

**Improved methods and actionable tools for enhancing HTA**

**Template for Outcomes-Based Managed Entry Agreement**

**of a Rare Disease Treatment**

**Draft for consultation by 1 February 2021**

**HTA BODY/HEALTHCARE PAYER NAME**

**OUTCOMES-BASED MANAGED ENTRY AGREEMENT**

**FOR <RARE DISEASE TREATMENT>**

**IN < REIMBURSED INDICATION>**

|  |  |
| --- | --- |
| Rare Disease Treatment | [Complete details]Brand name/Non-proprietary name |
| Indication | Reimbursed indication[[1]](#footnote-1) |
| Posology  | Dosing including method of administration |
| Signatories *[Alter as appropriate, delete this text]* |  |
| Healthcare Payer/Providers | Signature, name and role for each signatory |
| HTA body |
| Marketing Authorisation Holder |
| Registry Holder |
| Medical Association |
| Patient Organisations |
| Patient Groups |
| Date of Agreement[[2]](#footnote-2) | Date |
| Expected Duration of Agreement | X yearsStart date – End Date |
| Planned Re-Appraisal/Pricing and Reimbursement Renegotiation * Initiation of Process
* Publication of Decision
 | DateDate |

Further details from: staff lead email

Contents

[1. Purpose of this Agreement 3](#_Toc60741851)

[2. Basis for this Outcomes-Based Managed Entry Agreement 3](#_Toc60741852)

[2.1 Uncertainties to be Resolved in the OBMEA 3](#_Toc60741853)

[3. Patient Approval Process 4](#_Toc60741854)

[4. Patient Eligibility 5](#_Toc60741855)

[4.1 Inclusion criteria 5](#_Toc60741856)

[4.2 Exclusion criteria 5](#_Toc60741857)

[4.3 Continuation criteria 5](#_Toc60741858)

[5. Data Management 5](#_Toc60741859)

[6. Reviews 7](#_Toc60741860)

[7. Re-appraisal/Pricing and Reimbursement Renegotiation 7](#_Toc60741861)

[8. Responsibilities 8](#_Toc60741862)

**Acknowledgements**

This template has been developed as part of the EC Horizon 2020 funded project IMPACT HTA Work Package 10. It arises from mixed methods research with stakeholders about implementation of OBMEA for rare disease treatments and draws on OBMEA templates from

* Pharmaceutical Benefit Scheme, Australia
* National Institute of Health and Disability Insurance, Belgium
* National Institute for Health and Care Excellence, England
* Health Service Executive, Ireland.

# Purpose of this Agreement

After rigorous appraisal of all the available evidence for rare disease treatment (RDT) in indication to determine its added benefit/value for money, it has been agreed that an Outcomes-Based Managed Entry Agreement (OBMEA) should be undertaken. This decision has been made in accordance with the IMPACT HTA OBMEA checklist/is documented in Appraisal report XX.

The appraisal identified uncertainties in the clinical evidence (outcomes)/cost effectiveness modelling that seem feasible to resolve by additional data collection on all patients that will receive the RDT for the duration of the OBMEA.

This public document outlines the data collection plans for the OBMEA and the responsibilities of those involved. The aim is to enhance the quality and strength of evidence provided to decision-makers for future determinations of added benefit/value for money or to inform pricing and reimbursement re-negotiations.

A separate, confidential, pricing and reimbursement agreement outlines the conditions in place to ensure a fair price has been negotiated for the RDT, which is in accordance with national pricing policies.

# Basis for this Outcomes-Based Managed Entry Agreement

When substantial added clinical benefit is predicted in an appraisal but this effect is associated with major uncertainties, or when the most likely scenario analysis in an economic evaluation does not indicate value for money, standard processes may not recommend or fully reimburse an RDT. In this situation an OBMEA can be used if additional data can be collected within a specified timeframe to resolve the key uncertainties to better elucidate added benefit, optimize treatment use and demonstrate value for money.

In accordance with this premise and national legislation/policy XXX, this OBMEA has been developed for RDT in indication.

As the purpose of data collection in this OBMEA has the dual purposes of optimizing the treatment of individual patients and only their anonymized or pseudo-anonymized data will be used for health system purposes, this Agreement is covered by XXX legislation relating to consent and data sharing[[3]](#footnote-3).

## Uncertainties to be Resolved in the OBMEA

In the appraisal of RDT in indication, it was estimated that the prevalent population in the indication in country/region is PPP and the incident population is QQQ/year.

Key uncertainties to drive outcomes-based reimbursement/continuation of treatment for individual patients are

* X (e.g. successful infusion of treatment)
* Y (e.g. 6-month or 12-month survival)
* Z (e.g. early discontinuation due to Serious Adverse Event).

