How Does Regulatory Speed Impact Time to Final HTA Decision

HTA259

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INTRODUCTION

It is vital that patients have rapid access to innovative products for diseases where there is a significant unmet need.

With this goal in mind, the EMA can grant accelerated approval to therapeutic innovations that are deemed to be of major interest for public health. Accelerated assessment usually takes 150 days, rather than the 210 days for products going through the standard central marketing authorisation procedure. Products then need to undergo HTA evaluations in individual countries to inform pricing and reimbursement decision making.

We sought to explore if and how expediated regulatory approval impacts the time to final HTA decision to ensure full and rapid patient access to these innovative treatments.

OBJECTIVE

To investigate whether accelerated regulatory approval translates into swift HTA decision making for innovative new chemical entities (NCEs).

METHOD

We identified innovative NCEs approved in 2021 and 2022, based on whether they were considered to contribute "significant progress in their therapeutic areas", as classified in the EMA Human Medicines Highlights reports for 2021[1] and 2022[2], and/or if they went through the EMA's accelerated approval procedure.

The dates of European marketing authorisation were identified from the EMA website[3], and dates of UK marketing authorisation were taken from the MHRA website.[4] (N.B. All products approved by the MHRA relied on the EMA decision and CHMP advice through the European Commission Decision Reliance Procedure). The dates of the HTA decisions were identified from official HTA reports in France (HAS[5]), Germany (G-BA[6]) and England (NICE[7]).

The time (calendar days) between EMA/MHRA approval and the final HTA decision in each country was then calculated for each NCE. As there was a high degree of variation in the timelines across the NCEs, median values were used to compare the time to final HTA approval.

As oncology is considered a severe disease with significant unmet need for which new therapies are highly valued by the public, we also explored the time difference between approval and final HTA decisions between oncology and non-oncology products.

RESULTS

Twenty NCEs were identified that were considered to represent a "significant therapeutic progress" and/or went through the EMA accelerated approval procedure in 2021 and 2022.

The median time from regulatory approval to final HTA decision across all products was 208 days; however, there was significant variation, ranging from 89 to 671 days (Figure 1).

On average, Germany had the longest time from regulatory approval to final HTA decision: 246 days versus 178 days in France and 225 days in UK. This was driven by manufacturers delaying the start of the G-BA benefit assessment, either by not launching the drug on the market immediately after approval (e.g., Tecvayli and Mounjaro) or by requesting a delay to the assessment to include an update to the regulatory label (e.g. Beyfortus).

Across all markets, there didn't appear to be a significant difference in the time from regulatory approval to final HTA decision for products that received accelerated approval compared to those that didn't, 210 versus 206 days, respectively (Figure 2).

France

In France, there was little difference in the median time from regulatory approval to final HTA decision for products that received accelerated approval versus those that did not, 182 (103-537) versus 178 (89-671) days, respectively (Figure 2.).

France had the largest variation in time to final HTA decision with the TC publishing its decision for Imcivree 89 days after approval (SMR substantial; ASMR V; time-limited reimbursement 1 year) and 671 days after approval for Mounjaro (likely delayed by the manufacturer to combine assessments and pricing negotiations for both diabetes and obesity indications).

Germany

In Germany, there was a difference of ~2 months in median time from regulatory approval to final HTA decision for products that received accelerated approval versus those that did not, 220 (178-654) versus 278 (196-595) days, respectively (Figure 2.). However, this appears to be a random finding as the timelines do not appear to correlate with products receiving accelerated approval or not. As described above, it is largely manufacturers deciding when to commercialise in Germany that is driving the time to final HTA decision as the timelines for G-BA assessment are set in law.

UK

Only eight NCEs in the sample had a final appraisal document published by NICE. Of the others, one was not in scope for NICE, five had no evidence submitted, one withdrew evidence, four still have guidance in development, and one was deselected as offered no value to the NHS.

