



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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#### Update of 23 May 2025:

By its judgment of 28 October 2020 in Case T-594/18, the General Court annulled the Commission Implementing Decision of 17 July 2018 refusing marketing authorisation for Aplidin. The judgment was subsequently appealed before the Court of Justice in Joined Cases C-6/21 P and C-16/21 P. On 22 June 2023, the Court of Justice set aside the judgment and referred the case back to the General Court (Case T-594/18 RENV).

On 28 June 2024, the European Commission revoked the Commission Implementing Decision of 17 July 2018 refusing marketing authorisation for Aplidin. Following the adoption of [this decision](#), the Commission has requested EMA to re-assess the application for Aplidin.

Upon receipt of the final grounds of the re-examination request from the applicant for Aplidin, EMA's human medicines committee, the CHMP, will re-examine its opinion and issue a final recommendation.

20 December 2017

#### Questions and answers

## Refusal of the marketing authorisation for Aplidin (plitidepsin)

On 14 December 2017, the Committee for Medicinal Products for Human Use (CHMP) adopted a negative opinion, recommending the refusal of the marketing authorisation for the medicinal product Aplidin, intended for the treatment of multiple myeloma.

The company that applied for authorisation is PharmaMar.

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## **What is Aplidin?**

Aplidin is a cancer medicine that 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.

## **What was Aplidin expected to be used for?**

Aplidin was expected to be used to treat 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 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 [here](#).

## **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).

## **What were the CHMP's main concerns that led to the refusal?**

The CHMP 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.

Based on the above, the CHMP was of the opinion that the benefits of Aplidin did not outweigh its risks and recommended that it be refused marketing authorisation.

## **What consequences does this refusal have for patients in clinical trials?**

If you are in a clinical trial and need more information about your treatment, contact the doctor who is giving it to you.