Key uncertainties in the aggregated clinical/economic evidence were identified as:

* A (e.g. number of eligible patients)
* B (e.g. disease progression confirmed at two consecutive timepoints)
* C (e.g. Patient reported outcomes)
* D (e.g. survival)
* E (e.g. time on treatment and maintenance of effect).

The number of patients expected to enter the OBMEA is XX[[4]](#footnote-4) with XXX included in the analysis, with median follow-up of YY. These data will be combined with data from other international sources to enable resubmission.

# Patient Approval Process

Before considering entry of a patient into the OBMEA, the treating clinician should discuss treatment options and the requirements of the OBMEA with the patient or their carer/informal care-giver to ensure shared decision-making. This may include discussion of elements such as the benefits and risks of the treatment, how their eligibility will be determined, the expectations of the patient in the OBMEA beyond usual clinical practice (e.g. treatment adherence for the duration of the Agreement, prohibited medications, travel to clinic for regular assessments, treatment continuation according to specific criteria, restrictions on entering other clinical studies). If there are many requirements in addition to usual clinical practice, patients or their carer/informal care-giver may be asked to sign a Patient Agreement[[5]](#footnote-5).

*[Describe the system by which patients are approved for entry – a few simple explanations are suggested.]*

Baseline patient data are entered into an electronic system that automatically checks patient eligibility according to the pre-specified criteria. Dispensing notification is sent to the relevant pharmacist.

Baseline patient data are entered by a physician and reviewed by the local prescribing committee or a national expert panel.

All patients who transfer from a clinical trial or expanded access programme or who have been paying for private treatment will be deemed eligible for treatment in the MAA and will be subject to the continuation criteria, but due to the lack of baseline data, they will be analysed separately.

# Patient Eligibility

## 4.1 Inclusion criteria

List clinical criteria for inclusion….

## 4.2 Exclusion criteria

List clinical criteria for exclusion….

If it is not possible to measure an outcome in a group of patients, such as patients in a specific state (walk test in non-ambulant patients) or with a co-morbidity (cognitive impairment), then a joint clinical decision will be made about an alternative measure for all such patients (e.g. via the Monitoring Committee, section 6).

If a patient or carer/informal care-giver feels the assessments to determine eligibility for the OBMEA have been performed incorrectly, the patient may have the assessments repeated at another treatment centre within the health system jurisdiction. Costs for the second assessment will be borne by the patient.

## 4.3 Continuation criteria

The need for continuing treatment will be assessed at <x-monthly> intervals.

List clinical criteria for continuation of treatment….

A patient may withdraw consent to treatment and data collection at any time without prejudice to other treatment choices, but this will stop their access to RDT. They may not be permitted to re-enter the OBMEA.

# Data Management

Data will be collected on all patients in the OBMEA until the end of the Agreement (this includes data collection after treatment discontinuation) or when patient consent is withdrawn. Baseline data will be collected on all patients who are deemed ineligible for the OBMEA.

A plan outlining the required assessments and their frequency of measurement has been agreed among stakeholders, which seeks to avoid administrative burden on clinics but should also be sufficient to resolve the stated uncertainties. This includes patient identification, treatment information, demographics, eligibility criteria, key efficacy and safety outcomes and resource utilisation.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Data Itemx | Baseline | Follow-up 1 | Follow-up 2 | End of Treatment (EoT) | EoT +1 | EoT +2 |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |

xWith abbreviation to note data source in following table

Data to be used in the OBMEA will come from the following sources.

|  |  |
| --- | --- |
| **Data Source** | **Data Owner** |
| Bespoke national (treatment) registry | Health Provider/ Expert Centre |
| National or international disease registry | Registry Holder[[6]](#footnote-6) |
| Health system (prescribing, mortality, administrative, laboratory test, resource utilisation etc) | Health Provider/Payer |
| Clinic specific data, e.g. collected via eCase Report Form | Clinician/Expert Centre |
| Patient reported outcomes | Patient |
| Patients receiving treatment outside the OBMEA | MAH/Expert Centre/Clinician |

If data entry is not a pre-requisite for dispensing, treating clinicians will be required to enter all data within one month of treatment commencement and each clinic visit.

When data collection is substantially different from routine practice, training will be provided. This should occur before a centre starts entering patients into the Agreement, and after a few patients, to resolve queries.

Data will be subject to systematized verification and quality checks to improve accuracy and completeness. Given the real-world nature of clinic visits, data rules will need to be applied to the data (e.g. windows around treatment visits).

All data will be collected in accordance with EU General Data Protection Regulation/National Data Protection Legislation. Only treating clinicians will have access to de-anonymized data of their own patients for the purposes of optimizing individual patient care. For all other purposes data will be (pseudo)anonymized using national procedures to ensure good data governance. Data will be securely stored via…

Data collected from sources not owned by the health system will be transferred in anonymized form to <existing data source>/will be stored for no more than five years following the end date of this OBMEA, or no more than 10 years after initiation, whichever is shorter.

