WHAT DRIVES EU HTA DECISIONS IN MELANOMA? A TARGETED REVIEW ON CLINICAL EVIDENCE CRITIQUES

HTA362

Sequerra C,[1] Morton-West EG,[1] Povsic M[1]*
[1]Amiculum, Bollington, Cheshire, UK. *Email: manca.povsic@amiculum.biz

FINDINGS

We found that HTA agencies differed in their critique of the same data, resulting in conflicting appraisal outcomes. The German IQWiG consistently assessed risk of bias and criticized immature OS data, inappropriate comparators and incomplete QoL data. The French HAS is often aligned with the IQWiG in these areas, while the Spanish AEMPS and the Dutch ZIN frequently commented on clinical relevance. These differing emphases raise questions about how JCAs will reconcile national priorities.

As JCA reports are set to reflect multiple perspectives, they may become more critical by aiming to reflect the diverse perspectives of multiple agencies or may skew toward the views of more influential agencies. With the HAS and IQWiG frequently selected as assessors/co-assessors,[4] there is a possibility that the views of less established agencies may not be adequately represented. As the JCA process evolves, its success will hinge on delivering evaluations that are both methodologically balanced and representative of the diverse priorities across EU HTA systems.

INTRODUCTION

HTA practices originated in France over 50 years ago and have since spread across Europe and the rest of the world.[1] Given the heterogeneity of HTA appraisals and significant duplicated efforts, JCAs began in 2025, allowing coordination of European healthcare agencies and streamlined processes. However, aligning assessments remains challenging, as individual agencies evaluate the same evidence base according to localized influences, such as disease prevalence, patient population and treatment availability, alongside prioritizing various sources of information.[2]
Consequently, it is unclear how different national priorities will be managed as a unified EU-level assessment in the JCA. Melanoma is one of the first therapy areas to undergo JCA and shows highly variable survival rates across Europe, with access to treatments contributing to this disparity.[3]
We explored how divergent HTA approaches across Europe impact the appraisal of melanoma clinical evidence, ahead of the first JCA.

OBJECTIVE

To characterize key critiques of the clinical evidence in EU HTA of melanoma.

METHODS

We performed a targeted review of HTA reports in melanoma published between May 2020 and 2025. Four HTA agencies (IQWiG, HAS, AEMPS and ZIN) were chosen for their availability of melanoma clinical evidence assessments and their frequent selection as JCA assessors.[4] Key drivers of decision making were extracted and compared from appraisals of the clinical evidence.

RESULTS

- 21 melanoma HTA reports were analysed, with the IQWiG accounting for over one-third of papers and the HAS accounting for only two
- Seven technologies were identified; nivolumab monotherapy appeared in the largest number of reports (n=8), whereas nivolumab/relatlimab and tebentafusp appeared in reports from the greatest number of countries (n=3)
- Key drivers of decision making common to all HTA agencies included evaluation of choice of comparator, OS/AE/QoL data and extrapolation of data from adults to adolescents

IQWiG

- Placed great importance on **OS data**: critiqued the high risk of bias in studies with substantial missing follow-up OS data
- Often criticized **AE data**, such as deeming the company's AE analysis as unusable in one dossier because it relied on relative risk instead of time-to-event analyses, and only included AEs that investigators considered related to the study drug rather than reporting all AEs
- Criticized the integrity of **QoL data**: raised concerns in the survey time frames, included in results
- Heavily criticized **comparators**, mentioning company deviation from the appropriate comparator therapy in three dossiers, two of which were deemed unsuitable for complete a benefit assessment
- Did not accept extrapolation of data from adults to adolescents. Also criticized two other dossiers for small patient numbers and for including broader **populations** than those defined by the research question

