A value-based negotiation framework for improved managed entry agreement negotiations and faster access to innovative therapies

ISPOR Europe 2022

Alnylam® PHARMACEUTICALS

Workshop objectives

To *apply* a previously introduced *conceptual* value-based negotiation framework for managed entry agreements via a simplified mini-negotiation

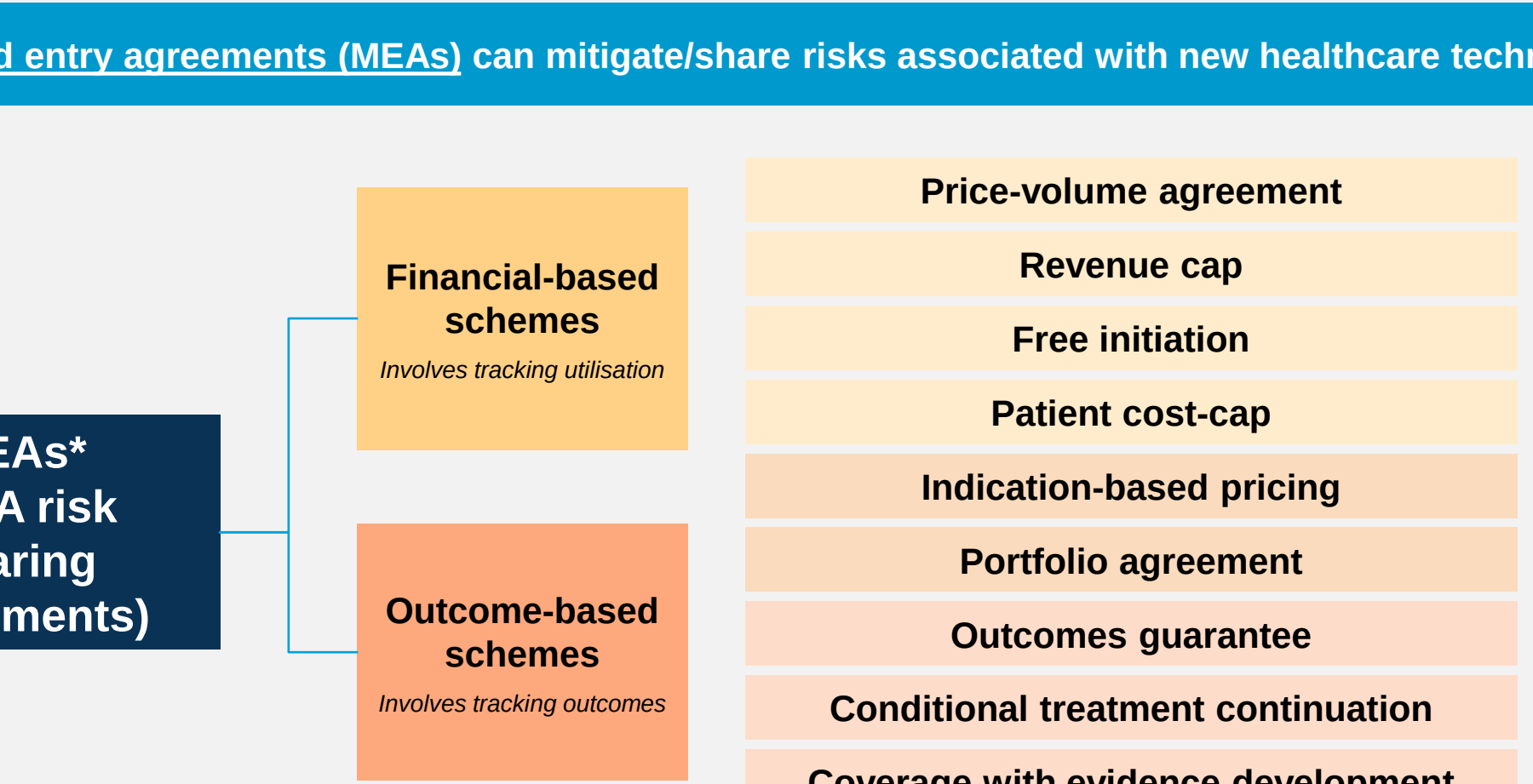
To discuss the experience and potential usefulness of the framework

Agenda

Topic	Presenter	Allocated time
Introduction: value-based negotiation framework (VBNF)	Amanda Whittal	10 min
Case introduction: fictitious disease and product	Amanda Whittal	10 min
Selecting managed entry agreements using the VBNF digital tool	Moderators and audience	30 min
Discussion	Claudio Jommi	10 min

