# Impact of European Medicines Agency clinical trial transparency policies on health technology assessment decisions in the uk

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## Background and objectives

The European Medicines Agency (EMA) aims to foster and protect public health, and considers transparency a key aim in service delivery to patients and society. To this end, the EMA has two policies that govern public access to clinical trial data: Policy 043,[1] which allows anyone to request clinical study reports (CSRs) and Policy 070,[2] which requires clinical trial overviews, summaries, and CSRs from centrally authorized market authorization applications to be published on the EMA's clinical data website. Policy 070 stipulates that clinical trial data should be published 60 days after the European Commission decision and publication of the European Public Assessment Report (EPAR). The policy came into effect in January 2015 for license extensions and in July 2015 for new indications. For older applications and data, or for data pertaining to non-centrally authorized products, Policy 043 applies.

To protect commercial business interests, the EMA allows commercially confidential information (CCI) to be redacted; however, the agency regards very little information to be truly confidential. In the first 5 months of the policy's enforcement, 495 documents were published (pertaining to 13 drugs), with a total of 321,563 pages; of these, only 10 pages had CCI redacted (for only three of the drugs).[3] Clinical data are being accessed under Policy 070: between October 2016 and February 2017, a total of 2,326 users accessed 35,633 documents.[3] The objective of this study was to analyze the use of these data in health technology assessments (HTAs).

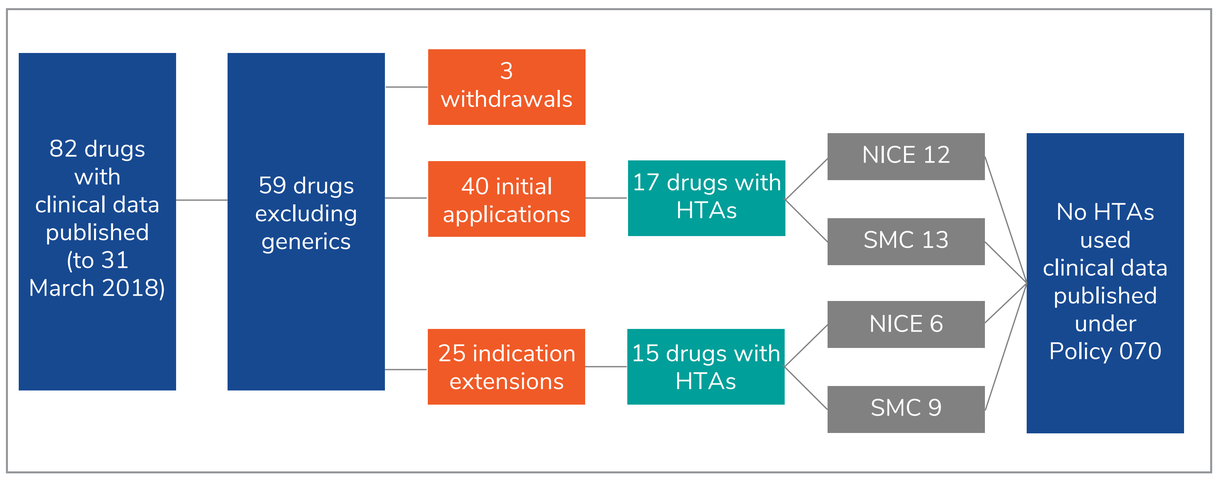
## Methods

The EMA clinical data publication website was searched for drugs with published clinical data (to 31 March 2018) and the EPAR publication date was located using the "find medicine" search function. The websites of National Institute for Health and Care Excellence (NICE) and Scottish Medicines Consortium (SMC) were searched for assessments of these drugs; the reference lists of the appraisal documents were then checked to determine whether the clinical data had been used in the decision-making process.

## Results

A total of 82 treatments had clinical data published up to the cut-off date (31 March 2018); the documents identified included 52 initial applications, 22 indication extensions, and 8 withdrawals of initial applications. When generics were excluded, there were 59 new indications and extensions; 18 had been assessed by NICE and 22 by the SMC.

