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First experiences with the HTA Regulation: **Challenges for small to mid-sized companies**

EAA/EUCOPE Preconference: EU HTA – Approaching Existing Gaps for SMEs
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OMPs and ATMPs present specific challenges

- Majority of Advanced Therapy Medicinal Products (ATMPs) and Orphan Medicinal Products (OMPs) in Europe are typically developed by small to mid-sized companies*

- **Development challenges specific to OMPs and ATMPs include *inter alia:***

  - Small, heterogenous and geographically dispersed populations
  - Lack of knowledge of natural history of disease
  - Target areas of high unmet need
  - Randomised Controlled Trials (RCTs) unethical or impractical
  - Need to rely on surrogate endpoints

- These challenges are recognised in the Regulation (EU) 2021/2282 on health technology assessment:

  - **Recital 24 and Articles 4 (1) and 4 (4) clearly prescribes that the methodologies shall consider the specificities of the health technology** to which the joint work relates, and specificities of new health technologies for which some data may not be readily available, listing *inter alia* OMPs, vaccines and ATMPs

1. Ten Ham RMT, Hoekman J, Hövels AM, Broekmans AW, Leufkens HGM, Klungel OH. Challenges in Advanced Therapy Medicinal Product Development: A Survey among Companies in Europe. Mol Ther Methods Clin Dev. 2018 Oct 11;11:121-130.
2. Tim Wilsdon, Michele Pistollato, Ryan Lawlor, Charles River Associates: "An evaluation of the economic and societal impact of the orphan medicine regulation. Final Report. 2017
3. REPORT FROM THE COMMISSION TO THE EUROPEAN PARLIAMENT AND THE COUNCIL in accordance with Article 25 of Regulation (EC) No 1394/2007 of the European Parliament and of the Council on advanced therapy medicinal products and amending Directive 2001/83/EC and Regulation (EC) No 726/2004
4. European Expert Group on Orphan Drug Incentives: "An EU HTA fit for rare diseases. Part 1: Clinical Evidence in Joint Clinical Assessments". 2023.

9 out of 25 expected JCAs have been started

- 4/9 JCAs started so far are for products from small or mid-sized companies
- 4/9 products have orphan designation
- 2/9 products are ATMPs
- Out of 17 oncology products and 8 ATMPs expected in 2025

International non-proprietary name (INN) / Common Name	Indication - Summary	Substance type (classification)
Autologous melanoma-derived tumor infiltrating lymphocytes, ex vivo-expanded	Treatment of melanoma	ATMP
Tovorafenib	Treatment of paediatric low-grade glioma (LGG)	Chemicals
Sasanlimab	Treatment of bladder cancer	Biologicals
Onasemnogene abeparvovec	Treatment of 5q spinal muscular atrophy (SMA)	ATMP
Lurbinectedin	Maintenance treatment of adult patients with extensive-stage small cell lung cancer (ES-SCLC)	Chemicals
Camizestrant	Treatment of adults with locally advanced or metastatic breast cancer	Chemicals
Tarlatamab	Treatment of extensive-stage small cell lung cancer	Biologicals
Catequentinib	Treatment of synovial sarcoma or leiomyosarcoma	Chemicals
Senaparib	Maintenance treatment of advanced epithelial high-grade ovarian, fallopian tube or primary peritoneal cancer	Chemicals

