Getting relevant health economics data from the clinical development pre-marketing phase of MS products

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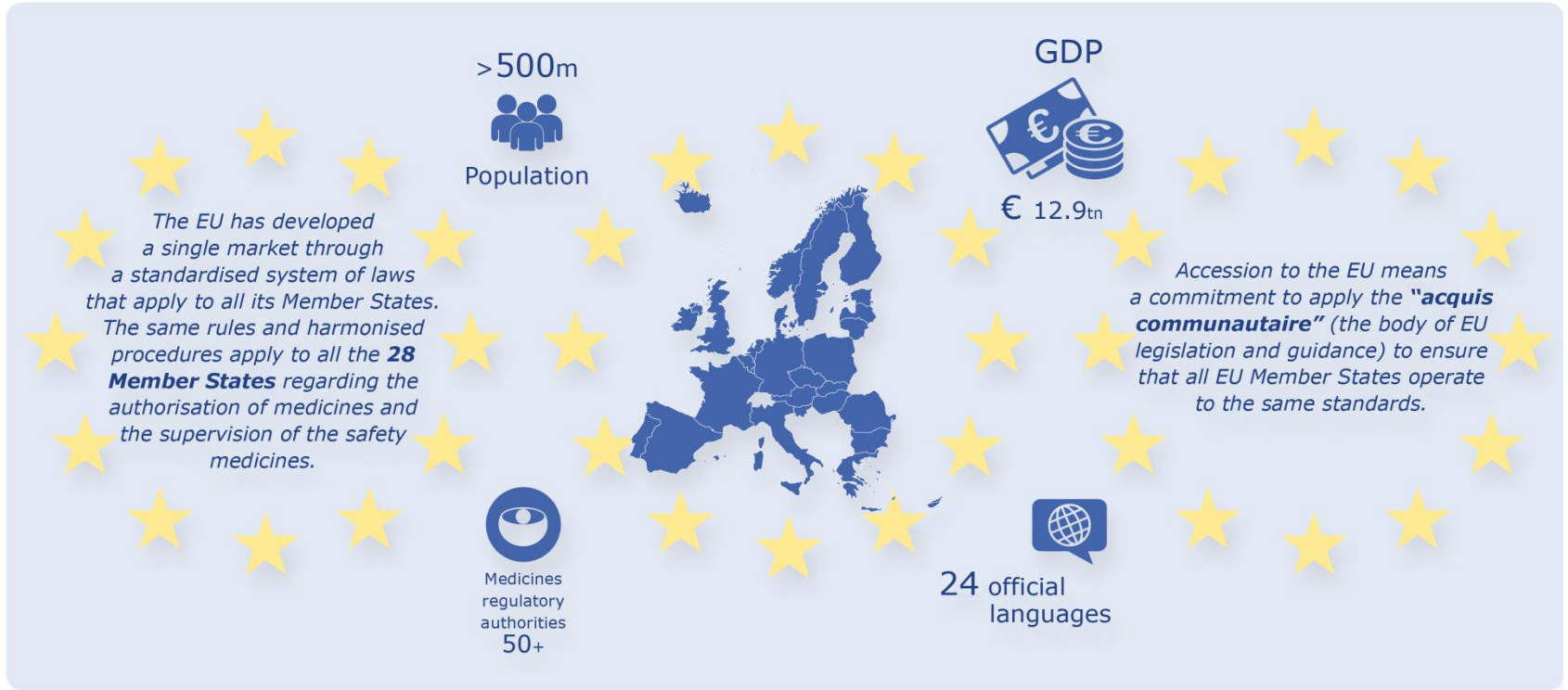
TIME MATTERS IN MS

Getting relevant health economics data from the pre-marketing clinical development of MS products

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EU Medicines Authorisation

>500m
Population

GDP
€ 12.9tn

The EU has developed a single market through a standardised system of laws that apply to all its Member States. The same rules and harmonised procedures apply to all the **28 Member States** regarding the authorisation of medicines and the supervision of the safety medicines.

