25 July 2025
EMA/243003/2025
EMEA/H/C/004354

Withdrawal of application for the marketing authorisation of Aplidin (plitidepsin)

PharmaMar withdrew its application for a marketing authorisation of Aplidin for the treatment of multiple myeloma.

The company withdrew the application on 23 July 2025 during a re-examination.

What is Aplidin and what was it intended to be used for?

Aplidin was developed as a medicine for treating adults with multiple myeloma (a cancer of the bone marrow) who have received at least three prior cancer treatments (including bortezomib and either lenalidomide or thalidomide). Aplidin was to be used in combination with dexamethasone (another medicine used to treat multiple myeloma).

Aplidin contains the active substance plitidepsin. It was to be available as powder and solvent to be made up into a solution for infusion (drip) into a vein.

Aplidin was designated an 'orphan medicine' (a medicine to be used in rare diseases) on 16 November 2004 for the treatment of multiple myeloma. Further information on the orphan designation can be found on the Agency's website.

How does Aplidin work?

The active substance in Aplidin, plitidepsin, blocks a protein called eEF1A2. eEF1A2 is involved in breaking down wrongly folded proteins, which are toxic to myeloma cells. By blocking eEF1A2, plitidepsin causes the accumulation of these proteins in multiple myeloma cells, damaging them and ultimately leading to their death.

What did the company present to support its application?

The company presented the results of one main study involving 255 patients with multiple myeloma who had been treated with at least 3 other cancer medicines. In this study, Aplidin plus dexamethasone was compared with dexamethasone on its own, and the main measure of effectiveness was progression-free survival (how long patients lived without their disease getting worse).

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

How far into the evaluation was the application when it was withdrawn?

The evaluation had finished and the European Medicines Agency had recommended refusing marketing authorisation. The company had requested a re-examination of the Agency's recommendation, but it withdrew the application before this re-examination had finished.

What did the Agency recommend at that time?

Based on the review of the data and the company's response to the Agency's questions, at the time of the withdrawal, the Agency had recommended refusing marketing authorisation for Aplidin for the treatment of multiple myeloma.

The Agency was concerned that the data from the main study showed only a modest increase of around one month in the time patients given Aplidin lived without their disease getting worse, compared with those treated with dexamethasone alone. In addition, improvement in overall survival (how long patients lived overall) was not sufficiently demonstrated. Regarding safety, severe side effects were reported more frequently with the combination of Aplidin and dexamethasone than with dexamethasone alone.

What were the reasons given by the company for withdrawing the application?

In its letter notifying the Agency of the withdrawal of the application, the company stated that their decision was based on a change in their marketing strategy.

Does this withdrawal affect patients in clinical trials?

The company informed the Agency that there are no consequences for patients in clinical trials with Aplidin. If you are in a clinical trial and need more information about your treatment, speak with your clinical trial doctor.