

# Template/Guidance for submission of documentation for Single Technology Assessment of pharmaceuticals

## Introduction

The national system for the introduction of new health technologies within the specialist health service will involve the rapid assessment of health technologies in relation to the introduction of medical devices, diagnostic methods, procedures and pharmaceuticals.

Two templates for Single Technology Assessment (STA) have been prepared:

1. Template on submission of documentation for the STA of medical devices, diagnostic methods and procedures.
2. Template on submission of documentation for the STA of pharmaceuticals.

**\*\*The System Description is the main document. We refer to it for information about the national system, and description of various types of Health Technology Assessments (HTAs) [Nettside- klikk her](#)**

**\*\* This template will be for submission of documentation to The Norwegian Medicines Agency for Single Technology Assessment (STA).**

The actual template should only be used by the manufacturers that are asked to send in documentation. The template is to be used after RHA Forum (Regional Health Authorities Forum for the commissioning of HTAs) requests (through the use of a proposal order) the Norwegian Medicines Agency to carry out a STA. The Norwegian Medicines Agency will then ask for documentation by the actual manufacturer in accordance with the guidance in this template.

Questions concerning the template or any requests for assistance, meetings, etc. in regard to submission of documentation should be sent to the Norwegian Medicines Agency at: [sykehus@legemiddelverket.no](mailto:sykehus@legemiddelverket.no) or phone: +47 22 89 77 00.

Economic analyses in the health technology assessments shall be based on recommendations derived from guidelines for health economic analyses by the [Norwegian Directorate of Health](#), the

[Norwegian Medicines Agency](#) and the template for reimbursement applications (the blue prescription scheme).

The Norwegian Medicines Agency asks manufacturers/marketing authorisation holders to ensure that documentation is presented in a systematic manner as proposed in this template. Any deviations from the template, including items/features/entries considered by the manufacturer as not being relevant, must be justified. Documentation may be submitted in either English or a Scandinavian language. The documentation should be submitted electronically. If a health economic model has been used to calculate cost-effectiveness, it is assumed that this will also be submitted.

Confidential information such as commercial secrets or data awaiting publication that should not be made public will be treated in accordance to applicable regulations in the Public Administration Act and the Medicines Act. The Norwegian Medicines Agency will publish completed reports on its website.

The template has been prepared by the Norwegian Medicines Agency in collaboration with the Norwegian Knowledge Centre for Health Services and the national group for the Introduction of New Health Technologies in the Specialist Health Service.

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## 1. Technology to be appraised

Briefly describe what task the submission of STA documentation is to respond to.

## 2. Information about the marketing authorisation (MA) holder/manufacturer's representative

Applicants contact information.

## 3. Description of the health technology

### 3.1 Description of the product

- Name of preparation/pharmaceutical
- Active ingredient
- Pharmaceutical form
- Strength
- Recommended daily dose
- Medically approved indication

What is the status concerning approval and use, in Norway, other European countries and the USA?

### 3.2 Description of the context for use

Refer to guidelines for Pharmacoeconomic Analyses; section 2.4

#### **Description of disease and epidemiology**

Describe the disease for which the medicine is indicated, including consequences of the disease in the short and long term, as well as severity of the disease. Describe the most relevant patient group(s), including current and anticipated developments in prevalence/incidence.

#### **Treatment regime with the pharmaceutical**

Dosage per day.

Anticipated treatment period (life-long treatment?).

Is the treatment continuous or intermittent? (E.g. six months per year).

What is the efficacy and side effects of the medicine for the relevant patient group(s).

Consumption of any supplementary medication.

#### **Overview of existing treatments**

Give a description of the Norwegian treatment tradition/practice for the indication concerned.

Describe the National clinical guidelines for the condition, if relevant.

Estimate the total number of patients indicated for medicinal treatment under this indication. Drug consumption, including supplementary medication, per preparation group and preparation (retail price and total number of DDD sold).

**Position of the new technology (pharmaceutical) in relation to the range of treatments available**

- Clinical advantages: What are the advantages compared to current treatment?
- Which treatment(s), including pharmaceuticals will be displaced – either partly or entirely – by the new technology?
- How many patients will be affected?
- Will the new technology (pharmaceutical) result in/lead to changes to the treatment pathway?
- Will the introduction of the new technology result in changes of the infrastructure (organisation of the health service, spatial requirements, training, monitoring, follow-up, administration or costs)?
- Could introducing the new technology have negative consequences for vulnerable patient groups?
- List ongoing studies or other documentation that can be available for assessment the next year or later years.

