Decision in case 222/2020/EWM on how the European Medicines Agency dealt with the authorisation of the medicine Kalydeco for use by children with a specific form of cystic fibrosis

Decision
Case 222/2020/EWM - **Opened on** 21/02/2020 - **Decision on** 03/06/2020 - **Institution concerned** European Medicines Agency (No maladministration found) |

The case concerned how the European Medicines Agency (EMA) dealt with a request to authorise a medicine called Kalydeco. Kalydeco is used to treat cystic fibrosis, a serious illness caused by a number of different gene mutations.

The complainant, whose three-year old son has a specific form of cystic fibrosis, expressed concerns that EMA had incurred delays in approving the drug for use in children with this specific form of cystic fibrosis.

During the inquiry, on 20 April 2020, EMA informed the complainant and the Ombudsman that its scientific experts had, after examining all the scientific and medical evidence they needed, approved Kalydeco for use in children with the form of cystic fibrosis that affects the complainant's child.

The Ombudsman found that no unjustified delays had occurred. EMA was also clear and transparent, and showed great care, in its contacts with the complainant.

The Ombudsman concluded that there was no maladministration by EMA and closed the inquiry.

Background to the complaint

1. The complainant's three-year-old son has cystic fibrosis, a serious genetic illness that affects the lungs, the digestive system and other organs. Various gene mutations can cause cystic fibrosis. The complainant's son has a R117H gene mutation.

2. The complainant considers that a medicine, Ivacaftor (trade name Kalydeco), can be used to treat his son. Early intervention with Kalydeco will, he hopes, prevent the organ damage

associated with cystic fibrosis, thus enabling his son to live a longer, healthier and more productive life.

3. In July 2012, the European Medicines Agency (EMA) approved the use of Kalydeco for the treatment of cystic fibrosis caused by **certain** gene mutations [1] [Link]. In 2015, it was approved for use **in adults** with cystic fibrosis caused by a R117H mutation. This meant that the only way children such as the complainant's son could have access to Kalydeco was through off-label [2] [Link] use or in the context of a clinical trial [3] [Link].

4. The complainant contacted EMA in December 2018 urging it to approve the use of Kalydeco for children with the R117H mutation. In his correspondence, he voiced his concerns that EMA has incurred delays in authorising the use of Kalydeco for children with this mutation.

5. EMA and the complainant exchanged correspondence between December 2018 and September 2019. EMA informed the complainant that in order for Kalydeco to be authorised for use in children, the company marketing Kalydeco, Vertex, had to apply to EMA for an extension of the marketing authorisation. Any such application for an extension would have to include evidence (for example from appropriate clinical trials) that would show that the use of Kalydeco in children with this gene mutation was safe and effective. EMA stated that it had not received any applications aimed at obtaining an authorisation to use Kalydeco in children with the R117H gene mutation.

6. EMA also informed the complainant of alternative ways his son could be treated with Kalydeco, namely through off-label use or in a clinical trial.

7. In August 2019, EMA informed the complainant that it had asked Vertex to send EMA all newly-obtained data that Vertex had on the use of Kalydeco in children with the R117H mutation. It assured the complainant that once it received the data, as part of an application for a marketing authorisation extension, it would assess it as quickly as possible.

8. In October 2019, Vertex submitted an application to EMA for an extension of the approval of the use of the medicine in children with the gene mutation.

9. On 4 February 2020, the complainant turned to the European Ombudsman.

The inquiry

10. The Ombudsman opened an inquiry into the alleged delays incurred by EMA in approving the use in of Kalydeco in children with the R117H gene mutation.

11. In the course of the inquiry, on 3 March 2020, the Ombudsman's inquiry team held a meeting with representatives of EMA [4] .

Arguments presented to the Ombudsman

12. The complainant stated that unless his son can use Kalydeco, he may have to undergo a double lung transplant and his life expectancy will be seriously affected. He stated that EMA had delayed approving the use of Kalydeco for children suffering from cystic fibrosis caused by the R117H gene mutation, despite the fact that there was evidence that Kalydeco works for these children. He expressed his fears that it would take a further 2 to 3 years before his son could have access to Kalydeco. In the meantime, his son may suffer irreversible and serious effects on his health.

The Ombudsman's assessment

13. It is not within the Ombudsman's mandate to question the merits of scientific evaluations carried out by specialised scientific agencies. The Ombudsman's inquiry therefore does not cover the substantive medical and scientific assessment of the safety and efficacy of Kalydeco. Moreover, it is crucial that scientific bodies are allowed to carry out their work in full serenity, free from undue external pressure. This is all the more important as regards the assessment of the safety and efficacy of medicines.

14. The aim of this inquiry was to clarify the status of EMA's assessment of the use of Kalydeco in children with the R117H gene mutation, to ensure that no unnecessary administrative delays had occurred and to ensure that EMA was keeping the complainant as informed as possible as regards the status of EMA's assessments.