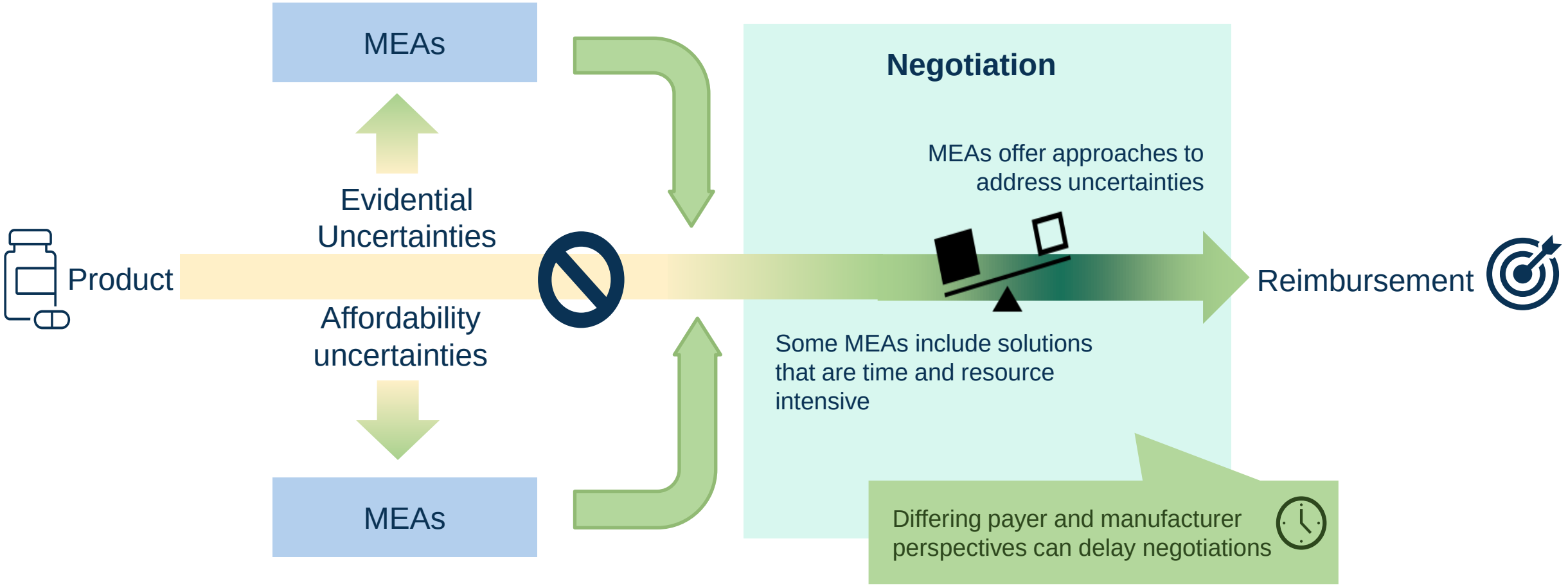
With more innovative therapies coming to the market…

Managed entry agreements (MEAs) can mitigate/share risks associated with new healthcare technologies



*non exhaustive list. Sources: Sear & Hutchings 2016. Abbreviations: **MEA**, managed entry agreement

MEAs can manage concerns associated with innovative therapies



BUT motivations for MEA negotiations differ

MANUFACTURERS

Maximize **reward for innovation**

Sustain a healthy business model to **ensure continued innovation**

Early access and **value** for patients

Earn **revenue** early in the product's life cycle

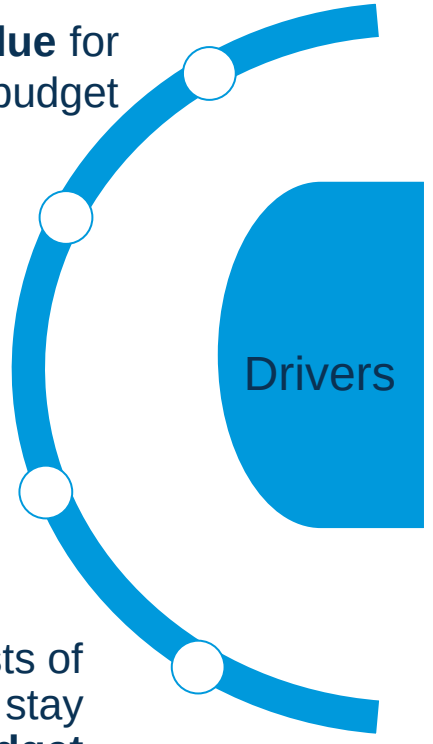
PAYERS

Maximize **value** for patients/money within budget

Support innovation that brings clinically meaningful products

Early access and **value** for patients

Reduce costs of treatment and stay within **budget**



Abbreviations: **MEA**, managed entry agreement

We propose a framework to better structure negotiations of MEA contract terms for innovative therapies