**4. Clinical effect**

Information about the new health technology/medicine and its mode of action should primarily be based on the summary of product characteristics or equivalent documentation submitted as part of the marketing authorisation application. (2.6 Guidelines for Pharmacoeconomic Analyses)

Additionally, systematic searches for studies involving the new health technology/medicine and comparison alternatives must be performed in relevant databases detailing relevant outcome objectives. The search strategy and the selection criteria of studies must be described. For more information about systematic searches see the Knowledge Centre’s health technology manual «slik oppsummerer vi forskning» (in Norwegian).

<http://www.kunnskapssenteret.no/verkt%C3%B8y/slik-oppsummerer-vi-forskning>

**4.1 Description of studies included**

**Overview of studies included in table form.**

Study (acronym, ID no.)	Reference	Population	Intervention	Comparison
Type of design				
Study 1				
Study 2				
Etc.				

Justification should be given if any of the identified studies is not to be used / incorporated in the health economic analysis.

**Detailed description of studies included**

Give a brief summary in text and describe details from each study in table form. Specify any important differences between the studies. See example of such a table.

Study (acronym, ID no.)	Study 1	Study 2	Etc.
Location/place of study/country			
Design/study type			
Duration of the study			
Randomisation method			
Blinding method (investigator, patient, outcomes assessor)			
Intervention (n=)			
Comparison/control (n=)			
Primary outcome (including measurement tools and measurement times)			
Secondary outcome (including measurement tools and measurement times)			
Follow-up time			

**4.2 Patient population in the studies**

**Describe the inclusion and exclusion criteria in the studies**

Study (acronym, ID no.)	Inclusion criteria	Exclusion criteria
Study 1	Important inclusion criteria such as age, gender, diagnosis, severity, etc.	
Study 2		
Etc.		

**Baseline characteristics of the patients in the studies included**

Study (acronym, ID no.)	Intervention	Comparison
Study 1 (n=)	(n=)	(n=)
Age		
Gender		
etc.		
Study 2 (n=)	(n=)	(n=)

**Endpoints**

Describe the endpoints in each study. The choice of endpoints should be in line with the guidelines developed by EMA (“European Medicines Agency's guidelines on the **clinical efficacy and safety of medicines**”).

Study (acronym, ID no.)	Primary outcome	Secondary outcome, including side effects
Study 1		
Study 2		
etc.		

### 4.3 Presentation of results

#### Present results for all relevant endpoints

Where possible, data must be presented as “intention-to-treat” analyses (analyses where all the patients are analysed in the group in which they started). Depending on the study design and type of endpoint, other types of analysis may also be relevant (e.g. “on-treatment” and “safety-on treatment”). Always define which patients are included in the analysis and, where applicable, the reasons why any patients were not included in the analyses. State clearly whether the analyses include patients that withdrew/had missing measurements and, if so, how this was handled.

Data should be presented in the form of text, table and graphics where possible.

#### Meta-analyses

In cases where meta-analyses are included, provide at least the following: selection method (random or fixed effects model, choice of effect parameter, sensitivity analyses) and test for heterogeneity.

#### Indirect comparisons

If there are no directly comparable studies (head-to-head studies), consideration must be given to the execution of indirect comparisons. See the Norwegian Medicines Agency’s guidelines for health economic analyses. Present clearly the assessment behind choices made, how the studies for indirect comparison were identified, how the data was extracted and the method adopted for analysis.

### 4.4 Summary of the key findings

Briefly summarize key findings of presently available clinical documentation, with a focus on effects and side effects. Give a brief summary of the strengths and weaknesses inherent in the documentation available for the new technology/medicine.

### 4.5 Relevance to Norwegian conditions

Briefly discuss how and to what extent the provided documentation is relevant for the application. Identify factors which could be of significance for the external validity of the study results when applied in normal clinical practice.

## 5. Cost-effectiveness analyses

The guidelines for health economic analyses prepared by the Norwegian Medicines Agency are also normative for the formulation of Single Technology Analyses of medicines that are to be used within the specialist health service.

