Pricing and Reimbursement of CFTR Modulator Medicines in Europe: A Comparative Analysis

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BACKGROUND AND OBJECTIVES

Cystic fibrosis is a rare condition characterized by abnormal thick mucus accumulation and affecting over 48,000 individuals in Europe. Innovative CFTR modulator therapies, Kalydeco®, Orkambi® and Symkevi® substantially ameliorated lives of people living with cystic fibrosis (PLWCF) by potentiating and/or correcting the dysfunctional CFTR protein. These revolutionary therapies have increased life expectancy of PLWCF to above 40, but have also brought on significant costs and affordability concerns for many jurisdictions.

In this analysis, we aim to map out accessibility to these interventions in twelve European countries by comparing publicly available list prices, reimbursement decisions, economic evaluations, budget impact analyses (BIAs), managed entry agreements (MEAs) and multinational collaborations.

METHODS

- Selected countries consisted of **Austria, Belgium, Denmark, France, Germany, Ireland, Poland, Spain, Sweden, Switzerland, the Netherlands and the United Kingdom**.
- Data was retrieved from **grey literature, pharmaceutical registries or formularies, health authorities' reports, press releases and government's healthcare databases** such as; Belgian NIHDI and BCFI, German G-BA and Rote Liste, Swedish TLV, Scottish SMC, English NHS and NICE, Dutch GVS, French CNHIM, Danish Lægemiddelstyrelsen, Austrian SV, Irish HSE and Swiss FOPH.
- List prices were converted into **prices per daily defined dose (DDD) or per average daily dose (ADD)**.
- For **economic evaluations and BIAs**, we compared **design** (model or target population, perspective, comparator, time horizon, costs and discounting), **incremental cost-effectiveness ratio (ICER) or BIA outcome and sensitivity analyses.**

RESULTS

- **Budget impacts** varied and were dependent on patient number, medication prices, (treatment-related) costs and discounting.
- International comparison of budget impact was complicated due to varying time horizons and inconsistent form of reporting results.
- Countries unanimously considered budget impact to be high.
- The Netherlands and Belgium (BeNeLuxA) **jointly assessed** Orkambi® in 2015 and concluded it not to be cost-effective without a price reduction of 82%.
- Ireland, Sweden, Denmark, England, Northern Ireland and Wales set up a unique **portfolio-deal agreement** for reimbursement of the company's current and future CF.
- Austria, Belgium, France, Germany, Spain, Switzerland and the Netherlands set up **managed entry agreements** coupled with clinical evidence generation and confidential discounts.

RESULTS

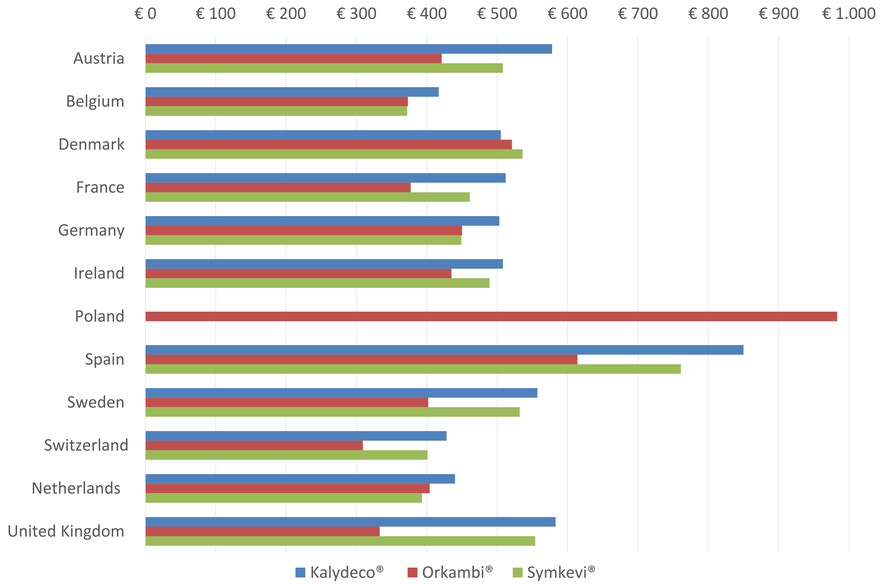
Overview of incremental cost-effectiveness ratios (ICERs) of CFTR modulators in a selection of European countries.

CFTR Modulator	Kalydeco®			Orkambi®	Symkevi®	
Indication	Gating class III ≥ 2 years	G551D ≥ 6 years	R117H ≥ 18 years		Homozygous for F508del	Heterozygous for F508del & residual function mutation
ICER (€; 2020 values)	-	-	-	€453,286/QALY (482,727)	-	-
	-	£771,297/QALY (1,001,336)	-	Company: £218,248/QALY (282,112) NHS: £221,992/QALY (286,951)	-	-
				€622 131/QALY (675,947)	-	Company: €945,278/QALY (980,110) NHS: >€1,000,000/QALY (>1,036,849)
	€465,546/QALY (487,122) or €636,237/QALY (665,723)	€449,035/QALY (500,195)	€444,466/QALY (463,288)	Company: €369,141/QALY (386,249) NHS: €649,624/QALY (679,731)	-	-
	£484,386/QALY (613,485) or £609,316/QALY (771,711)	£277,011/QALY (365,782)	£473,071/QALY (599,154)	£214,772/QALY (256,486)	£421,173/QALY (502,974)	£360,499/QALY (430,516)
	NHS: 5,556,831kr/QALY (533,034) - 7,005,198kr/QALY (671,968)	Company: 3,474,120kr/QALY (361,444) NHS: 5,840,000kr/QALY (607,588) - 10,440,000kr/QALY (1,086,167)	-	NHS: 1,541,295kr/QALY (147,723) - 1,650,000kr/QALY (158,275)	-	NHS: 5 675 522kr/QALY (544,420) - 7 035 099kr/QALY (674,836)
	Company: €172,278/QALY (191,910) HIF: €266,074/QALY (296,395)	-	-	€402,883/QALY (443,330)	€376,060/QALY (387,456)	-

ICER, incremental cost-effectiveness ratio; *NHS*, National Health Service; *HIF*, Health Insurance Funds, *QALY*, quality adjusted life years

RESULTS

Official list prices of CFTR modulators per DDD/ADD.*



*Consulted on September 22, 2021, VAT included and expressed in 2021 €. *DDD*, Defined Daily Dose. *ADD*, Average Daily Dose.

RESULTS

Reimbursement status of CFTR modulators in specific European countries. *

Kalydeco®	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✗	✓	✓	✓
Orkambi®	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✓	✓	✓	✓
Symkevi®	✓	✓	✓	✓	✓	✓	✓	✓	✗	✓	✓	✗	✓	✓	✓

✓, full reimbursement; ✗, no reimbursement (full out-of-pocket expenses) *as of June 2021

CONCLUSION

- Despite high list prices, lack of cost-effectiveness, an elevated budget impact and negative recommendations, Kalydeco®, Orkambi® and Symkevi® were reimbursed in majority of analyzed countries. This was mainly possible due to managed entry agreements, such as portfolio deals, but also criteria on equity and equal access, disease severity, innovation, patients' opinions, clinicians' views, patient advocacy, media attention and prevalence.
- Our findings point to unequal access, differential pricing and delayed availability of cystic fibrosis modulators in Europe.

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