EUnetHTA 21

Consolidated PICO

PICO EXERCISE III - POMBILITI

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DOCUMENT HISTORY AND CONTRIBUTORS

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The work in EUnetHTA 21 is a collaborative effort. While the agencies in the Hands-on Group actively wrote the deliverable, the entire EUnetHTA 21 consortium was involved in its production throughout various stages. This means that the Committee for Scientific Consistency and Quality (CSCQ) reviewed and discussed several drafts of the deliverable prior to validation. Afterwards the Consortium Executive Board (CEB) endorsed the final deliverable prior to publication.

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LIST OF ABBREVIATIONS

CEB	Consortium Executive Board
CSCQ	Committee for Scientific Consistency and Quality
EUnetHTA	European Network of Health Technology Assessment
GL	Guideline
HOG	Hands-on Group
HTA	Health Technology Assessment
HTAb	Health Technology Assessment Body
JCA	Joint Clinical Assessment
JSC	Joint Scientific Consultation
MD	Medical Devices
MP	Medicinal Products
PICO	Population, Intervention, Comparators and Outcomes
SOP	Standard Operating Procedure

1 INTRODUCTION

On 17 September 2021, the European Health and Digital Executive Agency (HaDEA) signed the Service Contract for the Provision of Joint Health Technology Assessment (HTA) Work Supporting the Continuation of EU Cooperation on HTA. The contract will run for 24 months, and until 16 September 2023. EUnetHTA 21 work will build on the achievements and lessons learned from the EUnetHTA Joint Actions and focus on supporting a future EU HTA system under the HTA Regulation. For all EUnetHTA 21 deliverables the future EU HTA Regulation will serve as a basis.

As part of this work the consortium have taken part in project work on developing PICO questions, based on methods developed during the service contract.

2 METHODOLOGICAL APPROACH

> "*The starting point for every assessment of a health technology is the scoping phase. During the scoping phase, an important goal is the definition of a concise research question that should be answered by the assessment. The PICO framework provides a standard format for the definition of a research question. Within the PICO framework, research questions are defined using (at minimum) the following components: Population (P), Intervention (I), Comparators (C) and Outcomes (O). Countries may differ in the exact PICO question they need to be answered. Therefore, during the scoping phase of EUnetHTA 21 agreement on the PICO questions should be reached.*"[1]

Despite multiple acquisition efforts by EUnetHTA 21, no medicinal product was submitted for the Joint Clinical Assessment work under EUnetHTA 21 contract. Regardless, EUnetHTA 21 has as one of its objectives to test the guidelines developed. To allow testing of procedures and gaining experience on JCA for medicinal products, EUnetHTA has conducted three PICO exercises. These exercises were very important as the D4.2 scoping guideline was one of the guidelines which would require the most capacity building. Furthermore, after these exercises, the D4.2 scoping guideline went under revision to implement the relevant learnings.

The PICO exercises were conducted on medicinal products which already obtained a positive CHMP opinion. Therefore, no confidential data was used for the PICO exercise.

The production with the focus on the scoping phase, i.e. to perform three JCA without a HTD submission. A JCA without submission is still allowed to apply lessons learned within the development of the templates and methodological deliverables developed under the EUnetHTA 21 service contract. Within the given timeframe, three scoping procedures without submission were conducted.

This document describes a test run for the definition of PICOs for an assessment of a medicinal product. This exercise aimed at testing and improving the process developed within EUnetHTA21. As such, it has no relevance and no consequences for national assessments of medicinal products.

Furthermore, heterogeneity in terms of wording and presentation between the 3 exercises was expected.

The below section provides a brief summary of the conducted scoping procedures.

3 PICO 3 - POMBILITI (CIPAGLUCOSIDASE ALFA)

Name of Product Pombiliti (cipaglucosidase alfa)
Company: Amicus Therapeutics Europe Limited
Date of CHMP & MA: 15.12.2022 more information here.