Goals of the framework

- ✓ Help identify cases when MEAs are appropriate to use

- ✓ Support identification of priority P&R risks & contract terms to address these risks

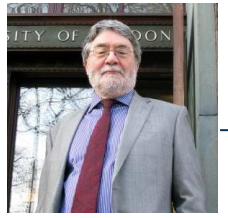
- ✓ Accelerate negotiations by offering a structured approach & a common language

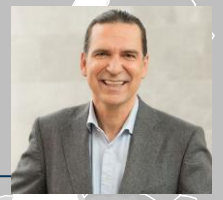
- ✓ Structured to be adaptable to different country systems

Not in scope

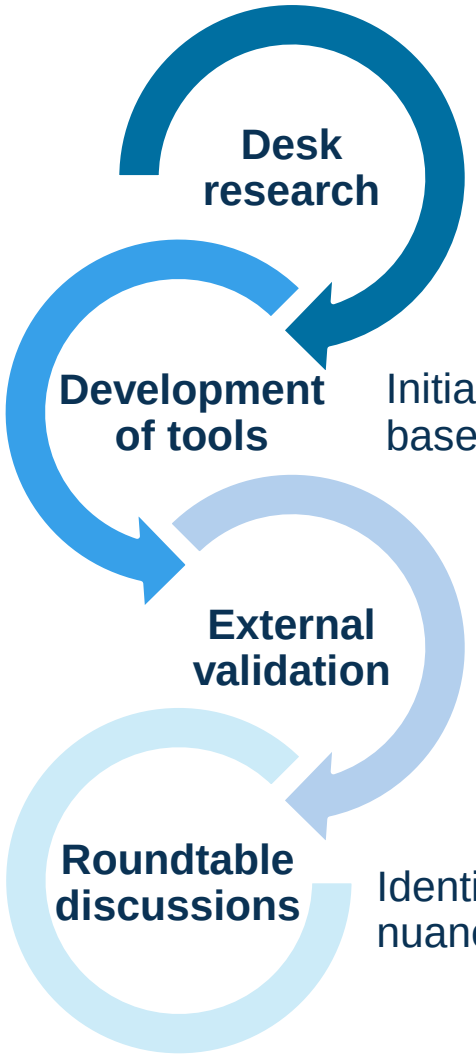
- × Not designed to suggest (more) complex MEAs
- × Does not assess the value or value for money of a product
- × Does not explain the cost of a product

The framework has been developed with European experts





Methodology



Scientific/grey literature

Initial framework and application tools based on literature and experience

Adaptation based on expert review and input

Identifying relevant country-specific nuances in local contexts

Deliverables

- Conceptual framework
- Corresponding application tools
- Article published in IJTAHC
- Practical application, collection and integration of country-specific input

Value-based negotiation framework

Assess
Product and disease profile

Prioritise
Risk and their impact

Identify
What combination of terms works?

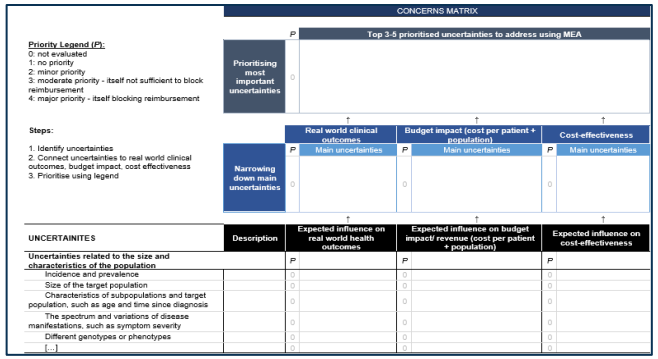
Decide
Most effective, least complex combination of agreement terms

Disease and product profile template

Objective: To present the incremental clinical benefit, incremental budget impact, level of evidence and level of innovation

