FINOSE

Evaluation report

January 2021

Background

FINOSE is a Nordic Health Technology Assessment (HTA) collaboration network between Finland, Norway and Sweden initiated in 2017 and established in 2018. The aims of the collaboration are to perform joint HTA assessments, gaining additional knowledge about the products, increasing quality of the assessment/s, as well as gaining insights in best practice and developing staff capacity. The collaborating agencies are Sweden's Dental and Pharmaceutical Benefits Agency (TLV), the Norwegian Medicines Agency (NoMA) and the Finnish Medicines Agency (Fimea).

The pilot stage of the collaboration ended in June 2020. In order to continue to explore ways to increase effectiveness and decrease administrative burden through the production of joint assessment reports across the Nordic countries, the three agencies Fimea, NoMA and TLV decided to prolong the FINOSE collaboration. Therefore, the Director Generals of each agency signed a new Memorandum of Understanding in June 2020. The collaboration under this Memorandum of Understanding will continue until 30 June 2023, with a possibility for extension if agreed by the involved parties.

A flowchart of the assessment process is presented in Figure 1 below.

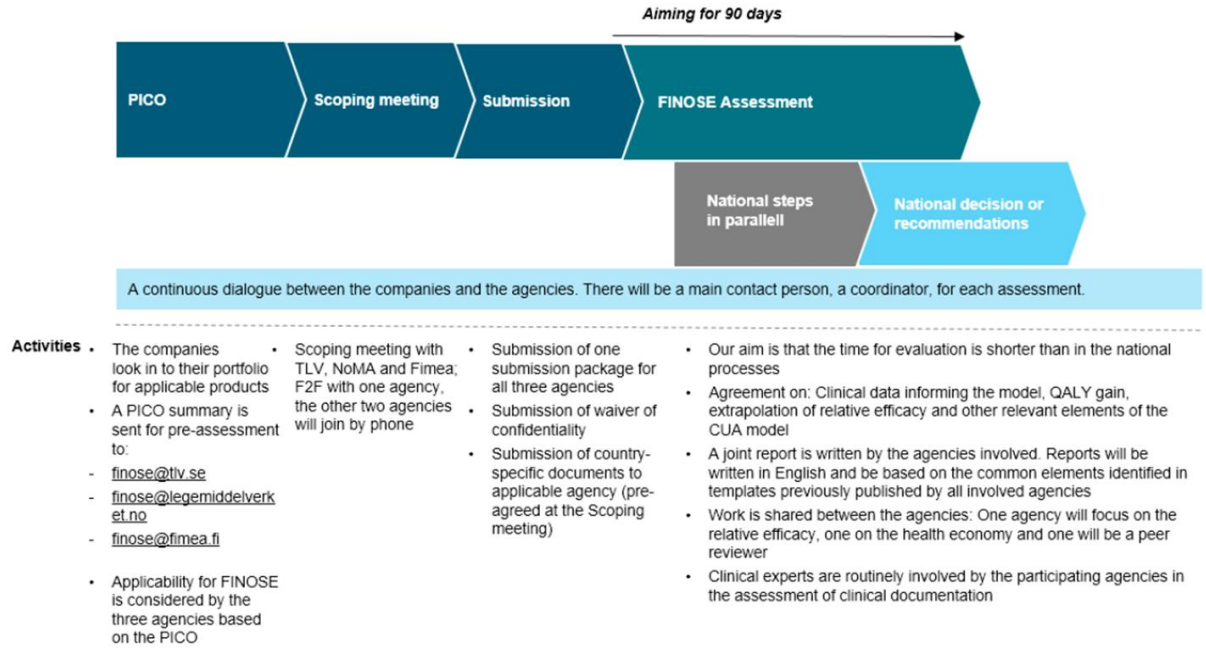

Figure 1: FINOSE process

The FINOSE collaboration network aims at (1):

- Supporting timely and equal access to medical technologies
- Gaining additional knowledge about the products
- Increased efficiency in production of assessment reports
- Less divergence in HTA methodologies and evidence requirements
- Reduced complexity in industry submissions

Consequently, the collaboration is expected to result in reduced workload and time to market.