Accession to the EU means a commitment to apply the **"acquis communautaire"** (the body of EU legislation and guidance) to ensure that all EU Member States operate to the same standards.
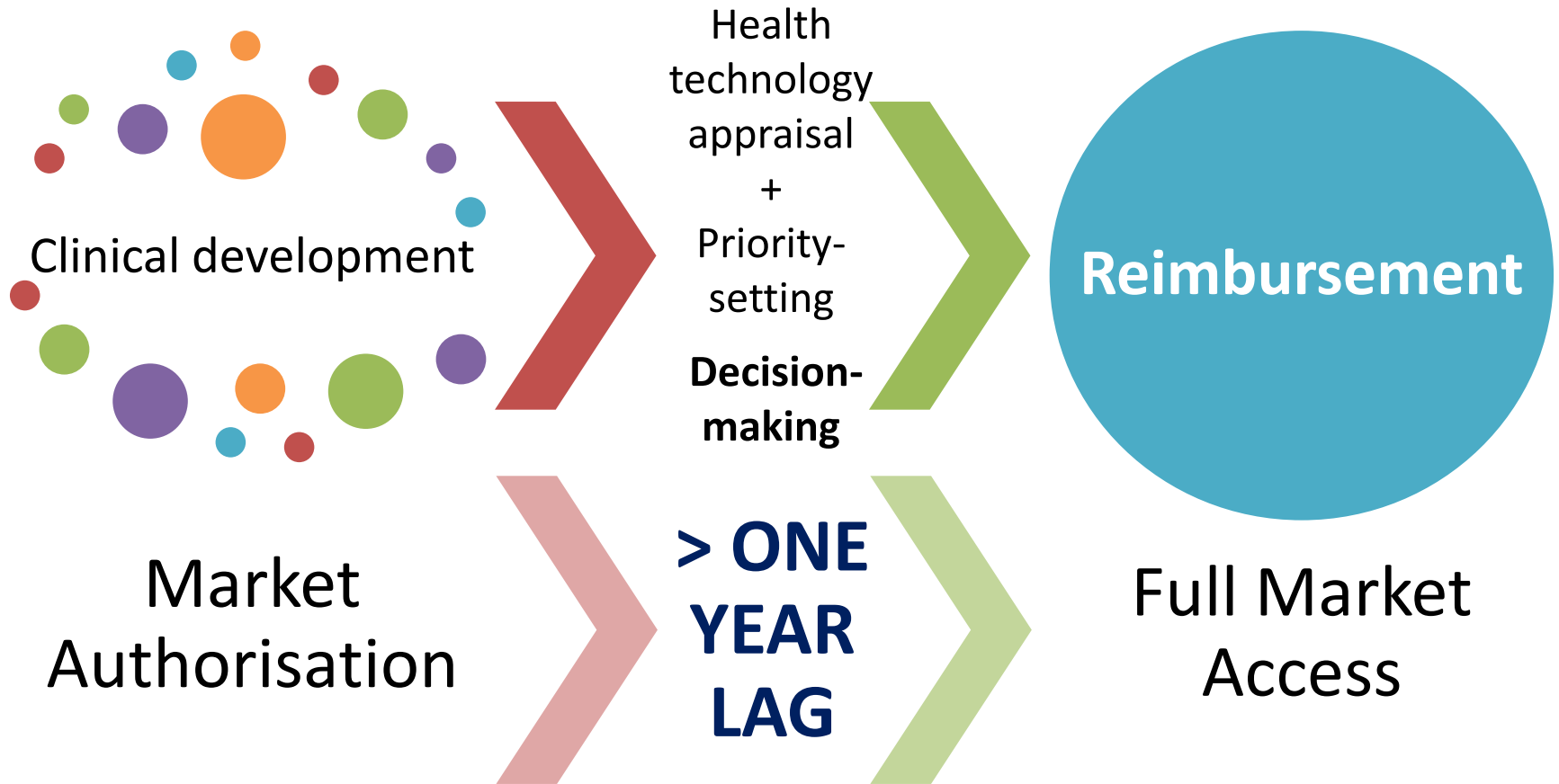
Medicines regulatory authorities 50+

24 official languages

EU Member States: 28

Austria Belgium Bulgaria Croatia Cyprus Czech Republic Denmark Estonia Finland France Germany Greece Hungary Ireland

Italy Latvia Lithuania Luxemburg Malta Netherlands Poland Portugal Romania Slovakia Slovenia Spain Sweden United Kingdom

The European Economic Area (EEA) is formed of the 28 EU Member States plus:

Iceland Liechtenstein Norway

Marketing Authorisation and Market access (EU)