15. EMA cannot authorise or extend the authorisation of a medicine without having received an application from the pharmaceutical company to authorise the medicine or to extend the authorisation. Prior to October 2019, Vertex had not submitted an application to EMA to extend the authorisation of Kalydeco to cover use in children with the R117H gene mutation.

16. Vertex submitted its application for an extension of the authorisation of Kalydeco to cover use in children at the end of October 2019.

17. Once it received the application, EMA transferred the application to its Committee for Medicinal Products for Human Use (CHMP), which is the EMA committee responsible for assessing the safety and efficacy of human medicines.

18. The CHMP **began its assessment of the application on 2 November 2019** .

19. The Ombudsman concludes that no delays were incurred at the start of the evaluation process.

20. EMA then informed Vertex that the CHMP would follow an accelerated 90-day-timetable for the assessment of the application, as foreseen in the relevant legislation. [5] [Link]

21. The relevant legislation allows EMA to extend this deadline if it requires additional information to complete its assessment. [6] [Link]

22. EMA has explained to the Ombudsman that the CHMP regularly requests additional data, or information on the interpretation of the data.

23. In the present case, the CHMP asked Vertex for additional information on 30 January 2020. The assessment was therefore placed in a default 'clock-stop'.

24. This clock-stop gave Vertex the opportunity to provide the CHMP with the requested information. This enabled EMA to conclude its assessment. On 30 April 2020, [7] [Link] the CHMP recommended extending the authorisation of Kalydeco for use in children with the R117H gene mutation. [8] [Link]

25. The CHMP has therefore concluded its assessment six months after Vertex submitted its application.

26. While EMA cannot authorise or extend the authorisation of a medicine without having received an application from the pharmaceutical company, the Ombudsman notes that EMA, in an effort to make more efficient the eventual assessment of the CHMP, held a pre-submission meeting with Vertex in April 2019 in which it discussed the availability of additional data supporting the use of Kalydeco in children with R117H mutation, and whether such data could be submitted as part of an extension of indication application.

27. In light of all of the above, the Ombudsman finds that no unjustified administrative delays occurred.

28. The Ombudsman finds that EMA corresponded clearly, transparently and with great care with the complainant.

29. EMA provided considerable information to the complainant as regards the status of its discussions with Vertex. It also informed the complainant about ways for his child to get access to Kalydeco (for example, via off-label use or via a clinical trial). It acknowledged the difficult situation of his son, but also sought to ensure that it did not create unrealistic expectations before the CHMP had arrived at its decision on the safety and efficacy of Kalydeco for use in children with the R117H gene mutation.

30. The Ombudsman also welcomes the speed and thoroughness with which EMA has responded throughout the inquiry, providing complete information on the approval process and background [9] .

31. The Ombudsman notes that on the evening of 30 April 2020, the day the CHMP approved the use of Kalydeco for use in children with the R117H gene mutation, EMA took the initiative to contact the complainant by email to inform him of this news.

32. The complainant contacted the Ombudsman soon thereafter to express his relief and happiness with the news.

33. The Ombudsman finds no maladministration as regards the manner in which EMA communicated with the complainant.

Conclusion

Based on the inquiry, the Ombudsman closes this case with the following conclusion:

There was no maladministration by the European Medicines Agency.

The complainant and the European Medicines Agency will be informed of this decision **.**

Emily O'Reilly

European Ombudsman

Strasbourg, 03/06/2020

[1] [Link] See https://www.ema.europa.eu/en/documents/product-information/kalydeco-epar-product-information_en.pdf [Link]

[2] [Link] Off-label use refers to the practice of prescribing a medicine that has been approved for at least one indication, age group, dosage or route of administration, for a use other than the approved indication, age group, dosage, or route of administration. Off-label use is generally legal unless it violates ethical guidelines or safety regulations.

[3] [Link] Kalydeco had been approved for the treatment of children with cystic fibrosis caused by nine specific gene mutations. The complainant's son has a different mutation.

[4] [Link]https://www.ombudsman.europa.eu/en/report/en/127891 [Link]. In light of the developing Covid-19 crisis, the meeting took place virtually.

[5] [Link] In this respect, see: Article 16(2), second subparagraph, of Commission Regulation (EC) No 1234/2008, in conjunction with Annex V.

[6] [Link] At Day 90, the CHMP will adopt the Opinion on the type II variation application or issue a request for supplementary information; in this respect, see: Article 16(3) of Commission

Regulation (EC) No 1234/2008 which states “Within the period referred to in paragraph 2, the Agency may request the holder to provide supplementary information within a time limit set by the Agency. The procedure shall be suspended until such time as the supplementary information has been provided. In this case the Agency may extend the period referred to in paragraph 2”.

[7] [Link] For more detailed information, please refer to the report of the meeting of 3 March 2020.

[8] [Link]https://www.ema.europa.eu/en/medicines/human/summaries-opinion/kalydeco-0 [Link] .

[9] [Link] See in this respect the detailed report of the meeting of 3 March 2020: https://www.ombudsman.europa.eu/en/report/en/127891 [Link].