Matrix 1	Core area	Topic	Sub topic	Rationale for consideration / objective
Disease background		Epidemiology	Prevalence	Impact on size of target patient population
			Incidence	Impact on cost profile over time
		Patient population characterization	Age of onset	
			Existence of patient subpopulations	Impact on willingness to pay
			Other patient characteristics (e.g. gender, ethnicity, risk factors, genetic mutation)	Impact on clinical uncertainties for specific subgroups
		Disease manifestation	Disease progression (e.g. acute vs. chronic, attacks)	
			Impact on mortality and life expectancy / prognosis	Characterise the disease profile, which sets up for the treatment goals
			Impact on morbidity	Identify the urgency to treat
			Impact on quality of life	
			Extent of variability in disease presentation and severity	
		Economic burden of disease	Economic and societal impact (e.g. missed school days, productivity)	Present a holistic view of the disease impact; this influences the perception of burden of disease sets up for discussion of spillover effects
		Diagnostic pathway	Time to diagnosis	
			Diagnosis method (e.g. biomarker test, clinical differential, diagnosis of exclusion)	Impact on start/stop rules, reimbursement criteria (e.g. restriction to sub-populations), budget impact
			Diagnosis rate	
			Other elements	
		Patient care pathway	Availability of clinical guidelines	
			Patient experience	Quality how the patient care experience is structured in the health system; this helps identify potential changes to the health system brought about by the novel treatment
			Treatment capacity in the healthcare system	
			Treatment location (e.g. centre of excellence)	
		Standard of care	Existence of (a) therapeutic option(s) (approved or off-label)	
			Efficacy of SoC	
			Safety of SoC	Quantify the extent of unmet medical need
			Cost of SoC	
			Date of introduction of SoC	
			Shortcomings of SoC	
Product profile description		Technology presentation	Treatment goal (e.g., curative, disease modifying, symptom management, slow progression, attack prevention)	
			Mechanism of action	Impact on perception of innovativeness
			Mode of administration	Impact on complexity of administration
			Posology (per label)	Impact on cost structure and variability in costs
			Duration of treatment (per label)	
		Regulatory background	Regulatory designations (orphan, PRIME)	
			Type of approval (e.g. conditional, under exceptional circumstances)	Impact on the perception of innovativeness and level of uncertainty
			Current and anticipated additional indications	Impact on size of the patient population (current population, extent of future

Uncertainties matrix



CONCERNS MATRIX

Priority Legend (P):
0: not evaluated
1: no priority
2: minor priority
3: moderate priority - itself not sufficient to block reimbursement
4: major priority - itself blocking reimbursement

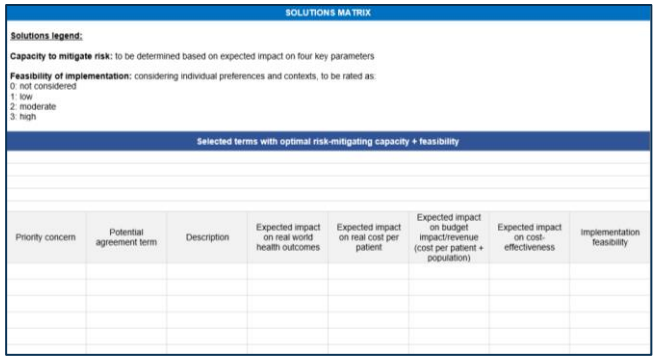
Steps:
1. Identify uncertainties
2. Connect uncertainties to real world clinical outcomes, budget impact, cost effectiveness
3. Prioritise using legend

	P	Top 3-5 prioritised uncertainties to address using MEA
Prioritising most important uncertainties	0	

	Real world clinical outcomes		Budget impact (cost per patient + population)		Cost-effectiveness	
	P	Main uncertainties	P	Main uncertainties	P	Main uncertainties
Narrowing down main uncertainties	0		0		0	

UNCERTAINITES	Description	Expected influence on real world health outcomes		Expected influence on budget impact/ revenue (cost per patient + population)		Expected influence on cost-effectiveness	
Uncertainties related to the size and characteristics of the population		P		P		P	
Incidence and prevalence		0		0		0	
Size of the target population		0		0		0	
Characteristics of subpopulations and target population, such as age and time since diagnosis		0		0		0	
The spectrum and variations of disease manifestations, such as symptom severity		0		0		0	
Different genotypes or phenotypes		0		0		0	
[...]		0		0		0	

Solutions matrix



SOLUTIONS MATRIX

Solutions legend:

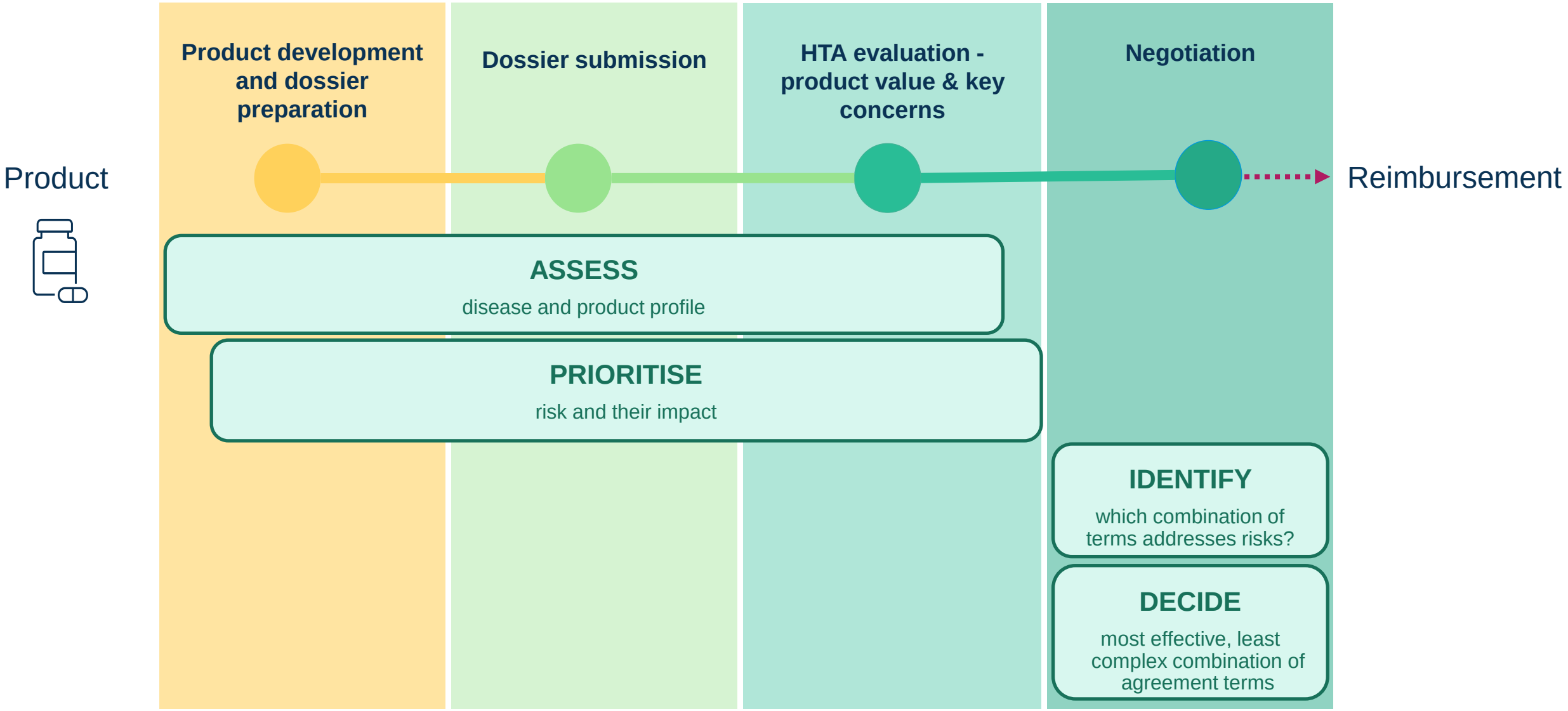
Capacity to mitigate risk: to be determined based on expected impact on four key parameters

Feasibility of implementation: considering individual preferences and contexts, to be rated as:
0: not considered
1: low
2: moderate
3: high

Selected terms with optimal risk-mitigating capacity + feasibility

Priority concern	Potential agreement term	Description	Expected impact on real world health outcomes	Expected impact on real cost per patient	Expected impact on budget impact/revenue (cost per patient + population)	Expected impact on cost-effectiveness	Implementation feasibility

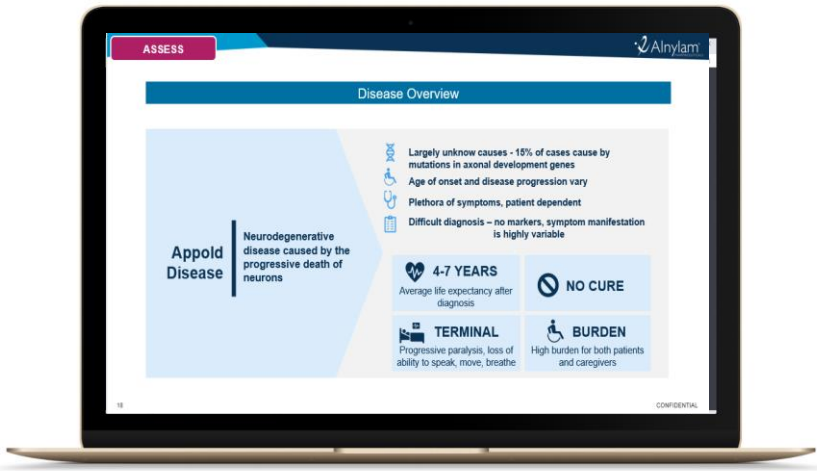
Contextualising the framework



Abbreviations: **HTA**, health technology assessment

Simplified case example

You will be asked to apply the framework approach for a new innovative drug:
Tamiolas for Appold Disease (ApD)



