Milan, 27 november 2023

European Medicines Agency

Domenico Scarlattilaan 6

1083 HS Amsterdam The Netherlands.

Dear Member of the Committee for Medicinal Products for Human Use,

We are responsible, as paediatric neurologists and neurologists, of the primary care for most of the Italian or Resident patients affected with Duchenne Muscular Dystrophy (DMD), due to stop-codon creating point mutations, deletions and other mutations within the dystrophin gene.

In our country, those patients affected by DMD gene stop-codon creating point mutations have been chronically treated with Translarna (ataluren) since EMA and AIFA conditional approval. The near totality (>95%) of the patients treated with Translarna had longitudinal clinical evaluations that have been prospectively recorded into the disease Registry STRIDE, therefore ensuring unbiased coverage of this sub-population. The quality of these data are of clinical study level, as all the centers treating these children are part of a national network that has been collecting prospective longitudinal data as part of an ongoing project on natural history. As part of this project since 2006 all the examiners undergo regular training sessions and assessments of interobserver reliability and the data are collected using the same platform with similar data dictionary. Many of these centers that have also been conducting relevant clinical studies in DMD in the last 20 years (outcome measures, antisense oligonucleotides, gene therapies, among others) using the same measures performed by the same examiners conducting natural history assessments.

The analysis of the age of loss of ambulation in the entire cohort of Italian patients included into the STRIDE registry is similar to that obtained in the whole registry and is significantly different from the data obtained in untreated patients from the CNRG registry.

United Kingdom is another European country with standards of care and epidemiology similar to Italy. Also in that Country, the adherence of our Colleagues and of patients and families to the STRIDE registry was very high, meaning that almost the entire population and not only the better performing patients were entered in this prospective observational study. The cumulative analysis of the Italy and UK treated patients versus the untreated CNRG cohort confirmed a statistically significant difference in favour of ataluren.

It is our individual experience that the clinical trajectories of the disease course in a substantial part of this cohort deviates favourably from what generally observed in DMD, both in terms of mobility, muscle strength and maintenance of lower/upper limb as well as pulmonary functions. Our patients are not only used to this drug, some of them being continuously exposed to it in the last 15 years, but have been reporting advantages in terms of quality of life.

A sudden discontinuation of the accessibility to this drug, while other potential therapeutic avenues are still in a clinical study phase, is likely to affect their quality of life, as well as that of their parents, relatives and caregivers.

It should be recognised that DMD is a severely progressive disorder, with markedly decrease life expectancy and marked disability along the course. Post-poning in a consistent way the critical step of deambulation loss is indeed a major achievement that reflects into better quality of life, higher social and educational

achievements, although also other therapeutic approaches will be needed in a coordinated way in order to cure this disorder.

For these reasons, we would like the express our support to keep Translarna™ (ataluren) as a medical option in the European Union and respectfully request that you grant a positive opinion on re-examination of the renewal of conditional authorization.

Sincerely,

GIACOMO PIETRO COMI
UNIVERSITA' DEGLI STUDI DI MILANO
30.11.2023 08:06:34 UTC

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