Coverage With Evidence Development For Medicines with Insufficient Evidence Of Clinical Benefit: Experience From The Netherlands

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Background:

- EMA special pathways (conditional marketing authorization (CMA), authorization under Exceptional circumstances (AECs), orphan designation products (OMPs)) enable market access with incomplete evidence, creating HTA/reimbursement challenges
- Coverage with Evidence Development (CED) addresses uncertainties through temporary reimbursement plus parallel data collection
- Dutch Conditional Inclusion Program (2019): CED program for OMPs, CMAs, and AECs with evidence gaps

Study Aim:

Evaluate the Dutch CED program procedures, the included medicines, and identify successes and improvement areas

Methods:

This study is a narrative policy review of the Dutch CED program based on data collection, document analysis, and expert consultations. Firstly, a description of the CED program implemented by ZIN, as commissioned by the MOH, is displayed in two flowcharts: one on the CED program within the Dutch reimbursement system and the other on the process, including stakeholder involvement. Secondly, characteristics of currently included drugs in the CED program are described. Lastly, a comparison with other countries' reimbursement recommendations for the included medicines is included.

Results:

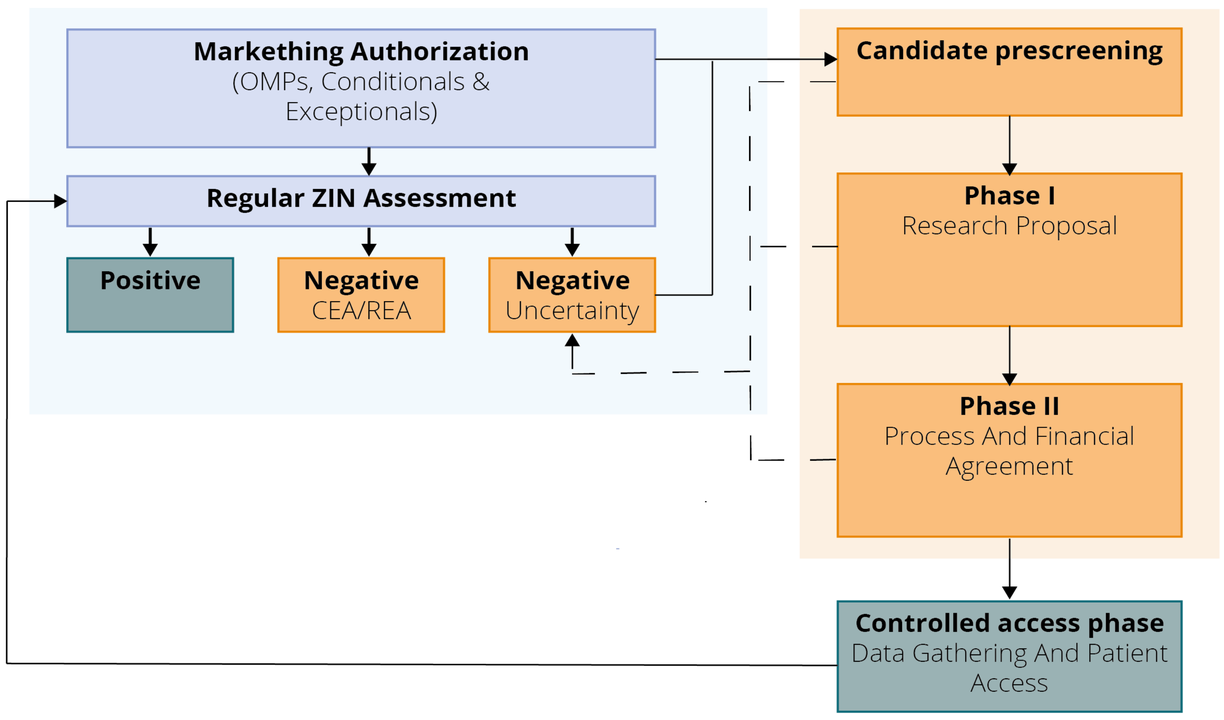

Figure 1: Schematic display of where the CED program fits in the regular ZIN assessment procedure. CEA, Cost-effectiveness analysis; OMPs, Orphan Medicinal Products; REA, Relative Effectiveness Assessment; ZIN, Dutch National Healthcare Institute.