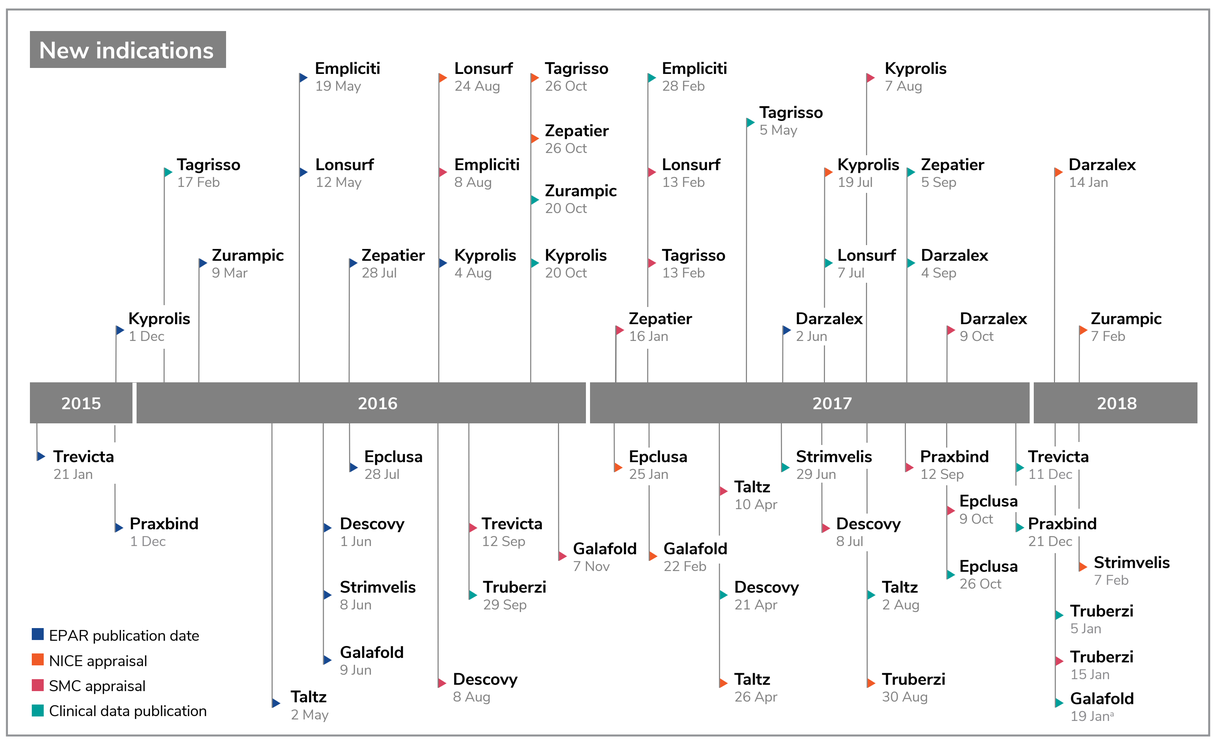
**Figure 1:** Flow diagram of drugs with clinical data published to 31 March 2018




HTA, health technology assessment; NICE, National Institute for Health and Care Excellence; SMC, Scottish Medicines Consortium

HTA decisions occurred between 1.5 and 15 months after publication of the EPAR (see Figures 2 and 3).

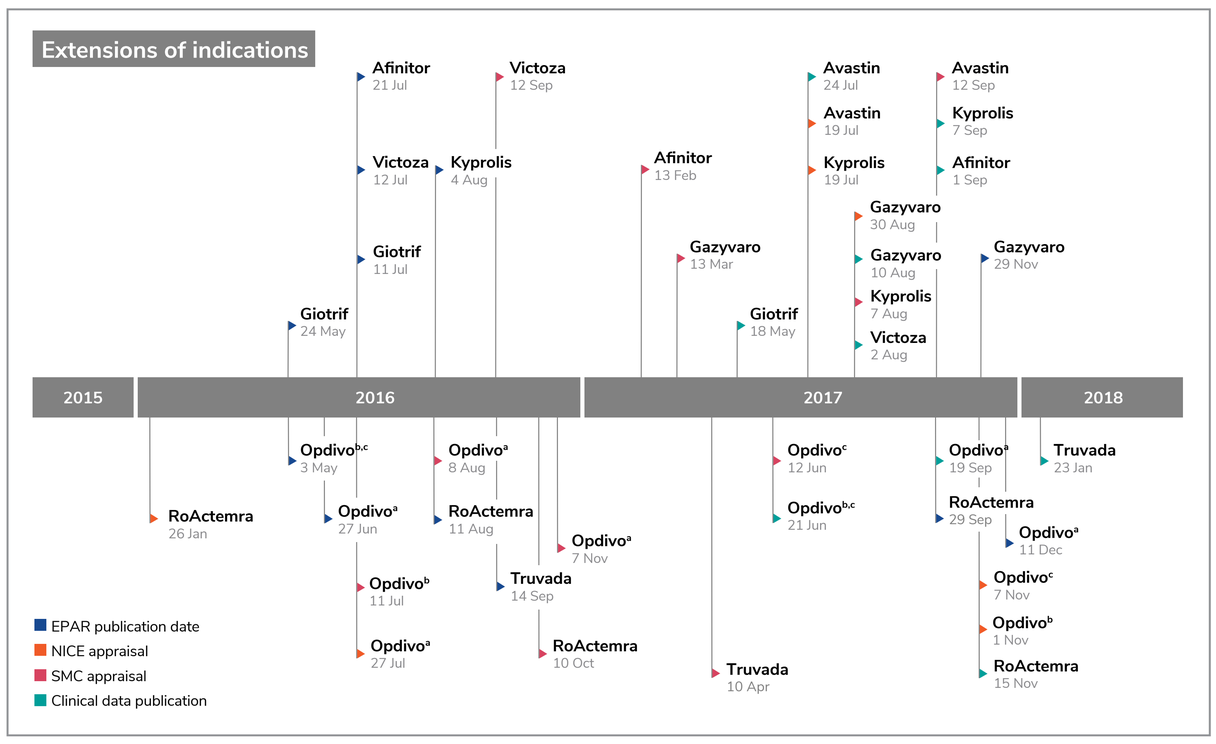
**Figure 2:** Timeline of EPAR, HTA, and clinical data publication for drugs submitted to the EMA for approval of a new indication