During the first stage of the collaboration four workshops where held in order to assess and discuss different viewpoints on important topics related to Health technology assessments between NOMA, TLV and Fimea. The topics discussed at these workshops were:

- Assessment of histology independent indications, NoMA, October 2018
- Assessment of combination therapies, at TLV, December 2018
- Assessment of potentially curative therapies, at Fimea, April 2019
- Using RWD at decision making, and different methods for discounting, at TLV, October 2019

During the first stage of the collaboration, three HTAs were performed. These will be will be discussed below.

Purpose

In the 2017 memorandum of understanding, it was decided that at the end of the first period, outcomes of the collaboration as well as the further developments in the proposed continued collaboration would be assessed. The purpose of this evaluation is to summarize the FINOSE process so far, and to identify challenges and what works well. Finally, new goals and improvements will be suggested.

In the process of making this report, questionnaires have been distributed to the FINOSE network, the companies that have had their pharmaceuticals assessed by FINOSE, as well as the Nordic procurement bodies responsible for the joint price negotiations for Zynteglo.

The content below reflects the answers received on the given questions, and can therefore not be considered to necessarily reflect the full perception of the involved parties regarding FINOSE.

HTA assessments

The pilot stage of FINOSE resulted in three joint HTA-assessments that are described in more detail below:

- Tecentriq for the treatment of non-small cell lung cancer
- Xtandi for treatment of prostate cancer
- Zynteglo for betatalassaemia

	Tecentriq (atezolizumab) – June 2019 (2)	*Xtandi (enzalutamide) – June 2019 (3)*	*Zynteglo (autologous CD34+ cells encoding βAT87Q-globin gene) – June 2020 (4)*
Indication	Tecentriq, in combination with bevacizumab, paclitaxel and carboplatin, is indicated for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC).	Treatment of adult men with high-risk non-metastatic castration-resistant prostate cancer.	Zynteglo for the treatment of patients 12 years and older with transfusion-dependent β-thalassaemia (TDT) who do not have a β^0/β^0 genotype, for whom haematopoietic stem cell (HSC) transplantation is appropriate but a human leukocyte antigen (HLA)-matched related HSC donor is not available.
Mode of action	Atezolizumab is an Fc-engineered, humanised immunoglobulin G1 (IgG1) monoclonal antibody that binds directly to PD-L1 and provides a dual-blockade of interactions between PD-L1 and the PD-1 and B7.1 receptors both of which can provide inhibitory signals to T lymphocytes. The blockade of PD-L1 enhances the magnitude of tumour specific T lymphocyte responses, resulting in improved anti-tumour activity.	Enzalutamide is a potent androgen receptor signaling inhibitor that blocks several steps in the androgen receptor signaling pathway. Enzalutamide treatment decreases the growth of prostate cancer cells and can induce cancer cell death and tumor regression.	Zynteglo is a novel, cell-based beta-globin gene therapy which comprises a lentiviral vector which inserts functional copies of a beta-globin gene into CD34+ haematopoietic stem cells, ex vivo. Gene therapy with Zynteglo requires myeloablative conditioning as pre-treatment. Zynteglo is a one-time treatment, which has the potential to increase haemoglobin production and eliminate or reduce dependence on chronic red blood cell transfusions. Zynteglo therapy requires qualified care centers and trained health care professionals, and the treatment will be offered in centers in some of the Nordic countries.
Roles	Authors: NoMA (medical assessor) and TLV (health economist) Reviewer: Fimea	Authors: NoMA (medical assessor) and TLV (health economist) Reviewer: Fimea	Authors: Fimea (medical assessor) and TLV (health economist) Reviewer: NoMA
Case processing time (excl. national steps)	188 days	174 days	170 days
Overall result	The report established a cost effectiveness ratio for one indication, while it did not consider the other indications to be clinically plausible. This report has led to a positive decision for atezolizumab and bevacizumab in EGFR-posistive NSCLC after targeted therapies in Norway. In Sweden the negotiations have not led to a price that was considered acceptable for reimbursement. The company did not launch this indication in Finland.	FINOSE concluded that that no added benefit was demonstrated, mainly due to sparse overall survival evidence. Since treatment duration and therefore treatment cost with Xtandi in the non-metastatic stage was significantly higher than in the metastatic stage, the report concluded that Xtandi was not cost-effective in the non-metastatic stage. Xtandi has not been reimbursed in any of the Nordic counties.	The joint assessment report was recently taken up as a basis for negotiations by the procurement functions in the five Nordic countries (Denmark, Iceland, Finland, Norway and Sweden), who have invited the Marketing Authorisation Holding company to enter a joint negotiation process. The FINOSE team had a meeting with the Procurement bodies on the 3rd of November 2020 to discuss joint negotiations and national processes and the role of the FINOSE assessment in the joint negotiations.

