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The assessment of alternative or abbreviated market access pathways for pharmaceutical reimbursement in 13 European markets

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Background

- Standard health technology assessment (HTA) processes for reimbursement of new drugs can be resource-intensive for small to mid-size pharmaceutical and biotechnology companies.
- For some treatments, the HTA resources required may exceed expected revenues and lead a company to decide not to launch in a particular market, depriving local patients of important therapeutic options.
- In order to address this issue, some countries offer alternative/abbreviated access pathways (AAPs) to ensure that such products can enter the market and become available to the local patient population.

Objective

- The study objective was to assess 13 European markets for existing AAPs that allow the commercialization of new drugs, as well as to summarize their key differences and similarities.

Methods

- Publicly available reimbursement policies, regulatory documents, and grey literature were reviewed for the following markets: Belgium (BE), Denmark (DK), Finland (FI), Germany (DE), Ireland (IE), Italy (IT), the Netherlands (NL), Norway (NO), Portugal (PT), Scotland (SCT), Spain (ES), Sweden (SW), and the United Kingdom (UK).
- Identified guidance was assessed based on applicant type, marketing authorization (MA) status, process eligibility criteria, evidence requirements, process duration, regional/national access, and pricing rules.
- Pathways included in this research needed to apply to new drugs, decision outcomes affecting a larger group of patients, and lead to revenue generation for the manufacturer. Therefore, pathways such as named patient programs and cases where manufacturers needed to provide products free of charge were excluded.

Results

- **AAPs are available in 11 of the 13 markets** (see **Figure 1**, **Table 1**). In 8 markets, these lead to reimbursement on a national level. In DK and SW, AAPs are conducted by region; therefore, to achieve national access, manufacturers need to engage with each region individually. In the UK, the AAP applies to England, Wales, and Northern Ireland. SCT has a separate but similar process.
- **Pathway eligibility varies strongly** across markets. In 5 markets (NL, NO, SCT, UK, IE), eligible treatments need to show similar efficacy to comparators, as well as a similar or lower budget impact. IT also applies an AAP for drugs used off-label. FI, DK, and SW allow regional assessments instead of national full HTAs; BE, NO, and PT, have dedicated AAPs for drugs that treat high-severity diseases and an expected high value for affected patients.
- **In 7 markets, AAPs can be initiated by the manufacturer.** In FI, IT, and SW, physicians or relevant medical/research organisations need to file the reimbursement request. In BE, the decision is political and made by the Commission of Reimbursement of Medicines (CRM), and the Ministry of Health (MoH).
- While **the extent of the evidence description required is smaller than in full HTAs**, in most markets, clinical evidence such as a description of the unmet need, clinical trials, and efficacy is required. In BE and PT, no clinical evidence is required to be submitted. In the Nordics (DK, NO, SW), requirements depend on the region/hospital.
- **Economic evidence required usually includes expected patient numbers, budget impact, and/or a cost comparison.** Some agencies request additional points of information, such as an overview of international HTAs, the orphan status, recommendations from medical societies, or hospital investments required to use the drug under consideration.
- **Process duration is not defined in 7 markets.** However, where processes are defined, these range between 4 (IE) and 26 (PT) weeks. These timeframes are similar in markets where information is gathered through experience (FI: 8-16 weeks; NO: 5 weeks).
- **In 6 markets, AAPs finalize in price negotiations.** In the UK and SCT, with the acceptance of the abbreviated process, prices are accepted as submitted. PT applies international reference pricing, and in BE and FI, it is not defined how prices are established.

Conclusions

- This analysis demonstrates that AAPs exist in most assessed markets.
- Particularly small and mid-size markets offer AAPs with flexibility related to data requirements. This indicates that agencies with limited resources, compared to those of larger markets, have established more pragmatic methods to ensure patient access to new drugs.
- Across markets, economic factors such as budget impact are key for process eligibility and success, excluding particularly innovative and comparatively expensive drugs from these processes.
- In summary, AAPs may offer viable options for small and mid-size companies or treatments with low budget impact and could help to overcome challenges in regular HTA processes with rigorous data requirements and a longer time for market access. However, such pathways are not available in all countries.