[a] Clinical data have not been published as the manufacturer has taken the EMA to court to prevent publication of CSRs

EMA, European Medicines Agency; EPAR, European Public Assessment Report, HTA, health technology assessment

**Figure 3:** Timeline of EPAR, HTA, and clinical data publication for drugs submitted to the EMA for approval of an indication extension




[a] Unresectable metastatic melanoma; [b] Non squamous non-small cell lung cancer; [c] Advanced renal cell carcinoma

EMA, European Medicines Agency; EPAR, European Public Assessment Report, HTA, health technology assessment

HTAs were conducted before the publication of clinical data for 50% and 13% of the drugs for NICE and SMC, respectively. Clinical data were published after the HTA for 50% and 87% of the drugs, respectively. When products underwent HTA before publication of the clinical data, NICE appraisals were published an average of 8.8 months (range: 1.6–21.6 months) and SMC appraisals an average of 8.1 months (range: 0.25–13.9 months) before publication. Conversely, when HTA occurred after publication of the data, NICE published its appraisals an average of 4.6 months (range: 0.6–8 months) and the SMC an average of 3.9 months (range: 0.3–10 months) after publication.

We found no evidence that NICE or the SMC were considering the data published under Policy 070. The clinical data assessed by these agencies were from the submitting companies' CSRs or internal data, or from EPARs, summaries of product characteristics, clinical trials published in journals, or HTAs of competitor products.

## Discussion

Transparency of clinical data is considered to be vital for clinicians, payers, and the general public to have confidence in the drugs they are prescribing, buying, and taking, respectively. Some manufacturers have already taken the initiative to publish all clinical trial data (e.g., GSK, which set up a study register in 2004). Conversely, other manufacturers have resisted publication: Amicus Therapeutics has recently taken the EMA to court to prevent the publication of the pivotal CSRs for Galafold.

While the role of the EMA is to assess the risks and benefits of a product, the objective of HTA agencies is to consider the value to patients and healthcare systems. They therefore consider much of the same data as regulators, from an alternative perspective, but also require access to additional data from trials. The German HTA agency, the Institute for Quality and Efficiency in Heath Care (IQWiG), strongly supported Policy 070 in a document summarizing the agency's comments on the draft policy. It stated: "There is overwhelming evidence, that so far publicly available trial data are insufficient to provide a complete and unbiased picture of a given healthcare intervention. HTA needs additional independent and high quality data sources."[4]

We were therefore surprised to find that the SMC and NICE do not appear to have used the data available through Policy 070. This could be because implementation of the policy is still in its early stages, and clinical data can be published up to 15 months after publication of the EPAR and up to 22 months after HTA. Publishing the clinical data closer to the target of 60 days after the EPAR could allow these data to be considered in the HTA process, although the time between EPAR publication and the SMC's HTA decisions was often short, sometimes only 1 month.

Furthermore, manufacturers already provide HTA agencies with additional, unpublished data, and NICE and SMC request additional analyses for some appraisals. However, HTA agencies could use data published under Policy 070 to gain a more complete view of the evidence, rather than that which the manufacturer chooses to present to them. In addition, both HTA agencies and manufacturers could access the complete trial data for comparator drugs.

Initiatives similar to Policy 070 are in development in Canada and the US. The Protecting Canadians from Unsafe Drugs Act (also known as Vanessa's Law) includes a provision relating to the publication of clinical trial information, which places an obligation on marketing authorization holders to ensure that prescribed information concerning clinical trials is published in a time and manner that will be set out in regulations. The method for this publication is still under development.

The US Food and Drug Administration (FDA) has a pilot program, known as the Clinical Data Summary Pilot (started in January 2018), in which companies have volunteered to publish their clinical data. Upon approval, sections of the pivotal CSRs (including the body of the report, the protocol and amendments, and the statistical analysis plan) will be made available alongside the FDA's regular action package for drug approval.

## Conclusions

The EMA publication site for clinical trial data is being underused in UK HTAs. This is likely to be due to delays in the publication of clinical data submitted in 2015 and 2016, and because HTA agencies have access to unpublished data. When preparing HTA submissions, manufacturers should consider the impact of HTA agencies' access to full trial data, and how they themselves can use the additional data for comparator products.


### References

1. EMA. European medicines agency policy on access to documents (related to medicinal products for human and veterinary use [Policy 043]). 2010.
2. EMA. European medicines agency policy on publication of clinical data for medicinal products for human use (Policy 070). 2014.
3. J G-B. Update on EU transparency in clinical trials Presented at EMWA symposium, Birmingham, 4–6 May 2017.
4. IQWiG. Submission of comments on 'Policy 070 on publication and access to clinical-trial data'. 2013.



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