Experiences with Joint Scientific Consultations

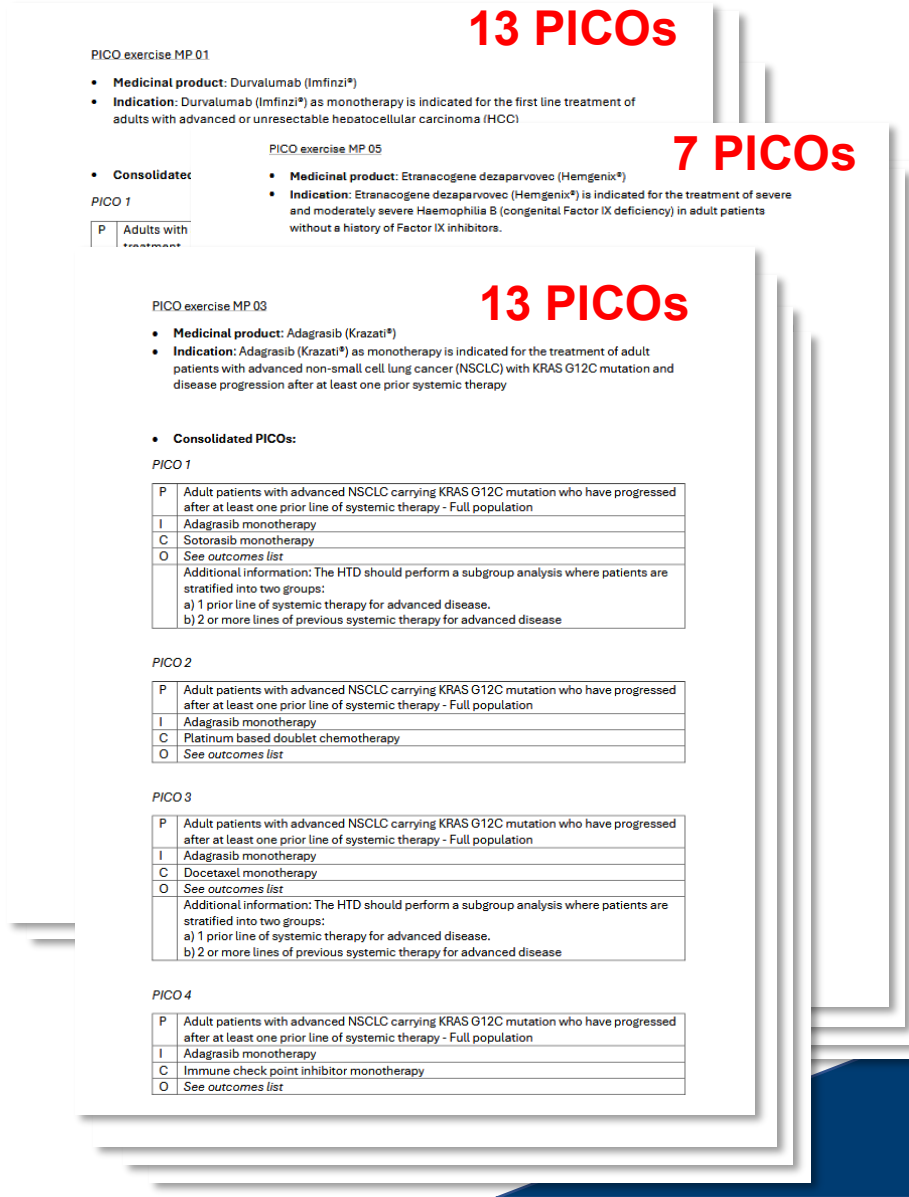
Current difficulties with accessing JSCs

- 7 JSC slots provided in 2025 over 2 request periods, HTA CG aims to gradually scale up the number of slots in 2026
    - **Challenging to get buy-in across teams to apply** for a slot that is not guaranteed
    - The **limited slots and short request periods** makes applying for a JSC difficult, due to shifting clinical trial timelines
    - **Additional guidance on the selection criteria would be helpful**, along more explanation on why specific criteria were not met
- Companies are leveraging national advice meetings, but these cannot provide joint advice for JCA
- With OMPs subject to JCA from 13 January 2028 **there is an urgent need for solutions to increase the JSC slots.** This could include:
    - Earlier introduction of the fee-paying mechanism
    - Collaboration between volunteer MS HTA bodies to provide additional slots
    - Alternative forms of advice, e.g. follow-up advice and written advice

Experiences with Joint Clinical Assessments

Companies need to prepare at risk for JCA

- **Lack of points of interaction** early in JCA means that companies have to prepare at risk for different PICO scenarios
  - Small to mid-sized companies will face a relatively larger burden to prepare for the many possible PICOs
  - The PICOs are communicated only 3 months after start of JCA, while **companies typically prepare for market launch 2 years in advance**
- The MS PICO survey yields a high number of PICOS with many different comparators and subpopulations
  - The **scoping meeting during the scoping phase can be leveraged** by HTA bodies to seek additional information from companies for developing the PICOs
  - Availability of evidence and chosen study designs will impact on the ability to provide answers to all the requested PICOs



Minor adjustment are needed in the beginning

- There is need for room for flexibility and to make adjustment in the first years of the JCA procedure
  - Further clarifications on procedure timelines may be needed
  - IT platform will need to be continuously tailored to users needs
  - Methodological guidance should be updated when needed, e.g. to cover AI and RWE
  - Opportunities for interactions between HTA bodies and companies should be fully leveraged
- Additional clarity on the scope of products subject to JCA is welcome
  - Continuous update and clarification of the scope of products subject to JCA will be needed

QUESTIONS **COMMENTS** **ANSWERS**