Figure 1. Type of AAPs available in assessed European countries

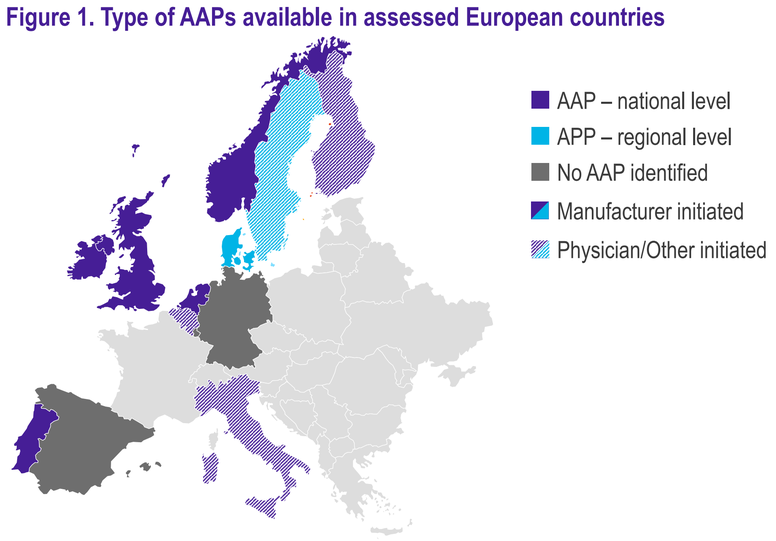

Table 1. Summary of alternative/abbreviated-access pathways (AAPs) by country

Country	AAP	Responsible agency	Applicant	MA status at time of request	Criteria for a drug to be eligible for the process	Evidence requirements: Clinical	Evidence requirements: Economic	Evidence requirements: Other	Process duration	Level of access	Pricing rules
Belgium[1,2]	Chapter V – List of reimb. pharmacy specialties	NIHDI CRM	• MoH & CRM (no dossier required, political decision)	• EMA approved	• Drugs not evaluated via a full HTA process and • Particularly valuable drugs with high need from a public health perspective (recognized by CRM and/or MoH)	None required	• Cost-price structure	None required	Not defined	National	Not defined Chapter V withdrawn once drug for same patient population is reimbursed
Denmark[3]	Individual regional procurements/contracts	Regions or DMC	• Manufacturer	• EMA approved	• Drugs not evaluated via a full HTA process	Situation-specific (agreement with agency)			Not defined	Regional	Negotiations
Finland[4]	Regional mini-HTA	FinCCHTA	• Treating physician	• EMA approved	• Drugs not evaluated via a full HTA process and • Hospital-administered drug and • Costs per patient >€30,000/year	• Burden of disease • Place in therapy • Trial descriptions • Clinical evidence • Comparators • PROs	• Costs per patient/year • BI • Cost comparison	• Organisational investments (training, new equipment, etc.)	Not defined (usually 8-16 weeks)	National	Not defined (Manufacturer may negotiate separately with hospital)
Germany	None identified	na	na	na	na	na	na	na	na		
Ireland[5]	Rapid Review	NCPE	• Manufacturer	• EMA approved or • Pending MA status	• Any new drug before the evaluation via a full HTA process	• Burden of disease • Place in therapy • Clinical evidence • Comparators	• BIM • Cost comparison	• International HTA	4 weeks (NCPE may request subs. full HTA, delaying timelines)	National	Negotiations • Manufacturer can decline full HTA and immediately negotiate, likely leading to discounts
Italy[6,7]	Law 648 – Article 1, sub. 4, Law 648/1996	AIFA CTS	• Physicians or • Scientific societies or • Health authorities or • AIFA CTS recommendation or • Universities or • Patient associations	• EMA approved or • Pending MA status	Drugs with no licensed alternative • MA gained in any European country, but not IT or • Not yet authorized, but in trials and phase 2 data available or • Off-label use, have undergone phase 2 trial Drugs with licensed alternative • Off-label use based on inexpensiveness & appropriateness, if compliant with research	In case of request, manufacturer will be informed by AIFA and asked to provide dossier, and participate in negotiations • Burden of disease • Place in therapy • Trial descriptions • Clinical evidence • Comparators	• Expected patient numbers • Costs per patient/year • BI on the SSN/year • Cost comparison	• MA status in IT and abroad • Drug reimbursement regime in IT (if applicable) • Rare disease/orphan status	Not defined	National	Negotiations
The Netherlands[8-11]	No-lock process	Hospital drugs CieBAG Out-patient drugs ZIN	• Manufacturer (supported by Medical Society & Health Insurers)	• EMA approved	Hospital drugs • BI <€20 million/year or • Costs per patient/year >€1,000 and <€50,000/year and annual costs <€10 million Out-patient drugs • Drugs that can be grouped in existing 'cluster of interchangeable medicines' and used in same pop	• Place in therapy • Trial descriptions • Clinical evidence	• Expected patient numbers • Costs per patient/year • Cost-effectiveness • Cost comparison • Incremental costs and effects	• Approved indications • Off-label use and compliance with research • Recommendations from scientific and medical associations	Not defined	National	Negotiations
Norway[12,13]	Simplified STA Rapid STA	NoMA	• Manufacturer	• EMA approved	Pre-meeting with NoMA to agree on required evidence • Small patient population and • Similar clinical effectiveness vs alternatives and • BI similar to alternatives evaluated via full HTA • Small patient population (<50 patients) and • High disease severity (at least 30 QALYs lost) and • Significant benefit expected (min. ~2 QALYs gained vs SoC)	Situation-specific (agreement with agency) could include: • Patient population • Burden of disease • Place in therapy • Trial descriptions • Clinical evidence • Comparator	• Costs per patient/year • Economic analysis and model • BI	• HRQoL • Relationship between relative efficacy, model parameters, and relevance for Norwegian clinical practice • Discussion of submitted evidence	Not defined (~5 weeks) Not defined	National	Negotiations
Portugal[14]	Early-Access Program	INFARMED	• Manufacturer	• EMA approved	• Drugs with no licensed alternative and • High disease severity (immediate risk of life or suffering from serious complications) • Mandatory to submit in parallel to reimbursed application	None required	None required	None required	26 weeks + clock stops (usually longer)	National	Price agreement based on IRP • Min. 210 days free-of-charge period
Scotland[15, 16]	Abbreviated submission	SMC	• Manufacturer	• CHMP-positive opinion or • Before final MHRA approval	SMC decides about eligibility, drugs may be eligible if: • Drugs with licensed alternatives and • Alternatives accepted for (restricted) use by SMC and • BI expected to be low	• Clinical evidence • Optional: ITC	• BI • Impact on resource allocation • Discount offered (if applicable)	• Any other relevant information	18 weeks	National	Price as submitted, (accept. price implied, as the process was accepted) • Restriction applied to comparators are applied to new drug
Spain	None identified	na	na	na	na	na	na	na			
Sweden[3]	Individual regional procurements/contracts	Regions	• Physician(s)	• EMA approved	• Not defined (processes not defined in rules and regulations on the regional level)	Situation-specific (regional process and agreement/requirements)			Not defined	Regional	Procurement/ negotiations
UK[17,18]	Cost Comparison Appraisal (updated former Fast Track Appraisal)	NICE	• Manufacturer	• CHMP-positive opinion or • MHRA approved	NICE decides about eligibility via scoping process: • New drugs and • Similar or greater clinical effectiveness compared to alternatives and • Alternatives accepted for (restricted) use by NICE and • BI similar to or lower than alternatives	• Unmet need • Burden of disease • Place in therapy • Trial descriptions • Clinical evidence • Comparators • ITC	• Cost comparison • Cost-effectiveness drivers of comparators in respective NICE appraisals	None required	23 weeks	• England • Wales • Northern Ireland	Price as submitted (similar or lower cost than competitors, with or without agreed discount)

