EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Stakeholder meeting on Translarna (ataluren)

Presented by Steffen Thirstrup, Chief Medical Officer (AF-CMO)
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Outline of the presentation

- Overview of the evaluation process for Translarna
- Stakeholders' involvement
- Evidence considered for the evaluation
- Scientific grounds for recommendation
- Transparency
- Next steps

Overview of the evaluation process for Translarna
2014

Duchenne Muscular Dystrophy

A rare disease with recognised seriously debilitating effects on patients

In 2014, Translarna was granted a conditional marketing authorisation (CMA)

- There was uncertainty about the effectiveness
- No major safety issues identified
- A study to confirm effectiveness was requested (Study 20)

Conditional marketing authorisation (CMA)

What is a CMA?

- An early access route for medicines in the EU
- For medicines that fulfil an unmet medical need
- Only granted if the benefit of immediate availability for patients is greater than the risk of less comprehensive data than normally required
- Valid for 1 year; can be renewed annually
- Comprehensive data is generated post-authorisation, according to agreed timelines

Medicines for which a CMA can be given include

- Medicines to target seriously debilitating or life-threatening diseases
- Medicines to fight public health threats in emergency situations (e.g. a pandemic)
- Medicines to treat rare diseases

CMA Info sheet

Overview of evaluation process for Translarna

From 2016 to 2024

2016

Study 20 conducted by the marketing authorisation holder did not confirm effectiveness but indicated a potential subgroup of patients who could be more sensitive to treatment

➡ Study 41 in this population requested

2023

Results from study 41 failed to demonstrate effectiveness

➡ CHMP negative opinion on renewal of CMA

2024

Non-renewal confirmed after re-examination

➡ Current status: CHMP opinion sent to the European Commission for decision

Stakeholders' involvement

- Patients are full members of:
  - COMP, which reviewed the orphan designation in 2005
  - PDCO, which reviewed the paediatric investigation plan (PIP) in 2010
- Patients contributed as experts in scientific advice (protocol assistance), provided for Translarna in 2007, 2012 and 2016
- Scientific Advisory Group (SAG) included:
  - Parents of patients with DMD in 2016, and 2023/2024
  - Clinical experts in 2013, 2016, 2019 and 2023/2024
- Oral explanations at CHMP included parents of patients with DMD from World Duchenne Organisation
- Review of medicine-related documents and news announcements

Evidence considered for the evaluation of Translarna

Applicant submissions

- Initial marketing authorisation application
- Study 20
- Study 41
- Registries

Scientific Advisory Group (SAG) input included

- Parents of patients with DMD in 2016, 2019 and 2023/2024
- Clinical experts in 2016, 2019 and 2023/2024

Oral explanations at CHMP included parents of patient with DMD

Third party interventions >50 received and reviewed by CHMP and EMA

Scientific grounds for recommendation of non-renewal

Two confirmatory studies (Study 20 and 41) did not confirm effectiveness

Data from two registries were not conclusive

- US registry (CINRG DNHS) of patients not treated with Translarna (2006–2016)
- EU registry (STRIDE) of patients treated with Translarna (2015–2022)
- Uncertainties linked to differences between the registries include:
  - Different time points for data collection
  - Use of non-pharmacological treatment (e.g. physiotherapy)
  - Use of other treatments such as steroids
  - Populations with different genetic mutations causing DMD

Transparency

The European Public Assessment Report (EPAR)

Published after European Commission decision

- Data provided by marketing authorisation holder
- CHMP assessment
- Advice from the SAG
- Overview of third-party interventions

Patient actively participating in regulatory meetings

- scientific advice
- scientific advisory groups and committees (COMP, PDCO, CHMP)

Next steps