Evaluation of the HTA assessment process

Comments from Fimea, Noma and TLV

All parties agree that the FINOSE collaboration has the potential to reduce divergence in HTA methodologies and evidence requirements between the Nordic countries, reduce workload and contribute to earlier access to new pharmaceuticals. The greatest value achieved in the pilot phase is perhaps the mutual increased knowledge on our different HTA-assessment systems and experience exchange on common challenges and how these issues are handled in our respective countries.

The FINOSE collaboration enables the countries to share the workload appropriately and to improve the capacity by optimizing productivity. Through FINOSE we were able to complement each other, save resources in our respective agencies and to have an earlier startup for the assessments.

The resource use is also decreased for the pharmaceutical companies in the FINOSE track as they can submit one dossier for all three countries, with only minor additional national requirements. Through joint FINOSE HTA assessments, new medicines have been assessed which otherwise would have been given low priority or where companies might not have sent applications to every single Nordic country due to a perceived excessive workload for too small markets.

During the assessments, Fimea, NoMA and TLV experienced fruitful discussion regarding the effectiveness of the treatments. Initial divergent opinions were discussed thoroughly, and joint understandings were reached.

As the agencies are located in different countries, some difficulties in handling and editing the same document were encountered. However, this will be solved in the very near future when all the agencies start using a common editing-tool.

Furthermore, there were challenges in differences in writing style and what issues were to be assessed between the medical and economic parts. The network will continue working on the consistency and connection between the medical and economic parts, whereas the writing style issue is expected to be resolved by the now available common template for the assessment report.

For some of the cases, the product or indication under assessment was not launched in Finland or was used in out-patient setting and are therefore nationally assessed by the Pharmaceutical Pricing Board (Prisnemden/Nämnden för läkemedelsförmåner/Lääkkeiden hintalautakunta). The latter resulted in that the company would have to submit the full reimbursement application irrespective of the FINOSE-assessment.

The FINOSE goal for case processing time is 90 days. So far the assessments have taken longer, more similar to a normal national assessment in Norway and Sweden. The first three years have been an important learning process on how other agencies express assessment of effect and health economic aspects. We expect a more effective assessment going forward. A common template, workshops discussing HTA methodologies and a joint editing tool will all help to reduce the workload and increase the effectiveness.

Joint price negotiations

Comments from procurement bodies in Norway, Sweden, Denmark and Iceland

Finland, Norway, and Sweden conducted a joint health economic assessment of Zynteglo through FINOSE.

Zynteglo was the first new drug to enter into a joint Nordic collaboration. Representatives from each country participated to find common terms and conditions for the five countries: Norway, Sweden, Finland, Denmark and Iceland. Based on the results of the common negotiation, each country has decision making authority whether the treatment should be financed.

The ICER results of the FINOSE report was utilized for the negotiation. The procurement bodies also mentioned that the report worked well in order to help them define a common goal.

Even though the procurement bodies did not all have a lot of experience using FINOSE reports, the report worked well as a platform for the negotiations. Some country specific demands were encountered.

The procurement bodies have suggested that communication between the negotiators and the FINOSE team should be established before the assessment begins. However, confidentiality issues needs to be resolved. The procurement bodies are confident that this could be solved.

The procurement bodies encourage further joint negotiations in the future based on FINOSE reports on new expensive treatments. They suggest that the process of finding candidates for FINOSE reports could be influenced by the negotiation functions in the Nordic countries.

Companies

Summary of company feedbacks

According to one company the FINOSE project is a great example of the ongoing efforts towards improving the HTA processes. It gives the possibility for sharing of workload between countries, both for the company and the national HTA-agencies. This ultimately saves resources for both industry and FINOSE-partners and has the potential to provide valuable and cost-effective treatments to patients faster. Nevertheless, as pointed out by all the companies there is still potential for improvements.