Only four of the eight products went through accelerated approval but despite the small sample, there appears to be little difference in the median time from regulatory approval to final HTA decision for products that received accelerated approval versus those that did not, 225 (168-343) versus 224 (138-394) days, respectively (Figure 2.). However, It should be noted that two products that went through EMA accelerated approval, Kimmitrak and Xenpozyme, are still undergoing evaluation by NICE as of 1 November 2024 despite receiving marketing authorisation by the MHRA in June and August 2022, respectively. If these innovative NCEs were included in the analysis this would substantially increase the median time to final HTA decision for products receiving accelerated approval in England.

Oncology vs non-oncology

There was little difference in the median time to final HTA decision between oncology and non-oncology NCEs in France, 178 versus 187 days, respectively (Figure 3.). However, in Germany, the median time to final HTA decision for oncology NCEs was much longer than for non-oncology NCEs, 298 vs. 220 days, respectively. This may be due to five of the oncology drugs relying on data from single-arm trials and manufacturers wanting to delay a negative opinion from the G-BA. Only two oncology products had final HTA decisions in the UK, which was an insufficient sample for analysis.

Figure 1. Time from regulatory approval to final HTA decision[3-7]

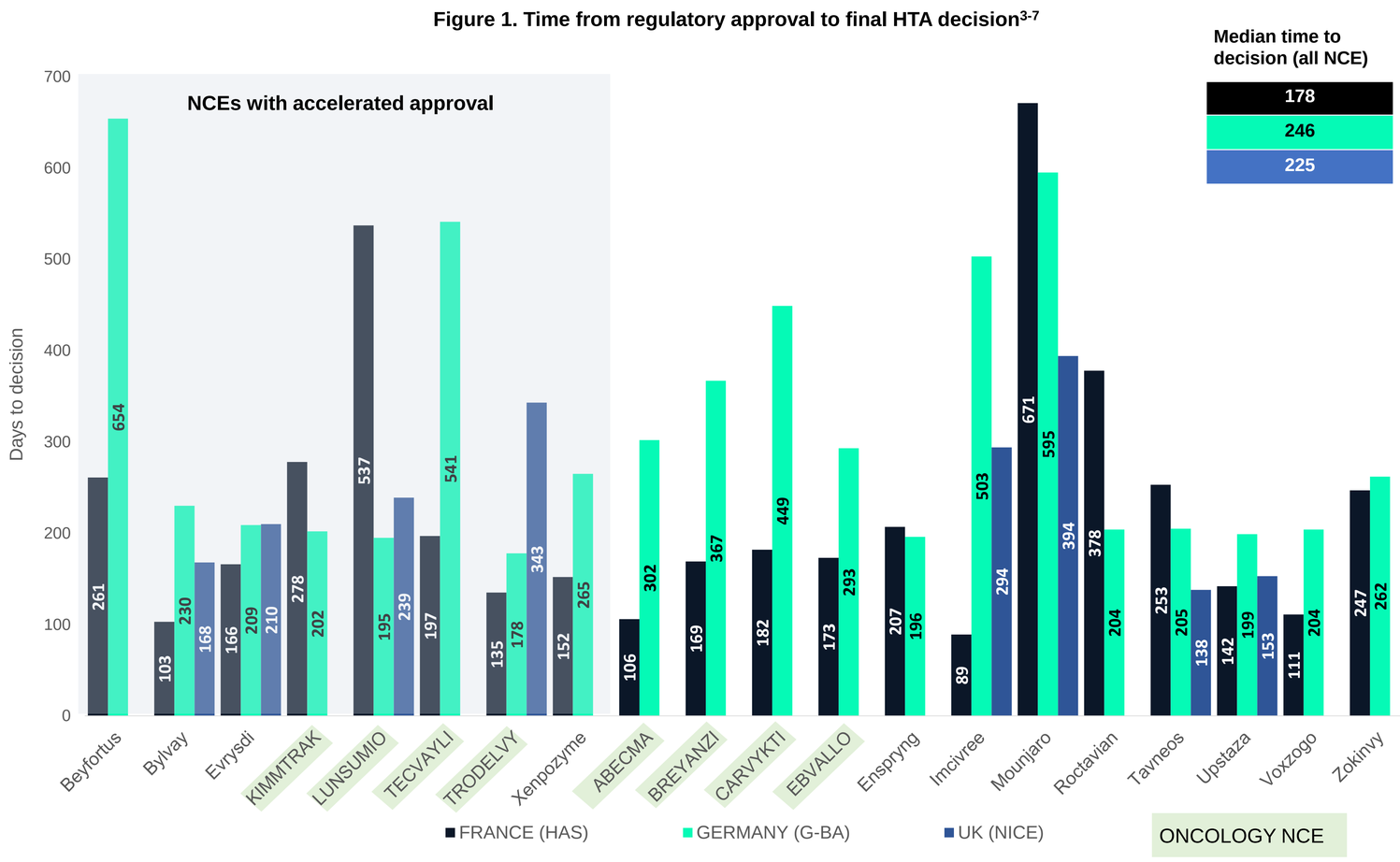