Clinical development

Health technology appraisal + Priority-setting

Decision-making

Reimbursement

Market Authorisation

> **ONE YEAR LAG**

Full Market Access

Marketing Authorization

3 hurdles to market …

Safety

Efficacy

Quality

Benefit
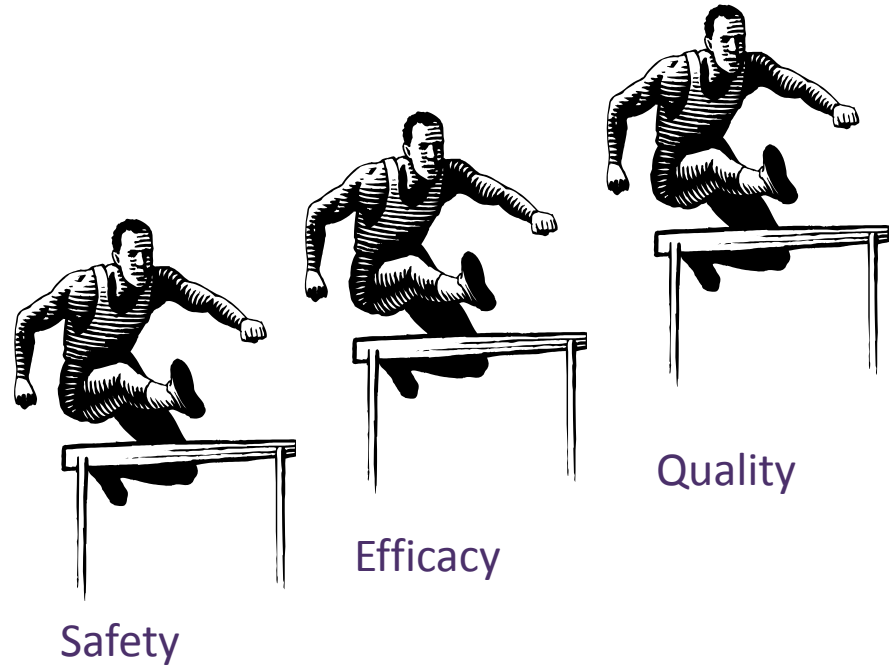
Risk

Marketing Authorization

4th hurdle…

And 5th…

Affordability

Cost-effectiveness

Therapeutic added value +

Value for money
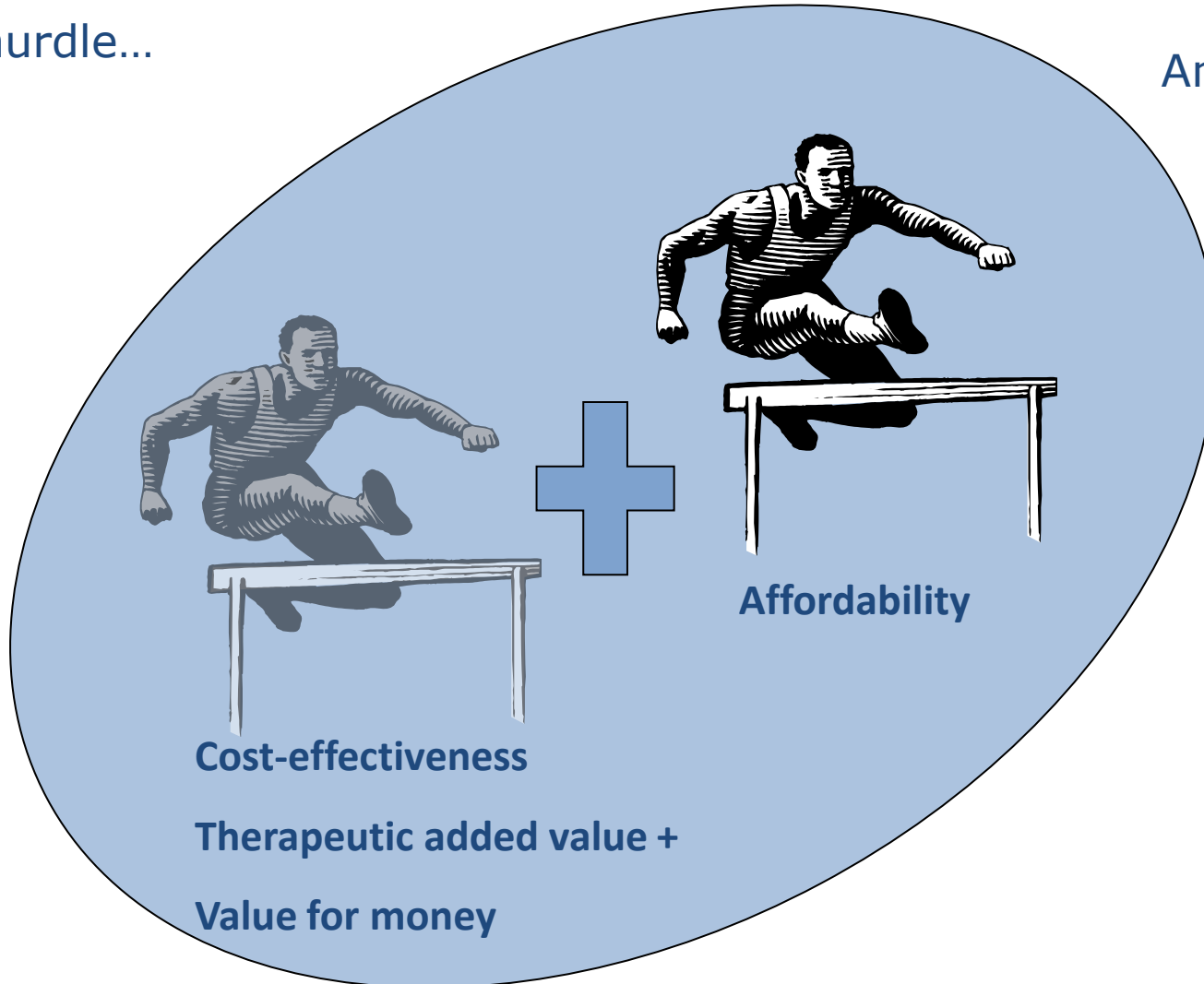
Classical triangle

Third payer:

Investment in future health gain
WITH
Cost control (containment)

Drug financing
Decision making

Pharmaceuticals:
Just Reward for the investment risk in I&D

Patients / society:
Prompt and unrestricted access to innovative medicines

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Early (phase 2/3) HTA quality data

Phase 2 trials

- Population
  - Homogeneous, RMS / PMS
  - EDSS 3-4.5 / 5-6 / >6
  - Small sample
- Short, proof of concept trial
- Biomarker based endpoint
  - MRI
- **Secondary / Exploratory endpoints in extension studies**
  - Disability endpoints
  - Up to 5 year data

Phase 3 trials

- Population
  - More heterogeneous, RMS + PMS
  - EDSS 3-6
- Medium duration trial
- Time to event endpoint
  - Lack of sustained double-blind follow-up
  - Event: relapse / sustained disability
- Disability endpoints

HTA in Multiple Sclerosis

- Delay / freezing of disability
  - Motor skills
  - Pain / sensation
  - Cognition / behaviour
  - …
- Improvement of patient capacity
- Cure
  - With sequelae
  - Without sequelae

Disability in Multiple Sclerosis

	Functioning and Disability		Contextual Factors	
	Body Functions	**Activities and Participation**	**Environmental**	**Personal**
Domain	Body functions	Life areas (tasks, actions)	External influence On disability	Internal influence On disability
Construct	Change in body function (physiological)	Capacity: Executing tasks in a standard environment Performance: Executing tasks in the current environment	Facilitating or Hindering impact of features of the physical, social and attitudinal world	Impact of attributes of the person
