HTA83

Assessing Health Technology Assessment (HTA) Outcomes for Conditionally Approved Drugs by the European Medicines Agency (EMA) in Germany, France, and England

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INTRODUCTION

The EMA grants conditional marketing authorisations (C-MAs) to medicines for debilitating/life-threatening diseases, including orphan drugs, when the benefits of faster availability outweigh the risks. C-MAs are valid for 1 year, renewable annually, with specific obligations to be fulfilled within set timelines.

OBJECTIVES

This study analyzes HTA outcomes in Germany, France, and England for medicines granted C-MA.

METHODS

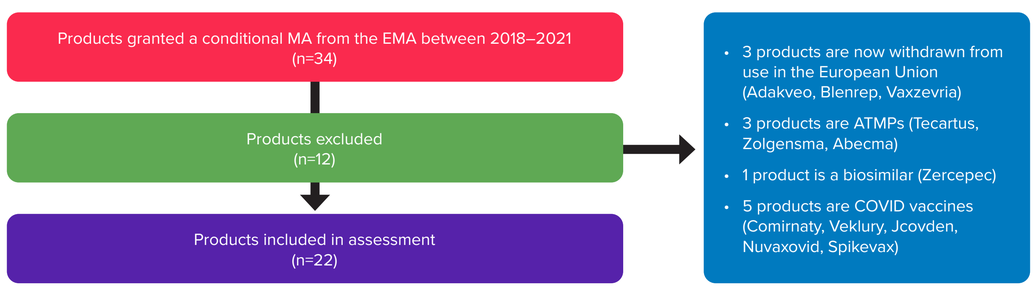
- Products granted C-MA between the years 2018 to 2021 were identified.
- Approvals after 2021 were excluded due to insufficient time for reimbursement procedures. Certain drug classes, including advance therapy medicinal products (ATMPs), biosimilars, and vaccines, were excluded.
- HTA outcomes were extracted from publicly available HTA opinions in Germany, France, and England in June 2024.

RESULTS

Timing to reimbursement

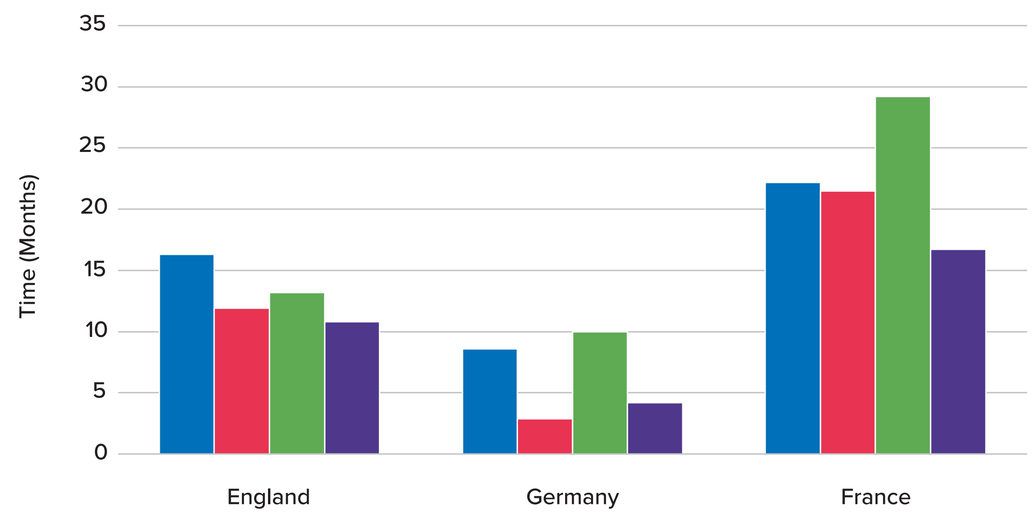
- Of 34 products receiving C-MA, 22 were included in the analysis (orphan, n=11; non-orphan, n=11) (Figure 1, Table 1).
- Average time to reimbursement for non-orphans with C-MA was longer than for all drugs across countries, and longer than for orphans with C-MA in France (29.2 vs 22.2 months) and Germany (10.0 vs 8.6 months) (Figure 2).
- Orphan products with C-MA took longer to reimburse than standard-approved orphan products in England (16.3 vs 11.9 months) and Germany (8.6 vs 2.9 months; 3-times longer) (Figure 2).
- In England, timelines were longer for negative outcomes.

Figure 1: Process of inclusion



Abbreviations: ATMP – Advanced therapy medicinal products; EMA – European Medicines Agency; MA – Market authorisation.

Figure 2. Time to reimbursement (months) for orphan vs non-orphan drugs with conditional approval and positive HTA outcome compared to averages



† Excluding ATMPs, COVID vaccines and biosimilars

Abbreviations:
HTA – Health technology assessment.

