Orphan Drug Compassionate Use Programmes: Impact on Reimbursement Decisions in France, Germany and England

POSB214

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OBJECTIVE

To understand the impact of compassionate use programmes on reimbursement decisions for orphan products in France, Germany and England.

BACKGROUND

- There is often a delay between the completion of Phase III clinical trials and positive regulatory and reimbursement decisions; it may take around 11 months for a marketing authorisation (MA) to be granted and an additional 12 months for reimbursement appraisals to be completed.[1] Compassionate use programmes (CUPs) involve a manufacturer providing a therapy on a temporary basis, often without charge, to enable patients to gain access to unauthorised medicines if they are ineligible for clinical trials and affected by a disease with a high unmet need for a medical treatment.[1,2]
- Such medicines include those with orphan drug designations (ODDs), which are intended for the treatment of life-threatening or chronically debilitating rare diseases with a prevalence of ≤5 in 10,000 people.[3] CUPs are particularly important for products with ODDs, as few if any treatments exist for many rare diseases, and affected patients are therefore particularly reliant on new treatments being made available.[1]
- This research follows on from Newell *et al.*,[4] who focused on products with ODDs in France, Germany and England, and demonstrated that the majority of identified orphan products with CUPs successfully gained MA, suggesting CUPs may offer a benefit with respect to regulatory decision making.

METHODS

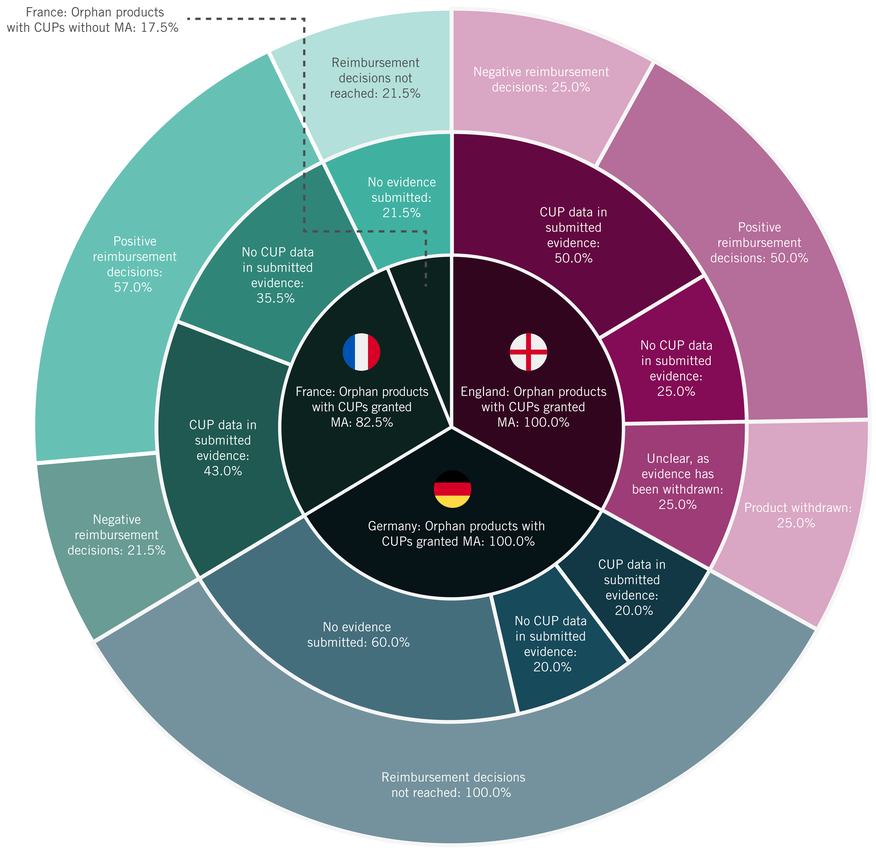
- Local regulatory bodies were searched in June 2020 to identify products made available through CUPs in France, Germany and England. Those treatments that had been awarded EMA ODDs between January 2010–June 2020 were then identified through searching the Community Register of orphan medicinal products.[4,5]
- In May 2021, the EMA website was searched to investigate the latest MA status of these products.
- Websites of French (Haute Autorité de Santé), German (Institute for Quality and Efficiency in Healthcare; Der Gemeinsame Bundesausschuss) and English (National Institute for Health and Care Excellence) health technology assessment (HTA) bodies were searched to determine the use of CUP data in published appraisal documents for the previously identified orphan products with MAs.