[1] EUnetHTA 21 D4.2 Deliverable https://www.eunethta.eu/d4-2/

Indication: Pombiliti (cipaglucosidase alfa) is a long-term enzyme replacement therapy used in combination with the enzyme stabiliser miglustat for the treatment of adults with late-onset Pompe disease (acid α-glucosidase [GAA] deficiency).
Date of PICO survey: 24.03.2023 to 07.04.2023 **Date of CSCQ validation:** 11.07.2023
Number of MS participated: 10
Number of associated HTAb participated: 4
Consolidated PICOs: 9

4 CONSOLIDATED PICOS

Below you can find the nine consolidated PICOs, which were validated by the EUnetHTA 21 CSCQ.

Two formats of PICO tables were presented. Both formats contain the same information but they are presented in a different manner. When presented to CSCQ members, consensus was not reached regarding the preferred method of presentation. Thus, both are presented here.

Table 1 - Parameters for the assessment scope of Pombiliti

	PICO A	PICO B	PICO C
Population	Full Population: Adult patients with late onset Pompe disease	Subpopulation: Adult patients with late onset Pompe disease, who are ERT-naive	Subpopulation: Adult patients with late onset Pompe disease, who are ERT-experienced
Intervention	Cipaglucosidase alfa in combination with miglustat		
Comparator	Alglucosidase alfa AND Avalglucosidase alfa AND BSC AND Physicians choice for control arm, with at least: - Alglucosidase alfa - Avalglucosidase alfa	Alglucosidase alfa AND Avalglucosidase alfa AND BSC	Alglucosidase alfa AND Avalglucosidase alfa
Outcomes	See outcomes table		
Note	PICO A comprises 4 separate comparisons/ datasets to be submitted by HTD	PICO B comprises 3 separate comparisons/ datasets to be submitted by HTD	PICO C comprises 2 separate comparisons/ datasets to be submitted by HTD

Abbreviations: BSC: Best supportive care; ERT: Enzymatic replacement therapy; HTD: Health Technology Developer.

Table 2 - Parameters for the assessment scope of Pombiliti (1 PICO per comparator)

Description of PICO elements	P	I	C	O
PICO 1	Full Population: Adult patients with late onset Pompe disease	Cipaglucosidase alfa in combination with miglustat	Alglucosidase alfa	See outcomes table
PICO 2	as for PICO 1	as for PICO 1	Avalglucosidase alfa	
PICO 3	as for PICO 1	as for PICO 1	BSC	
PICO 4	as for PICO 1	as for PICO 1	Physicians choice for control arm, with at least: - Alglucosidase alfa - Avalglucosidase alfa	
PICO 5	Subpopulation: Adult patients with late onset Pompe disease, who are ERT-naive	as for PICO 1	Alglucosidase alfa	
PICO 6	as for PICO 5	as for PICO 1	Avalglucosidase alfa	
PICO 7	as for PICO 5	as for PICO 1	BSC	
PICO 8	Subpopulation: Adult patients with late onset Pompe disease, who are ERT-experienced	as for PICO 1	Alglucosidase alfa	
PICO 9	as for PICO 8	as for PICO 1	Avalglucosidase alfa	

Abbreviations: BSC: Best supportive care; ERT: Enzymatic replacement therapy.

Outcomes table

Overall survival
Ventilator-free survival
Changes in mobility (incl. measurement by 6MWT and documented use of wheelchair)
Changes in respiratory function (incl. measurement by FVC in sitting and upright positions)
Changes in muscle strength (by validated scales)
Changes in motor function (by validated scales, e.g. quick motor function test)
Respiratory symptomatology associated with Pompe disease
Gastrointestinal symptomatology associated with Pompe disease
Quality of life (as assessed using disease-specific (preferably) and/or generic questionnaires)
Health status (measured preferably by the EQ-5D)
Patient-reported outcomes to include R-PAct scale, and any other patient-centered outcome assessed by means of a patient-reported outcome measure
Adverse events (AEs) (incl. hypersensitivity, infusion reactions, immunogenicity)
Serious AEs (SAEs)
Severe AEs
Discontinuation and interruption of treatment due to AEs
Mortality due to AEs

Abbreviations: 6MWT: 6-minute walking test; AE: Adverse event; EQ-5D: EuroQoL five-dimension scale questionnaire; FVC: Forced vital capacity; R-PAct: Rasch-built Pompe-specific Activity.