Table 1: EMA approval overview

Product	CHMP Opinion Date	Marketing Authorisation Date	Indication	Therapeutic Area
Rucaparib[1]	13 Dec 2018	23 May 2018	Ovarian neoplasms	Oncology
Lorlatinib[2]	28 Feb 2019	6 May 2019	NSCLC	Oncology
Andexanet alfa[3]	28 Feb 2019	26 April 2019	Anticoagulation reversal due to life-threatening/uncontrolled bleeding	Hematology/ coagulation
Volanesorsen[4]	28 Feb 2019	3 May 2019	FCS	Metabolic disorders
Cemiplimab[5]	26 April 2019*	28 June 2019*	Squamous cell carcinoma, BCC, NSCLC, cervical cancer	Oncology
Larotrectinib[6]	25 July 2019	19 Sept 2019	Solid tumors with NTRK gene fusion	Oncology
Polatuzumab vedotin[7]	14 Nov 2019	16 Jan 2020	DLBCL	Oncology
Pretomanid[8]	26 March 2020	31 July 2020	Drug resistant tuberculosis	Infectious diseases
Entrectinib[9]	28 May 2020	31 July 2020	Solid tumors expressing a NTRK gene fusion, ROS1-positive NSCLC	Oncology
Bulevirtide[10]	28 May 2020	31 July 2020	Chronic hepatitis delta virus	Infectious diseases
Imlifidase[11]	25 June 2020	25 Aug 2020	Desensitisation treatment of highly sensitised adult kidney transplant patients	Transplantation/ immunology
Avapritinib[12]	23 July 2020	24 Sept 2020	GIST + advanced systemic mastocytosis	Oncology
Trastuzumab deruxtecan[13]	10 Dec 2020**	18 Jan 2021**	HER2-positive, HER2-low breast cancer, gastric cancer	Oncology
Selpercatinib[14]	10 Dec 2020	11 Feb 2021	NSCLC, thyroid cancer, MTC	Oncology
Selinexor[15]	28 Jan 2021	26 Mar 2021	Multiple myeloma	Oncology
Pemigatinib[16]	28 Jan 2021	26 Mar 2021	Cholangiocarcinoma	Oncology
Dostarlimab[17]	25 Feb 2021	21 April 2021	Endometrial cancer	Oncology
Selumetinib[18]	22 April 2021	17 June 2021	Neurofibromatosis type 1	Genetics/ oncology
Tafasitamab[19]	24 June 2021	26 Aug 2021	DLBCL	Oncology
Pralsetinib[20]	16 Sept 2021	18 Nov 2021	RET fusion-positive NSCLC	Oncology
Amivantamab[21]	14 Oct 2021	9 Dec 2021	NSCLC	Oncology
Sotorasib[22]	11 Nov 2021	6 Jan 2022	NSCLC	Oncology

[a]**Bolded products are orphan drugs.**

Abbreviations: BCC – Basal cell carcinoma; CHMP – Committee for Medicinal Products for Human Use; DLBCL – Diffuse large B-cell lymphoma; FCS – Familial chylomicronaemia syndrome; GIST – Gastrointestinal stromal tumour; HER2 – Human epidermal growth factor receptor 2; MTC – Medullary thyroid cancer; NSCLC – Non-small cell lung cancer; NTRK – Neurotrophic tyrosine receptor kinase; RET – Rearranged during transfection

Reimbursement conditions

- Products were reimbursed as per the EMA label most frequently in Germany (96%) followed by England (50%) and France (32%).
- More non-orphan vs orphan products were reimbursed: Germany (55% vs 41%), England (27% vs 23%), France (18% vs 14%).
- France had the most drugs with reimbursement restrictions (36%), followed by England (23%), with none in Germany.
  - England: requirements for further evidence, stopping criteria, specific eligibility criteria, and conditions for treatment administration.
  - France: requests for patient registries and restrictions to specific lines of therapy or patient subgroups.
- In England, ~50% of products were included in the Cancer Drugs Fund to collect additional evidence.
- In Germany, one drug received “considerable additional benefit” while others had “unproven” or “non-quantifiable” benefit due to lack of data.
- France had the highest denial rate (18%), followed by England (14%), with none in Germany.

CONCLUSIONS

C-MAs lead to extended reimbursement decision timelines compared to standard approvals, regardless of orphan status. These delays highlight challenges in achieving timely market access even with expedited regulatory pathways. Furthermore, additional restrictions in France and England not only complicate the reimbursement process but may also reduce the number of patients eligible for treatment, limiting the overall impact of innovative therapies.

REFERENCES

1. Rubraca (rucaparib), SmPC, 23 May 2018.
2. Lorviqua (lorlatinib), SmPC, 6 May 2019.
3. Ondexxya (andexanet alfa), SmPC, 26 April 2019.
4. Waylivra (volanesorsen), SmPC, 3 May 2019.
5. Libtayo (cemiplimab), SmPC, 28 June 2019.
6. Vitrakvi (larotrectinib), SmPC, 19 September 2019.
7. Polivy (polatuzumab vedotin), SmPC, 16 January 2020.
8. Dovprela (pretomanid), SmPC, 31 July 2020.
9. Rozlytrek (entrectinib), SmPC, 31 July 2020.
10. Hepcludex (bulevirtide), SmPC, 31 July 2020.
11. Idefirix (imlifidase), SmPC, 25 August 2020.
12. Ayvakyt (avapritinib), SmPC, 24 September 2020.
13. Enhertu (trastuzumab deruxtecan), SmPC, 18 January 2021.
14. Retsevmo (selpercatinib), SmPC, 11 February 2021.
15. Nexpovio (selinexor), SmPC, 26 March 2021.
16. Pemazyre (pemigatinib), SmPC, 26 March 2021.
17. Jemperli (dostarlimab), SmPC, 21 April 2021.
18. Koselugo (selumetinib), SmPC, 17 June 2021.
19. Minjuvi (tafasitamab), SmPC, 26 August 2021.
20. Gavreto (pralsetinib), SmPC, 18 November 2021.
21. Rybrevant (amivantamab), SmPC, 9 December 2021.
22. Lumykras (sotorasib), SmPC, 6 January 2022.
23. EFPIA patients W.A.I.T. Indicator 2022 survey. European Federation of Pharmaceutical Industries and Associations (EFPIA). April 2023. https://www.efpia.eu/media/s4qf1ego/efpia_patient_wait_indicator_final_report.pdf