Positive aspect	Functional and structural integrity	Activities Participation	Facilitators	
Negative aspect	Impairment	Activity limitation Participation restriction	Barriers / hindrances	Person role

Disability in Multiple Sclerosis

Examples of activities limited by disability in MS	Walking fast	Keeping up appointments / double tasking	Reading magazines / leaflets	Using cutlery, writing, keyboard	Family decisions, having fun
Body functions impaired	Walking	Higher cognitive functions	Sight	Muscle power/ movement control	Higher executive functions/ Mood
Components of body function	Speed	Speed of thought/ Memory/ Attention	Visual acuity/ visual fields	Fine hand use/ Eye-hand coordination	Planning/ Depression
Assessment tools	T25FW	SDMT/ CVLT/ BVRT/ 7-24 SRT/ Stroop	LCVA	9-HPT	MADRS

T25FW: Timed 25-Foot Walk test; SDMT: Symbol Digit Modalities Test; CVLT: California Verbal Learning Test; BVRT: Benton Visual Retention Test; 7-24 SRT: 7/24 Spatial Recall Test; Stroop: Stroop Test; LCVA: Low-contrast visual acuity; 9-HPT: 9-Hole Peg Test; MADRS: Montgomery–Åsberg Depression Rating Scale

HTA assessment tools in MS

Multiple specific tools

- Detailed information (each test informs about specific MS items)
- Too cumbersome to apply all tests to all trial participants
- Most are not Patient oriented (not PROs), and provide information on clinical signs rather than daily life functioning
- Less variability
- Good to confirm that stabilisation / improvement is related to a change in MS

Global functional tools

- Clinical Global Impression (CGI)
- Patient Global Impression
  - Change
  - Improvement
  - Severity
- High variability
- Depression bias
- Training issues
- Must be complemented with other scales to confirm that improvement is related to MS symptom improvement

Good News!

- Academia, Pharmaceutical Industries, Patient representatives and Regulators on the same path:

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