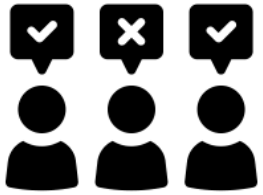
STEP 1
Uncertainty identification

STEP 2
Top uncertainty

STEP 3
Identification of agreement terms

STEP 4
Negotiation

Breakouts and digital tool



DISCLAIMER

Disease, drug and related information in this exercise are fictious

The exercise is **illustrative** only

The exercise is an **over-simplification** of a real-world scenario

For the exercise, please try to think not in a local context, but more abstractly

Disease Overview

Appold Disease

Neurodegenerative disease caused by the progressive death of neurons

- **Causes largely unknown - 30% of cases cause by mutations in axonal development genes**
- **Age of onset and disease progression vary**
- **Plethora of symptoms, patient dependent**
- **Difficult diagnosis – no markers, symptom manifestation is highly variable**

4-7 YEARS
Average life expectancy after diagnosis

NO CURE

TERMINAL
Progressive paralysis, loss of ability to speak, move, breathe

BURDEN
High burden for both patients and caregivers

Hypothetical case – designed to illustrate and discuss the framework

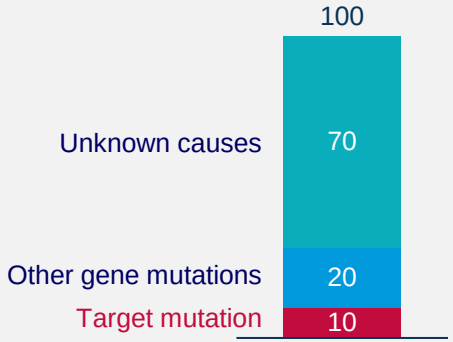
Product profile | Mode of Action | Posology and administration | Clinical trial results

Mode of Action

Prevents further axons disruption, stopping disease progression

Eligible population

10% of patients with ApD carry the mutation targeted by Tamiolas



Administration

Treatment is administered in a specialized center

One day prior to infusion, hospital administered pre-treatment

Treatment administered as intravenous infusion over 3 hours

The product is **immediately available** in specialized centres for patients with confirmed target mutation

Dosage and Frequency

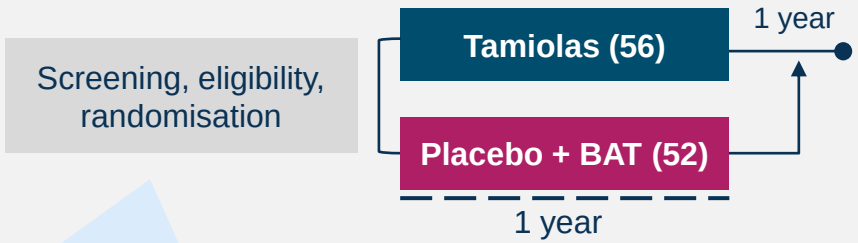
One-off treatment
1 vial / 75 kg

Tamiolas is a one-time treatment, but potential need for retreatment unknown

Hypothetical case – designed to illustrate and discuss the framework

Clinical Trial Design

Phase III multicenter double-blind RCT (n=108)



Adults with early-stage ApD with **confirmed target mutation by genetic test**

Endpoints (ApD validated)

PRIMARY

- ApD Functional Rating Scale

SECONDARY

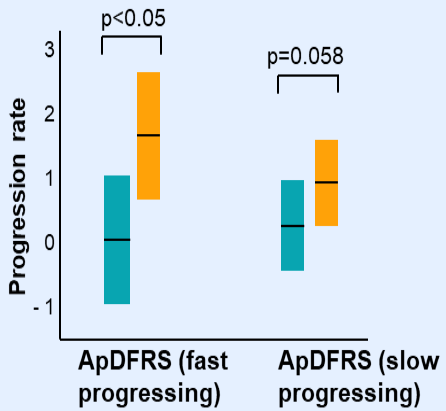
- Muscle strength
- Progression free (ventilation assistance-free) survival
- HRQoL assessment (EQ-5D: mobility, usual activities, pain and discomfort and anxiety and depression)

Abbreviations: **ApDFRS**: Appold disease Functional Rating Scale; **HRQoL**, health related quality of life; **OS**, overall survival; **p:** p-value