Guidelines for health economic analyses can be found here:

[http://www.legemiddelverket.no/Blaa\\_resept\\_og\\_pris/soeknad\\_om\\_refusjon/mal\\_for\\_refusjonssoeknad/Documents/Retningslinjer%20per%201%20mars%202012.pdf](http://www.legemiddelverket.no/Blaa_resept_og_pris/soeknad_om_refusjon/mal_for_refusjonssoeknad/Documents/Retningslinjer%20per%201%20mars%202012.pdf)

### 5.1 Previously published cost-effectiveness analyses

If published health economic analyses that are relevant to the case exist, the Norwegian Medicines Agency wishes that such analyses are enclosed.

Fill in the following table summarizing identified studies.

Study	Year	Country in which the study was conducted	What type of model analysis?	Patient population (age, gender, state of health, etc.)	Incremental QALY*	Incremental costs	ICER**	Comparison
Study 1								
Study 2								
Etc.								

\* QALY: Quality-Adjusted Life Years

\*\* ICER: Incremental Cost-Effectiveness Ratio

### 5.2 In-house Cost-Effectiveness Analysis

The Instructions for Official Studies and Reports (FAD 2005) and the Ministry of Finance's Guideline on socio-economic analyses (FIN 2005) form the basis for why and how socio-economic analyses shall be conducted in order to provide a sound decision basis as concerns public sector investment in Norway. At lower levels, specific institutions which assess socio-economic analyses can have their own, more detailed requirements or recommendations. An example of this is the Norwegian Medicines Agency's requirements regarding pharmacoeconomic analyses submitted in relation to applications for the admission of medicines/pharmaceuticals under the blue prescription scheme.

The Norwegian Medicines Agency refers applicants to the **Pharmacoeconomic Analysis Guidelines** of 1 March 2012 in relation to the formulation of in-house cost-effectiveness analyses. The guide for pharmacoeconomic analyses sets out requirements and recommendations concerning how pharmacoeconomic analyses should be *conducted/carried out*. The key points here are analysis perspective, what costs and beneficial effects to include and how they are to be calculated. The recommendations offer some evaluation of both analysis methods and methods for the measurement of quality of life. Explanatory justifications are provided as concerns choices made, along with some supplementary guidance.



[http://www.legemiddelverket.no/Blaa\\_resept\\_og\\_pris/soeknad\\_om\\_refusjon/mal\\_for\\_refusjonssoeknad/Documents/Retningslinjer%20per%201%20mars%202012.pdf](http://www.legemiddelverket.no/Blaa_resept_og_pris/soeknad_om_refusjon/mal_for_refusjonssoeknad/Documents/Retningslinjer%20per%201%20mars%202012.pdf)

Deviations from these recommendations apply to the selection of the analysis' perspective and are specified in more detailed in a separate section below.

### **Deviations from the recommendations in the Pharmacoeconomic Analysis Guidelines**

- **Analysis perspective**

Pharmacoeconomic Analysis Guidelines: *Section "2.1, Standardanalyse" (2.1, Standard Analysis) and "2.7, Perspektiv og synliggjøring av konsekvenser for ulike aktører" (2.7, Perspectives and awareness about their consequences for different actors)* the recommended perspective in the standard analysis used in connection with assessments relating to admission to the blue prescription scheme is *"Samfunnsperspektiv, med begrensninger"* (narrow societal perspective).

In STAs for pharmaceuticals/medicines within the specialist health service, the analysis must be carried out using both the "narrow societal perspective" and the health care perspective.

### **5.3 Budgetary consequences of the new technology**

The manufacturers/applicants must provide/present an analysis of their technology's budgetary consequences. The Norwegian Medicines Agency will then evaluate and possibly carry out own calculations where necessary.

The applicant must calculate and provide the budget implications on program category 10:30 of the National State Budget (Specialist health care services). The budget impact/implication is hereby defined as the additional costs incurred i.e. the total costs of introducing the new technology minus the total costs of not doing so.

These calculations/analyses are intended for the national level. Budget calculations at the regional or local level should be done regionally or locally.