Timelines:
For some companies it has been a bit unclear to how long the total timeline of the process would be (i.e. including the national report). Shorter assessment times than the national processes would incentivize more companies to take part in FINOSE. A common agreement on the timelines for the national report, and an update of the written information that further clarifies this would make the process more predictable for the companies and hence the FINOSE track more attractive.

The process:
One company commented that it was a bit unclear what information was shared between the FINOSE HTA-agency participants, and what was not shared. Country specific or country confidential information was not intended to be shared between the FINOSE HTA-agencies. The communication between the companies and the assessors should be continuous in the future, in order to be able to clarify information as needed.

Report content:
Severity is defined differently in the three countries and should be left to the national parts of the report, according to one company.

Although certain differences in the base case are expected and should be considered reasonable, e.g. based on national specific data (e.g. cost Inputs or patient numbers) or differences in guidelines (e.g. discount rate for cost and efficiency), most of the larger efficacy assumptions should be the same. This was not the case for one of the reports. One of the companies also mentioned that the report went further towards concluding on cost-effectiveness than was agreed upon in the pre-submission phase. One company suggested improving the template and making it clearer in what information is required.

Finalizing and publishing the report:
One FINOSE report was released in all countries before any of the countries had made a decision on reimbursement. The fact that the countries have different timelines for decision makes the content of the report all the more important. For one company the FINOSE report was released in Norway before the company could assess confidentiality. In addition, one agency commented on cost-effectiveness on their homepage even though cost-effectiveness was out of scope of FINOSE for one assessment. The company perceived this as unfortunate. One company also suggested that it would be appropriate to have the possibility to comment on the FINOSE report (i.e. similar to the Norwegian HTA-process, where the last two pages of the report is reserved for the company to comment on the assessment).

Findings, Conclusions and Recommendations

The FINOSE pilot has resulted in three joint assessments. One of the reports has been used in a joint price negotiation. Furthermore, it has been a great learning experience and based on the experiences from the pilot the Nordic agencies will focus on streamlining the processes and communication as we take FINOSE in to the future.

In this evaluation report, several challenges have been identified and possible solutions are suggested:

We have recently agreed on a **common FINOSE reporting template** and expect to implement a **common communication-platform** in the near future. This might resolve some of the former mentioned issues that we have faced during the pilot phase.

A **more thorough description of roles and timelines** should also be considered to make the process as seamless as possible. It is important that expectations and requirements are thoroughly discussed with the companies before submission of the data-package in order to avoid delays ("clock stop") in the assessment. Good dialogue between the company and the assessors and a common FINOSE template will help to achieve shorter assessment times.

The procurement bodies encourage further joint negotiations in the future based on FINOSE reports on new costly treatments. They suggest that the process of finding candidates for FINOSE reports could be influenced by the negotiation functions in the Nordic countries. Further **dialogue with the procurement bodies** on how to achieve this should be undertaken, as this will reduce the workload and increase efficiency in the production of HTA assessments.

Good dialogue with the companies prior to finalizing and publishing the report is essential to avoid misunderstandings. As the countries have different timelines for decision making, information on this process should be more openly shared with the companies in order for them to be prepared on what to expect.

The COVID-19 pandemic has triggered a lot of opportunities and learnings for collaboration between areas of expertise and organizations. For example, the National Institute of Health and Care Excellence (NICE) moved from an output focused HTA to a collaborative Rapid-C19 -process including five key stakeholders (payers, regulators, HTA, guideline, R&D) in the assessment of investigational drugs for COVID-19 (5). The key question is how the Nordic countries can better co-operate to efficiently form their strategies, procurement and decision making and what kind of role could FINOSE take in this co-operation.

The FINOSE project is an important effort towards improving and simplifying the HTA processes. It has given the Nordic HTA-agencies and companies the possibility for sharing of workload and thereby saving resources. The FINOSE process has the great potential to provide new and cost-effective treatments faster to patients. Also, importantly, new treatments have been assessed which otherwise would have been given low priority or where companies might not have sent applications to all Nordic Countries due to an excessive workload for small markets in terms of population.

After a 3 year pilot phase, the Nordic countries are now looking forward to work together for another 3 years through the FINOSE collaboration. By addressing the challenges and working on possible solutions, we expect to further improve the FINOSE collaboration and streamlining the processes in order to achieve faster patient access to innovative medicines.

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