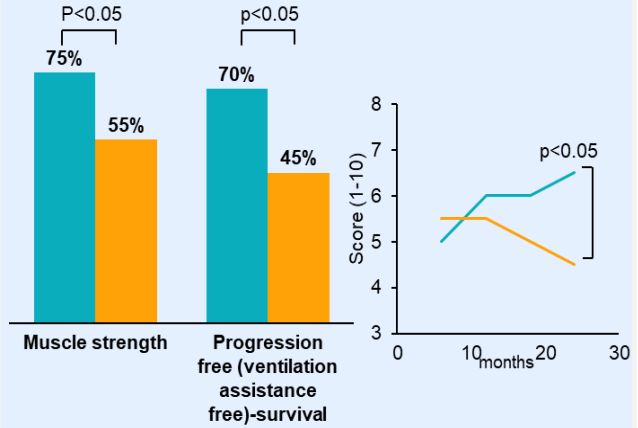
Clinical Trial Results (1 Year)

Trial was not long enough to conclude survival effect, but clinical experts anticipate the improvement in clinical markers will translate into clinically relevant survival improvement

Primary endpoints



Secondary endpoints



Safety

- **21%** of patients had **moderate** adverse events*
- **15%** of patients had **severe** adverse events*

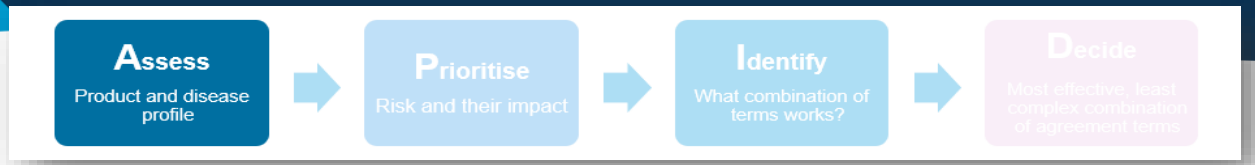
Adverse events resolved within 14 days with no lasting effects

*Related to the treatment

Hypothetical case – designed to illustrate and discuss the framework

Tamiolas price point and economic considerations

Price per patient	**1,500,000 €** per patient (weighted average)
Treatment posology	**One-off** treatment, weight based (1 vial / 75 kg)
Eligible prevalent population	Estimated prevalence: **0.3 in 100,000 people** – eligibility **to be confirmed** by **genetic testing**
Budget impact	Estimated at **60,000,000 € in the first year**
QALY gain	**5 incremental QALY from SoC** - QALY gain is based on early data and may change following results of additional utility study
Cost-Effectiveness	Healthcare utilisation is estimated between **50,000-150,000 €** per patient Cost-effectiveness **400,000 €/QALY**



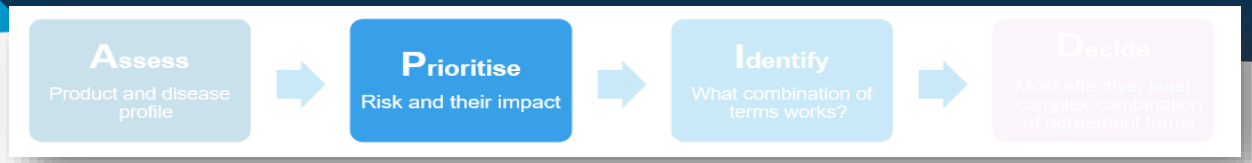
The ‘Assess’ step helps identify concerns

What are the affordability/evidential uncertainties concerns that → translate into P&R risks?

- Outcomes
- Cost per patient
- Budget/Revenue
- Cost-effectiveness

Abbreviations: **P&R**, pricing and reimbursment

PRIORITISE



Uncertainty	Expected influence on baseline			
	Real world health outcomes	Cost per patient	Budget/Revenue	Cost-Effectiveness
Size of eligible population	Unknown effect of the drug on patients with other mutations, **20% of total ApD population**		**Eligible population could be up to 50% larger** than current estimates - risk of under and misdiagnosis due to lack of clear diagnostic test	
Size of treatment effect	Large effect in fast-progressing patients, but **no significant improvement in slow progressing patients (50% of population)**			**Potential 40% ICER increase** in slow-progressing patients
Effect durability	Clinical trial limited to 1 year. 35-year time horizon predicted; **high uncertainty around longevity of the effects**		Potential indirect cost due to disease progression in the long-term – could result in **60% BI increase** if effect is not durable	Decreased QALY gains if effects are not durable, **potential 80% ICER increase**
Adverse events	Trial limited to 1 year. Similar therapy proven safe	**Potential 5% increase in cost related to adverse event management**	**Potential 15% BI increase due to unknown long-term effects**	