The time horizon in relation to budget analyses of pharmaceuticals shall be five years. This is because it is assumed that the broad usage of new pharmaceuticals is well established after five years. For other technologies, the time horizon may vary depending on the economic life and/or depreciation of the technology.

Calculation of the additional costs shall be based on the following factors:

1. Costs incurred by the specialist health service during the calculation/analysis period.
2. The estimated market share of the new technology, in relation to the patient group the technology targets, in each of the relevant years after the decision to use the technology is made.
3. Deductions of: costs of competing technologies that will be completely or partially replaced by the new technology, any increases in patient payments and increments in user fees during outpatient treatment.

- Other costs related to the technology assessment (change in bed-days, commodity costs, personnel costs, nursing costs, depreciation, travel expenses covered by the specialist health care service, administrative expenses, etc.) should only be included if there are significant differences between the competing technologies and/or if the differences constitute a large proportion of the additional costs.

The table below shows an example of how calculation of the additional costs can be done. Costs are calculated in two scenarios - one where the technology is introduced into the specialist health service (green table) and one where this is not the case (orange table). In each of the scenarios, costs are only presented for the indication that the new technology will cover. It is possible to provide where applicable; various treatment procedures, different measures, different pharmaceuticals used for treatment of the indication i.e. the new technology and several alternatives/comparators. It is also possible to have a scenario where a certain percentage of patients receive the new technology while a certain proportion of patients receive the alternative comparison technology.

Number or share of patients if the new technology is adopted					
	Year 1	Year 2	Year 3	...	Year x
The New Technology					
Alternative/comparator A					
Alternative/comparator B					
Alternative/comparator C					

Number or share of patients if the new technology is NOT adopted					
	Year 1	Year 2	Year 3	...	Year x
The New Technology					
Alternative/comparator A					
Alternative/comparator B					
Alternative/comparator C					

Cost (Yearly cost per patient * Number of patients per year)					
	Year 1	Year 2	Year 3	...	Year x
The New Technology					
Alternative/comparator A					
Alternative/comparator B					
Alternative/comparator C					
<b>Total COST</b>					

Cost (Yearly cost per patient * Number of patients per year)					
	Year 1	Year 2	Year 3	...	Year x
The New Technology					
Alternative/comparator A					
Alternative/comparator B					
Alternative/comparator C					
<b>Total COST</b>					

Budget Impact	Year 1	Year 2	Year 3	...	Year x
+ Cost if the New technology is adopted					
- Cost without adoption of the New Technology, i.e. Current situation					
- Out-of-pocket charges during outpatient treatment					
- Payment by individual patients					
<b>Total added cost</b>					

Budget calculations/analysis should cover both the new technology and the competing technology(ies) if the extent of use is affected by the possible introduction of the new technology.

This will in turn make it possible to calculate a total budget impact. The budget impact is the difference between the two scenarios in each of the relevant years of the analysis (tables below). Year 1 is the first full calendar year after a decision is made about introducing the new technology into the specialist health care service.

The budget impact calculations must show the following:

- 1 What proportion of the total additional costs is the result of an increase in patient numbers and what proportion is due to the transition to a more expensive technology
- 2 The basis for key assumptions in the calculations.

Additionally, the following calculations may apply in special cases:

- 1 Subgroup analyses such as in cases where it is prudent to prioritize giving the new technology to only a subset of the total population.
- 2 Analyses with added costs/impact on other patient groups not targeted by the new technology but whom none the less use the technology.
- 3 Sensitivity analyses where key assumptions and data are tested in order to check to what extent results and estimates used are sensitive to changes. This is particularly relevant if critical assumptions in the analyses are very uncertain.

## 6. References

1. Statens legemiddelverk (2012), Retningslinjer for legemiddeløkonomiske analyser.  
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8. [http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000085.jsp&mid=WC0b01ac0580027549](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000085.jsp&mid=WC0b01ac0580027549)
9. [http://www.legemiddelverket.no/Blaa resept og pris/soeknad om refusjon/bagatellgrensen og budsjettberegninger/Sider/Beregning-av-merutgifter-for-folketrygden.aspx](http://www.legemiddelverket.no/Blaa_resept_og_pris/soeknad_om_refusjon/bagatellgrensen_og_budsjettberegninger/Sider/Beregning-av-merutgifter-for-folketrygden.aspx)