The MAH/Payer/Expert Centre will be responsible for the analysis of data from all sources. XXX procedures ensure safe data access and sharing.

Publication of any data collected in this Agreement is not permitted by any party until after the OBMEA is complete.

# Reviews

A multi-stakeholder Monitoring Committee[[7]](#footnote-7) will be established to review progress and recommend actions to support successful conduct and completion of the OBMEA.

The MAH will provide information about any major alterations to the SmPC that may impact treatment[[8]](#footnote-8).

The MAH/Payer/Expert Centre will provide six-monthly/annual reports summarizing the number of patients treated under this Agreement in each participating clinic. Information about data quality and quantity will be scrutinized according to the planned patient entry numbers. Clinical monitoring activities will be undertaken to improve recruitment and data collection in individual centres.

Issues arising in several centres in relation to patient treatment or data collection will be discussed and addressed in a Frequently Asked Questions document to all centres ([see example from the MPS Society](https://d422994b-53f1-40f8-a3df-62dbcbf28377.filesusr.com/ugd/8acb9b_c238f04593f547e585a1fcaca3f56658.pdf)). This will be a living document throughout the lifetime of this Agreement.

A review may trigger revision of the end date – to lengthen due to limited data, or to expedite given concerns.

Approximately halfway through the Agreement, a Statistical Analysis Plan will be created and agreed by the Monitoring Committee.

# Re-appraisal/Pricing and Reimbursement Renegotiation

Nine months before the planned date of review, the MAH will submit evidence for re-appraisal/pricing re-negotiations, presenting analyses based on data from this Agreement and other international sources, to address the uncertainties outlined in the appraisal. Evidence will be submitted on HTA/Payer submissions forms. This should include new epidemiologic studies (such as natural history), new trials, long-term follow-up information (including the latest EMA Periodic Safety Update Report), analyses relating to the clinical uncertainties, a revised economic model (showing how assumptions have been changed in light of new evidence).

Signatories to this Agreement will be given the opportunity to contribute to the review process. Patient groups and clinicians should be involved as outlined in IMPACT HTA guidance[[9]](#footnote-9) or according to HTA body/PAYER stakeholder involvement processes.

Outcomes from the review may be to:

* Extend the OBMEA without changes, defining a new review date
* Extend the OBEMA with changes and a new review date
* Terminate the OBMEA and put the medicine on the general reimbursement list
* Terminate the OBEMA and withdraw the medicine from use.

# Responsibilities

This Agreement has been entered into with the approval of the “signatories”, for action by them and *[list any stakeholders who are not signatories but who will be expected to act in accordance with this agreement]* clinicians, prescribers and patients*.*

Signatories to the agreement are given the right to contribute to the review of the agreement.

The Payer agrees to pay the agreed price for appropriate use of the RDT (eligible patients, in accordance with continuation criteria) and in accordance with any individual patient outcomes-based agreement (e.g. based on early response or refund due to lack of response).

The MAH/Payer/Expert Centre is responsible for the cost of collecting, cleaning and analysing the data.

The MAH must commit to the planned pricing and reimbursement/appraisal review(s), bearing any costs and in accordance with processes at the time of the review (which may be different from the initial appraisal).

Clinicians are responsible for entering the necessary data on their patients within 4 weeks and responding to data queries within 2 weeks.

Any party wishing to publish data from the OBMEA (after completion) must obtain approval of the data owner and for this case of rare diseases take particular care that no patient can be re-identified. All publications should acknowledge the OBMEA signatories and share a final copy with them.

If the MAH does not respect this Agreement, the Payer is entitled to revise it in consultation with the other signatories.

1. Throughout this document “indication” refers to reimbursed indication which will be the licensed indication or subset as stated in the appraisal or pricing and reimbursement agreement, with specification of any restrictions. [↑](#footnote-ref-1)
2. *If possible, this Agreement should be published at the same time as the final appraisal report/reimbursement decision, without causing any delay to the usual appraisal process.* [↑](#footnote-ref-2)
3. *Most health systems have exemptions for secondary use of patient data to improve individual patient care, but if a formal clinical trial is established, ethical approval will be required.* [↑](#footnote-ref-3)
4. Include a sample size determination if possible [↑](#footnote-ref-4)
5. See NICE Example, page 16 onwards <https://www.nice.org.uk/guidance/hst12/resources/managed-access-agreement-pdf-6968825245> [↑](#footnote-ref-5)
6. E.g. European Reference Network, Specialist Society [↑](#footnote-ref-6)
7. Add link to Monitoring Committee ToR [↑](#footnote-ref-7)
8. E.g. eligibility criteria, safety issues to be considered at discontinuation [↑](#footnote-ref-8)
9. *Link to patient group submission template to be added after consultation* [↑](#footnote-ref-9)