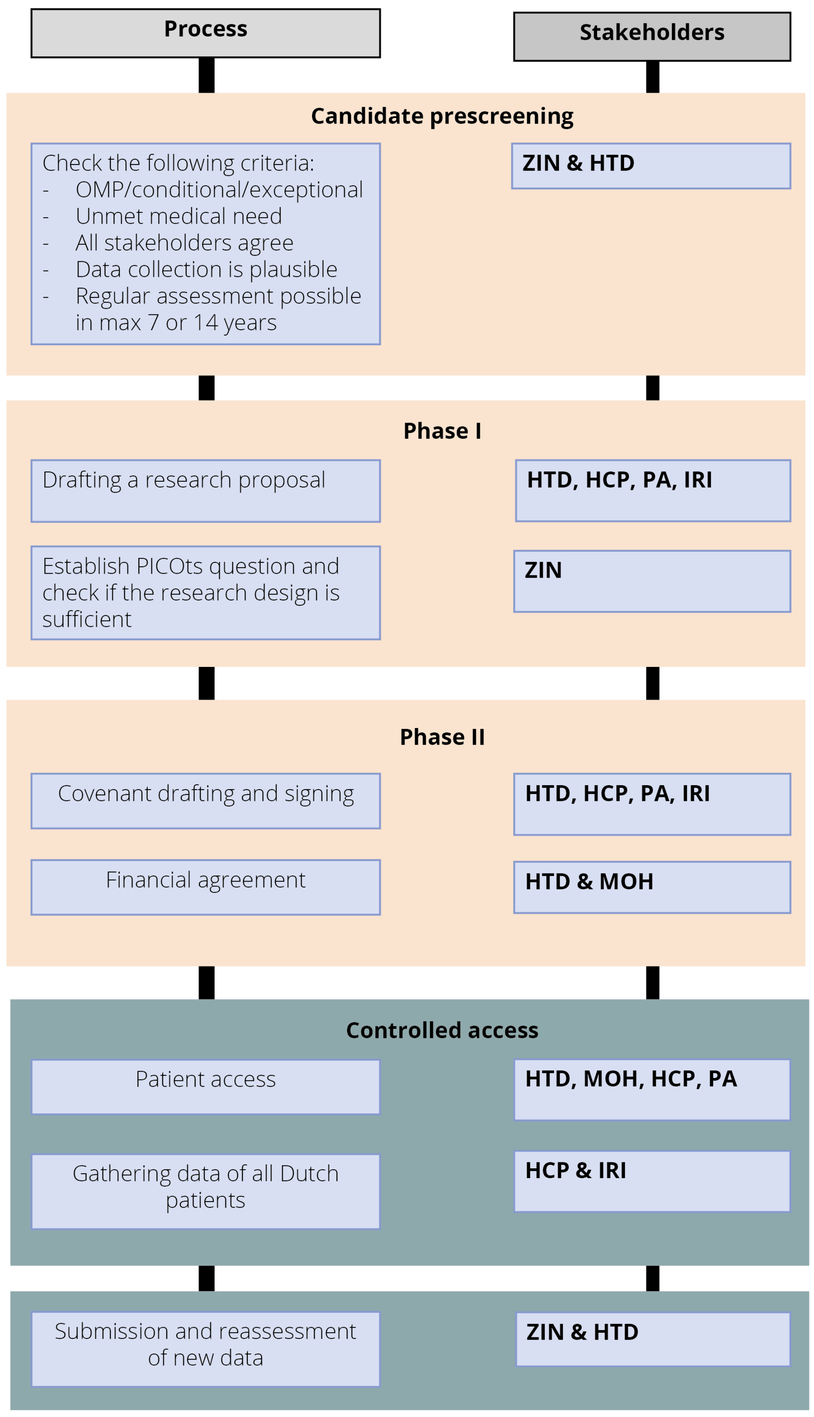

Figure 2: Detailed process description of the CED program with stakeholder involvement. Abbreviations: HCP, Association of Health Care Providers; HTD, Health Technology Developer; IRI, Independent Research Institute; MOH, Ministry of Health; OMP, Orphan Medicinal Product; PA, Patient Association; ZIN, Dutch National Healthcare Institute.

Table 1: high-level description of medicines previously, currently, or soon to be enrolled in the CED program.

Medicine name	entrectinib (Rozlytrek®)	larotrectinib (Vitrakvi®),	rhPTH 1-84 (Natpar®)	ataluren (Translarna®)	teduglutide (Revestive®)	CD34 (Libmeldy®)
Current status	Normally reimbursed after CED program completion	Normally reimbursed after CED program completion	Coverage terminated – production issues	Coverage terminated – EMA authorization revoked	Currently covered in the CED program	Candidate for the CED program
Evidence gap	The current assessment framework is not ready for tumor-agnostic products	The current assessment framework is not ready for tumor-agnostic products	The studied population did not match the population in the Dutch package question.	Effectiveness for so-called mid-range patients.	If there is an effect on quality of life in a specific sub-population of the indication	For the subgroup of early symptomatic patients, ZIN requests more data on efficacy as the pivotal study included too few patients
Evidence collection	Clinical trial + Additional data gathering in the Netherlands on efficacy, Drug Access Protocol	Clinical trial + Additional data gathering in the Netherlands on efficacy, Drug Access Protocol	A Dutch registry, the NatPar monitor	Clinical trial + Duchenne-Ataluren register in the Netherlands	A Dutch registry, the Revestive monitor NL	International multicenter MLD registry study
(envisioned) duration	1 year and 9 months	1 year and 9 months	3 years 2 months	2 years 11 months	5 years	TBD

Discussion & conclusion

- The Dutch CED program that started in 2019 gathers additional clinical data and facilitates access to OMPs, CMAs, and AECs that have insufficient evidence for regular reimbursement.
- Until now, six medicines with different types of evidence gaps have been included or are candidates in the program.
- Important facilitating factors of the current program are the involvement of all stakeholders, the "only-in-research" approach of data gathering, and the case-by-case evidence generation requirements and duration.
- However, the program does not yet include the expected number of medicines, and no conclusion can be drawn so far on the usefulness of the data collection, as there has not yet been a reassessment in the regular CED program until today. Continuous evaluation is needed to generate insights about the value of this program.

Want to know more?

Check out the website of the Dutch National Healthcare Institute through the QR below!

Get in touch by emailing me at j.Versteeg@uu.nl or by messaging me on LinkedIn through the QR below!