Key: AAP – alternative/abbreviated-access pathways; AIFA – "Italian Medicines Agency"; BE – Belgium; BI – budget impact; BIM – budget impact model; CHMP – Committee for Medicinal Products for Human Use; CieBAG – "Commission for Add-on Drugs"; CRM – "Commission of Reimbursement of Medicines"; CTS – "Scientific Technical Advisory Committee"; DE – Germany; DK – Denmark; DMC – "Danish Medicines Agency"; EMA – European Medicines Agency; ES – Spain; FI – Finland; FinCCHTA – "Finnish Coordinating Center for Health Technology Assessment"; HRQoL – health-related quality of life; HTA – health technology assessment; IE – Ireland; INFARMED – "Portuguese National Authority of Medicines and Health Products"; IRP – international reference pricing; IT – Italy; ITC – indirect treatment comparison; MA – marketing authorization; MHRA – Medicines and Healthcare products Regulatory Agency; MoH – Ministry of Health; na – not applicable; NCPE – National Centre for Pharmacoeconomics; NICE – National Institute for Health and Care Excellence; NIHDI – National Institute for Health and Disability Insurance; NL – the Netherlands; NO – Norway; NoMA – "Norwegian Medicines Agency"; PRO – patient-reported outcome; PT – Portugal; QALY – quality-adjusted life-year; SCT – Scotland; SMC – Scottish Medicines Consortium; SoC – standard of care; SSN – "Italian National Health Service"; STA – simplified single technology assessment; SW – Sweden; UK – United Kingdom; ZIN – "Dutch National Healthcare Institute".

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