HAS

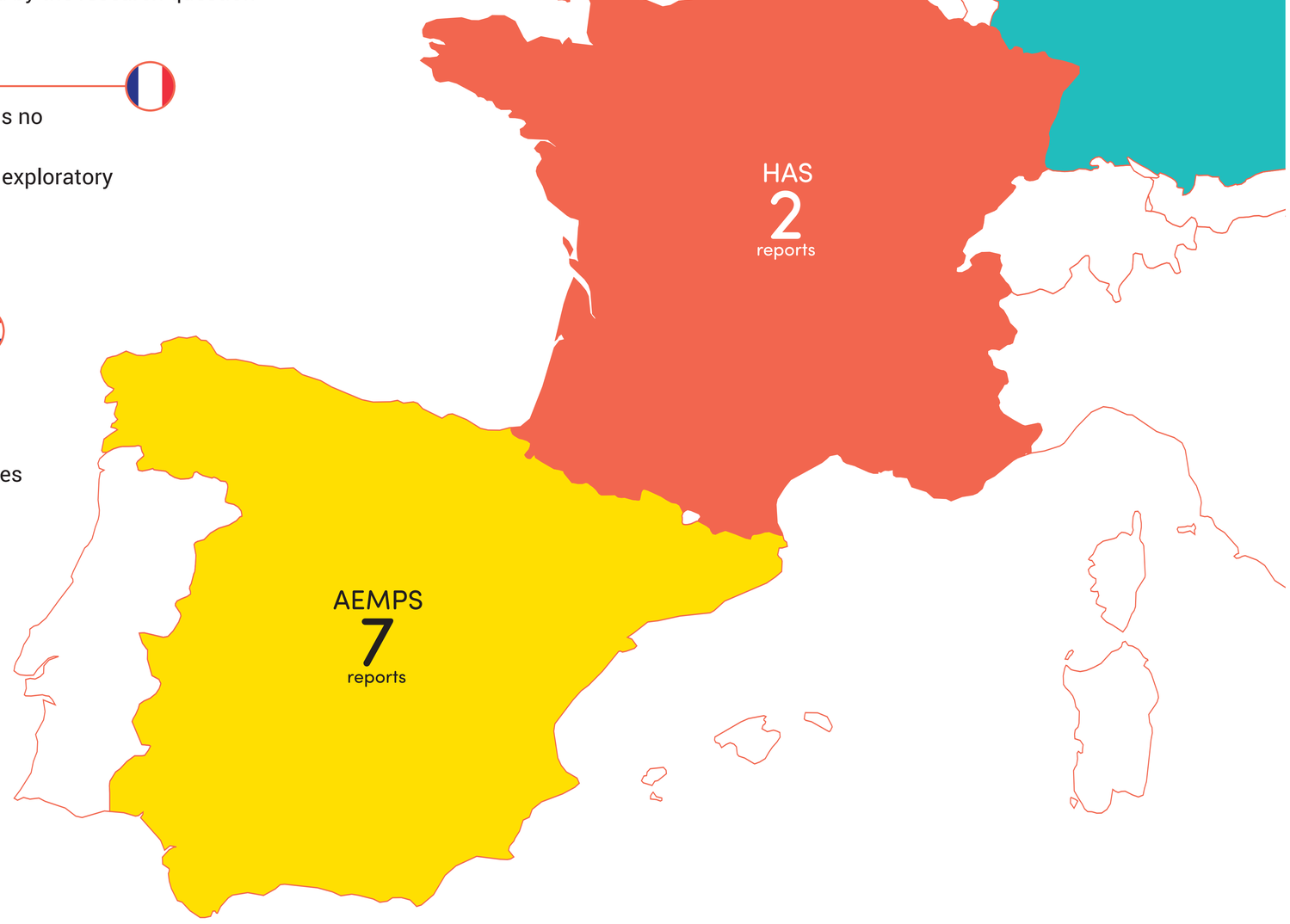
- Placed great importance on **OS data**: granted a low ASMR rating when there was no statistically significant gain in OS
- Criticized the robustness of **QoL data**: would not draw formal conclusions from exploratory analyses of QoL data
- Accepted extrapolation of data from adult **populations** to adolescents

ZIN

- Granted positive approvals in two-thirds of instances, whereby low quality of evidence and indirect comparisons were used for **OS data**, or a surrogate endpoint was accepted because of no OS data
- Considered **AE data** acceptable if QoL remained unchanged and approved medications even with low quality of evidence for SAEs and discontinuation rates
- Linked **QoL data** to conclusions surrounding toxicity
- Placed less emphasis on choice of **comparator** therapies, with comparators often accepted as presented
- Accepted extrapolation of data from adult **populations** to adolescents

AEMPS

- Despite criticizing immature **OS data**, accepted RFS as a suitable surrogate endpoint to infer the effects of treatment
- Accepted the validity of exploratory **QoL data**
- Placed less emphasis on choice of **comparator** therapies, with comparators often accepted as presented
- Accepted extrapolation of data from adult **populations** to adolescents



References

1. Fernandez J *et al. Presse Med* 2025;54:104282
2. Akehurst RL *et al. Value Health* 2017;20:67–76
3. Nurla LA, Forsea AM. *Ital J Dermatol Venereol* 2024;159:128–34
4. European Commission. Updated – list of ongoing joint clinical assessments. 2025. Available at: https://health.ec.europa.eu/latest-updates/updated-list-ongoing-joint-clinical-assessments-2025-09-02_en (accessed September 2025)

Abbreviations

AE, adverse event; AEMPS, Spanish Agency of Medicines and Medical Devices; ASMR, Added Medical Service Rendered; HAS, National Authority for Health; HTA, health technology assessment; IQWiG, Institute for Quality and Efficiency in Healthcare; JCA, joint clinical assessment; OS, overall survival; QoL, quality of life; RFS, relapse-free survival; SAE, serious adverse event; ZIN, Dutch National Healthcare Institute

Amiculum®