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‘Don’t Cut Corners’ If You Want To Succeed, EMA Orphan Drug Head Tells Sponsors

by Eliza Slawther

The head of orphan medicines at the European Medicines Agency has encouraged sponsors to engage with regulators early and take “a little bit longer” to develop their product, rather than cut corners, to boost their chances of marketing authorization success.

Pharmaceutical companies developing drugs for rare diseases should use the European Medicines Agency’s scientific advice and protocol assistance services to avoid delays during the assessment of their marketing authorization applications, according to the EMA’s head of orphan medicines, Kristina Larsson.

During a presentation on 8 May at the RAPS Euro Convergence meeting 2024 in Berlin, Larsson acknowledged that in the orphan drug space, companies often face challenges in generating evidence to support marketing authorization applications.

“Where you have so few patients, you have to make the research that you do count,” she told attendees of the meeting, adding that she “did not want to see studies coming to the agency where we cannot use the data because too many corners have been cut.”

In response to a question from the *Pink Sheet* following her presentation, Larsson said that too often, the regulatory procedure for rare disease medicines “takes quite a long time because there are questions” around the data.

However, she acknowledged that it was “always easy to look with hindsight and think ‘that should have been done’.”

Sponsors can maximize their chances of regulatory success by trying to plan their development process “well in advance,” and should “discuss with regulators to see if an endpoint is [suitable] to be used for a statistical analysis plan,” Larsson continued.

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“My take home message is that it is really good to have early and repeated engagement with the agency on your development,” she said.

She also recommended that companies “take a little bit longer” to develop medicines, for instance by waiting until the 12-month mark to perform a statistical significance analysis of their endpoint, rather than doing this at six months.

For some medicines, reaching statistical significance might not be necessary, Larsson said, but the EMA “would maybe have to look at the totality of data” instead, and would also need to see evidence of a drug providing a measurable benefit to patients.

The EMA can help companies early on in the development process by offering scientific advice and protocol assistance. These are provided by the agency’s human medicines advisory committee, the CHMP, on the recommendation of the scientific advice working party (SAWP).

Companies can seek advice at any stage of the development process. The EMA provides scientific advice by answering specific questions from the drug developer regarding a specific medicine.

Protocol assistance is very similar to scientific advice, but it is only available to developers of designated orphan medicines for rare diseases.

Companies can also benefit from using the EMA’s PRIME scheme for promising medicines for unmet medical needs, although the scheme has a high rejection rate and might not be suitable for all medicines. (Also see "*PRIME Scheme: EMA Says Yes To Hookipa, Bluejay & 89bio But No To Six Others*" - Pink Sheet, 5 Apr, 2024.).

HTA Regulation Benefits

Larsson also spoke about the positive benefits of the upcoming Regulation (EU) 2021/2282 on health technology assessment (HTA), which will begin to apply from January 2025. A major component of the regulation is joint clinical assessments (JCAs), which are essentially relative effectiveness assessments and will be conducted by designated national HTA experts at the EU level.

As JCAs will be carried out in parallel with the EMA's centralized marketing authorization process, it would mean that the HTA and regulatory stakeholders “will talk together and exchange quite a lot of information,” Larsson said.

“Instead of sort of sprinting after each other, we can now hopefully gently jog along together,” she added, noting that “hopefully at the end, the outcome is that the HTA will be done just after the regulatory assessment,” meaning that patients would be able to access medicines more quickly.

The HTA Regulation will be rolled out in a phased manner, meaning that it will initially only apply to medicinal products with new active substances for oncological indications and to advanced therapy medicinal products (ATMPs).

JCAs will apply to orphan drugs from 13 January 2028 onwards, and to all other medicines approved under the EU centralized procedure from 2030.

The HTA Regulation has not been without criticism, however. Many industry representatives have argued that the proposed timelines for JCAs, which will see member states given 140 days to prepare the assessment scope but companies just 90 days to prepare their dossiers in response, are unworkable. (Also see "*Lack Of Industry Involvement In EU HTA Scoping Process Exacerbates 'Unworkable' Timelines*" - Pink Sheet, 19 Apr, 2024.).