HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

CHMP-CAT inter-committee ad hoc working group on "Comprehensiveness" of clinical data in marketing authorisations

CAT Industry interested parties meeting

Presented by Maura O'Donovan on behalf of the working group

Virtual meeting October 26th 2021

Comprehensiveness“ of clinical data
Background and baseline considerations

- Same standards regarding B/R assessment and comprehensiveness apply for all chemicals and biologicals including ATMPs
- Need for consistency across products of the same indication when looking at B/R and comprehensiveness -> be consistent within one indication
- Need for consistency in the assessment and opinion making across committees on principles, arguments, criteria
- Agreed that both RCTs and SATs can lead to comprehensive as well as non-comprehensive data -> SATs are not per se non-comprehensive

Comprehensiveness“ of clinical data
Background and baseline considerations

- At MAA submission, Applicant should discuss regulatory options for approval (standard marketing authorisation, conditional marketing authorisation, authorisation under exceptional circumstances)
- Elaborate on reasons for and the requirements for conditional approval or approval under exceptional circumstances
- In the frame of the discussion on comprehensiveness the criteria should be considered and discussed.

Comprehensiveness criteria

1.Quality of evidence: (including feasibility considerations)

Methodological strengths and weaknesses of the clinical program, with focus on pivotal trial(s). Credibility /attributability of treatment effect and safety findings (both efficacy and safety). Trial conduct and GCP (prohibitive GCP findings?). The judgment of "Quality of evidence" should include feasibility considerations.

Which data/trial designs (e.g. RCT or SAT) can be reasonably expected based on epidemiological considerations? Are there limitations due to the rarity of disease? Is randomization feasible?

Comprehensiveness criteria

2.Efficacy; estimate effect size:

Precision to measure/determine effect size/quantify efficacy, biostatistical considerations.

3.Efficacy: clinical meaningfulness of the endpoint

Clinical endpoint versus biomarker or endpoint with clear mechanistic link to clinical outcome measure. Biomarker could also reflect pharmacological activity but not necessarily reflect clinically relevant outcome.

Comprehensiveness criteria

4.Efficacy; duration of efficacy

Maturity of efficacy follow-up in the context of disease setting and aim of treatment.

5.Safety: exposure

e.g. patient numbers to understand the safety profile, in the context of what can be expected based e.g. on the mechanism of action of the product and specific characteristics of the disease. Have AEs of special interest been captured?

Comprehensiveness criteria

6.Safety; length of follow-up: detection of acute, medium, long-term toxicities. Maturity of follow-up and granularity of AE/ADR detection.

7.Target population vs study population

Has the target population (e.g. age, line of treatment) been covered in the trial population or is part of the indicated patient population missing? If extrapolation is used, is an explicit confirmation by data (post approval) required? Is efficacy driven by a subpopulation which is not representative of the target population?

Comprehensiveness criteria

8.Pharmacological rationale: strong pharmacological rationale e.g. monogenetic disease treated by replacement of the defected gene or gene product by gene therapy or enzyme replacement therapy

9.Natural history/course of the disease: Is additional information added/included that helps in the interpretation of the data and adds context?

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Next steps

- CAT has started Pilot applying the criteria to MAA assessments.
- A revised template, including the comprehensiveness criteria, to be used for procedures starting or restarting from September/October.
- The updated Rapporteur's AR template with guidance is available on the EMA external website: https://www.ema.europa.eu/en/human-regulatory/marketing-authorisation/assessment-templates-guidance#day-80-and-day-120-assessment-report-templates-(containing-guidance)-section
- Review results pilot after 6-12 months.

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Thankyou for your attention ☺
Questions ?