RESULTS

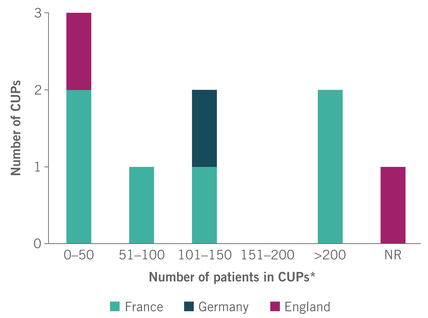
Regulatory and Reimbursement Decisions

- In France, Germany and England, 14/17 (82.5%), 5/5 (100.0%) and 4/4 (100.0%) of the identified orphan products with CUPs had been awarded MAs, respectively **(Figure 1)**.
- In France, evidence had been submitted and a reimbursement decision had been reached for 11/14 (78.5%) products: 8/14 (57.0%) were positive, 3/14 (21.5%) were negative **(Figure 1)**.

1 Regulatory and reimbursement decisions for orphan products with CUPs



2 Number of CUP patients reported in reimbursement submissions



*Total number of patients enrolled in all the CUPs reported in each reimbursement submission.

1 Use of CUP data in appraisals where CUP data were reported

Product where CUP data were used in the submission	Reimbursement decision	CUP data used in the submission	Number of patients in the CUP
France			
Chlormethine	Negative	Safety and tolerability data	478
Inotuzumab ozogamicin	Negative	Tolerability data	11
Lutetium (177Lu) oxodotreotide	Positive	Safety data	268 (152 from French CUP, 116 from US CUP)
Metreleptin	Positive	Usage data	35
Midostaurin	Positive	Usage data	114
Polatuzumab vedotin	Negative	Usage data	88
Germany			
Fenfluramine hydrochloride	Awaiting decision	Safety data	149 (97 from German CUP, 52 from Italian CUP)
England			
Tafamidis	Negative	Usage data	NR
Volanesorsen	Positive	Safety, efficacy and usage data	20

- In Germany, evidence had been submitted for 2/5 (40.0%) products, but no decisions had been made at the time of the searches **(Figure 1)**.
- In England, evidence was available for 3/4 (75.0%) products; one product had been withdrawn from the UK market in January 2020, with concomitant withdrawal of the reimbursement decision.[6,7] Positive and negative reimbursement decisions had been reached for 2/4 (50.0%) and 1/4 (25.0%) products, respectively **(Figure 1)**.

Use and Impact of CUP Data

- A total of nine appraisals mentioned data from CUPs: 4/9 appraisals received a positive opinion (France: 3/6; England: 1/2), 4/9 of the appraisals received a negative opinion (France: 3/6; England: 1/2). Additionally, one appraisal in Germany, for which no reimbursement decision had been reached, mentioned data from CUPs **(Table 1)**.
- Data from CUPs that were commonly used to support evidence from clinical trials in appraisals were safety and/or tolerability and usage data, whereas efficacy data from a CUP were used to support clinical trial evidence in only one appraisal **(Table 1)**.
- The total number of patients treated in the CUPs varied, ranging from 11–478 **(Table 1** and **Figure 2)**, with no clear correlation between the size of the CUP and the reimbursement decision **(Table 1)**.
- Most appraisals only reported data from a CUP in the same country as the HTA body. However, two appraisals reported data from an additional CUP from a different country outside of the submitting HTA body **(Table 1)**.

CONCLUSIONS

A large proportion of HTA appraisals for products with a CUP mentioned data collected from a CUP, including safety, tolerability, usage and efficacy data. This suggests that data from CUPs may add value to technology appraisals.

However, the results do not demonstrate any direct association between inclusion of CUP data and a positive reimbursement decision, though it should be noted that the number of products on which this analysis could be based was small.

References

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Abbreviations: CUP: compassionate use programme; NR: not reported; MA: marketing authorisation.

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