Figure 2. Average time from regulatory approval to final HTA decision for NCEs with and without accelerated approval[3-7]

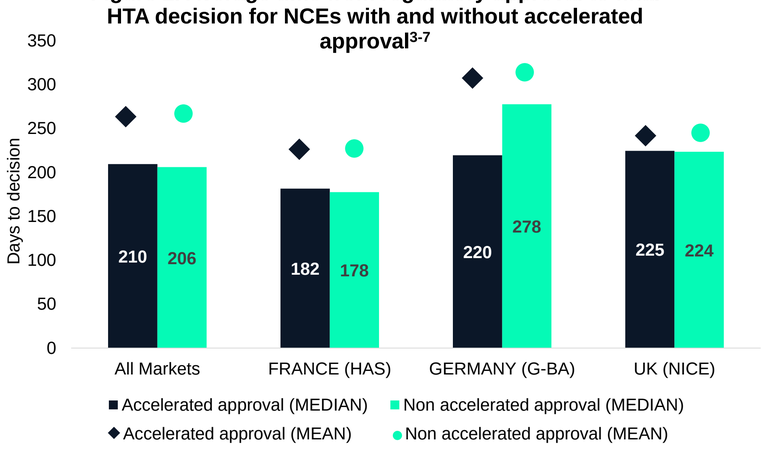
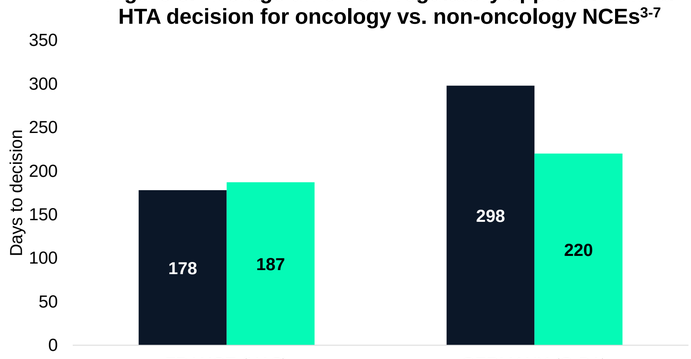


Figure 3. Average time from regulatory approval to final HTA decision for oncology vs. non-oncology NCEs[3-7]



CONCLUSIONS

There appears to be no clear impact on the time from marketing authorisation to final HTA decision for products that went through accelerated approval compared to those that did not.

In general, timelines appear to be impacted due to delays by manufacturers, which in some cases, may be a result of strategic decision-making. For example, in Germany, manufacturers may want to delay placing the product on the market if they feel that the benefit assessment will not be favourable and may result in a suboptimal net price that, until recently, would be visible to other markets. Similarly, in England, manufacturers may not want to make a submission to NICE if they know that their product is unlikely to be cost-effective, which unfortunately has severely limited access to these innovative treatments.

REFERENCES

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Abbreviations: CHMP: Committee for Medicinal Products for Human Use, EMA: European Medicines Agency, G-BA: Federal Joint Committee (Gemeinsamer Bundesausschuss), HAS: French National Authority for Health (Haute Autorité de santé), HTA: Health Technology Assessment, NICE: National Institute for Health and Care Excellence