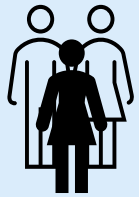
Summary from the *Assess* and *Prioritise* steps

Priority uncertainties

1 EFFECT DURABILITY

- Long-term data beyond clinical trial period is currently missing – no information on durability of response
- Concern is driven by lack of knowledge on long-term efficacy and treatment impact

2 SIZE OF ELIGIBLE POPULATION



- Confidence in exact number of eligible population is low
- Unknown effect of the drug on other mutations
- Genetic testing is needed to confirm patient eligibility

Potential MEA solutions

3) IDENTIFY

Which terms work best to address the top uncertainties?

Identify how the different MEA terms affect the impact of the uncertainty and their implementation feasibility

4) DECIDE

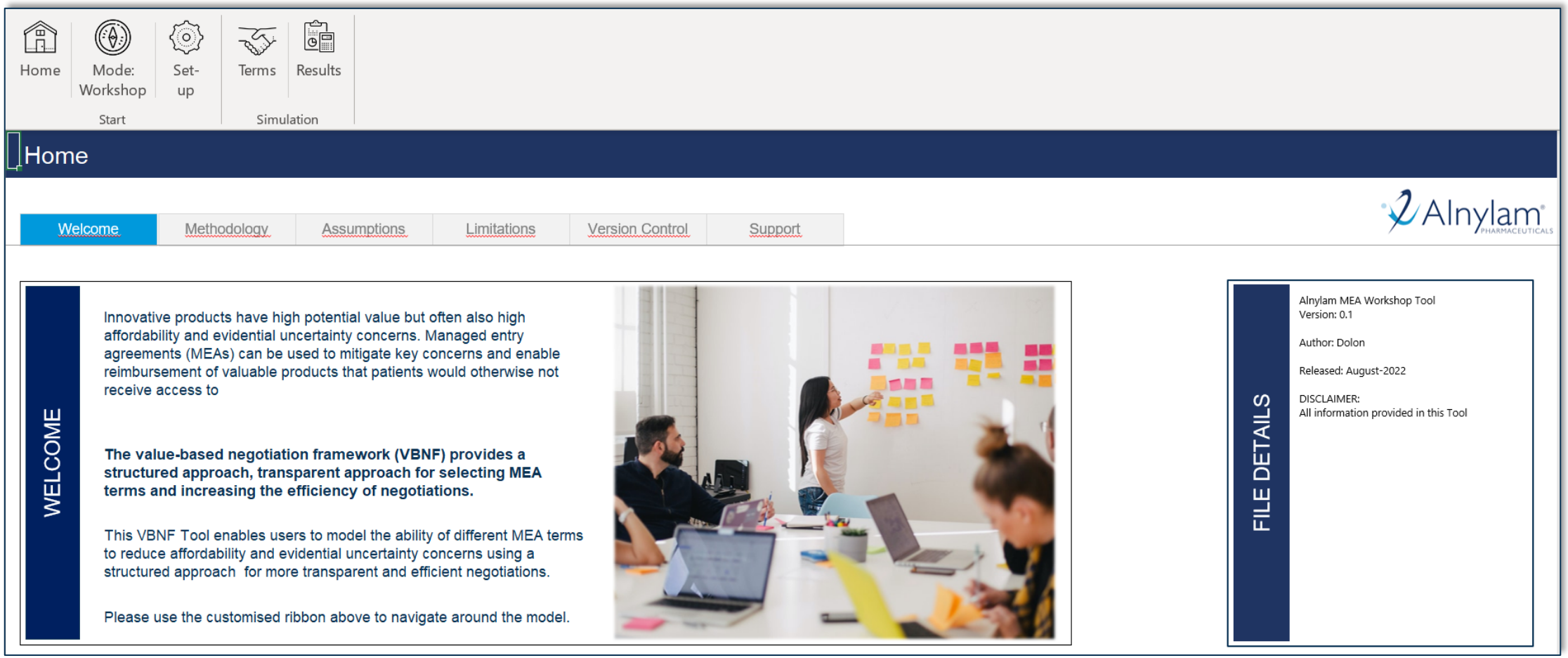
What is the most effective, least complex combination of agreements?

Identify the combination of MEA terms considering implementation feasibility and how it will affect the different parameters

Negotiation approach: commitment to achieving a transparent deal that considers the other side

You will be divided into groups of payers and manufacturers

With the help of your moderator, use the digital tool to suggest your ideal MEA for Tamiolas



Feedback and discussion

Experience?
Usefulness?
Possibilities for application in practice?