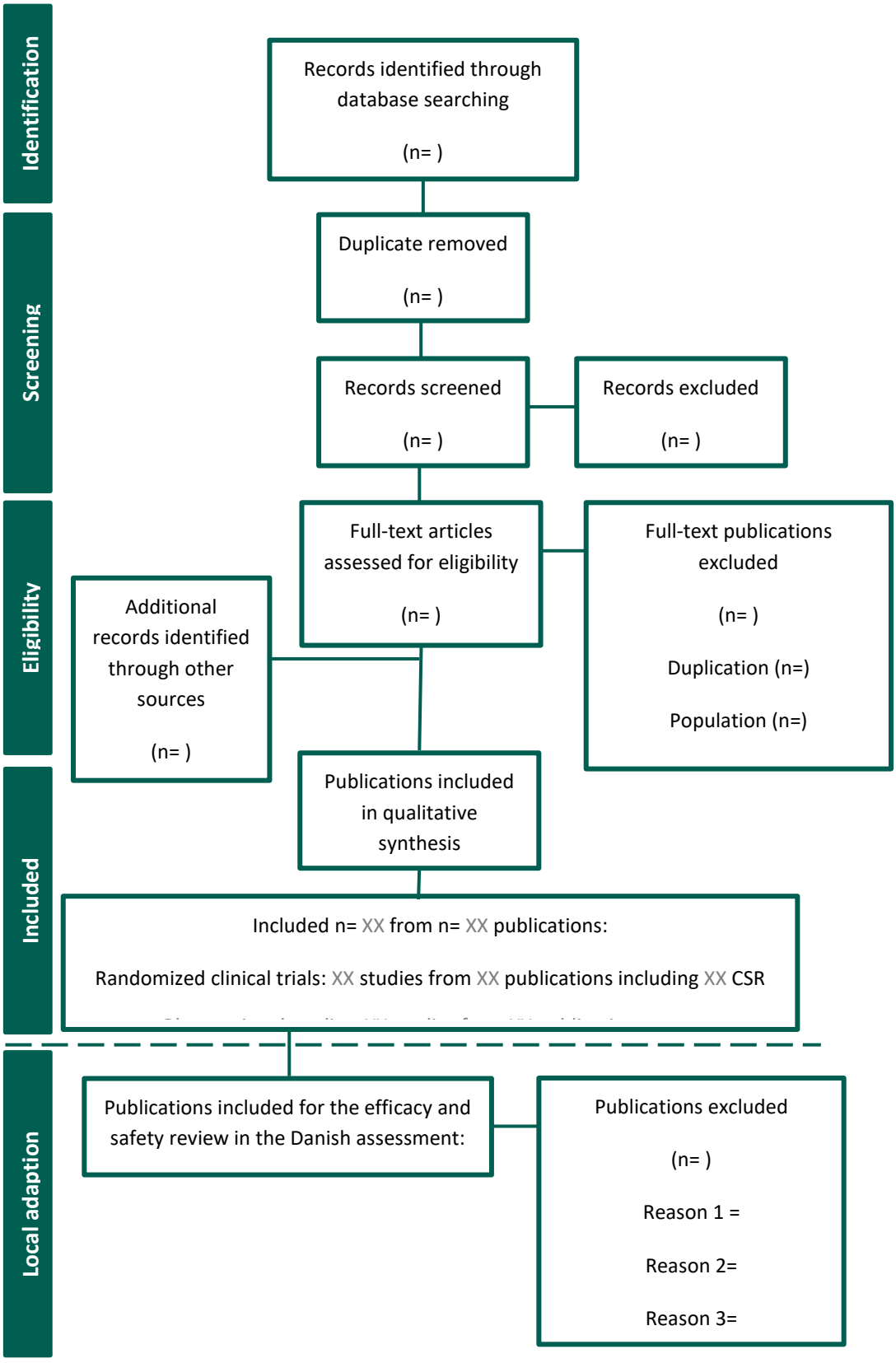
D.1.4 Quality assessment

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

D.1.5 Unpublished data

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

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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