IMPORTANT NOTICE

IN AGREEMENT WITH THE ITALIAN MEDICINES AGENCY (AIFA)

18th July 2024

Manidipine-based medicinal products: risk of the development of a cloudy peritoneal effluent associated with the use of manidipine in peritoneal dialysis patients

Dear Doctor,

The marketing authorisation holders of manidipine-based medicinal products would like to inform you, in agreement with the Italian Medicines Agency (AIFA), of the following:

Summary

- **Serious cases of a cloudy peritoneal effluent have been reported with the use of manidipine in patients undergoing peritoneal dialysis.**
- **The cloudiness is due to an increase in the concentration of triglycerides in the peritoneal effluent and tends to resolve after stopping manidipine.**
- **The association between manidipine and the cloudy peritoneal effluent should be recognised, as the latter could be confused with infectious peritonitis resulting in unnecessary hospitalisation and the administration of empirical antibiotic therapy.**

General information on the safety issue

Manidipine is a dihydropyridine calcium channel blocker with antihypertensive activity and nephroprotective properties, which is authorised to treat mild to moderate essential hypertension and, in combination with delapril, patients whose blood pressure is not adequately controlled with delapril or manidipine alone.

Some serious cases of cloudy peritoneal effluent have been reported in patients undergoing peritoneal dialysis and being treated with medicinal products containing mandipine.

After considering the evidence available in pharmacovigilance databases including the European database (EudraVigilance), and in the published scientific literature, as well as data submitted by a marketing authorisation holder based on post-marketing experience, the Pharmacovigilance Risk Assessment Committee (PRAC) of the European Medicines Agency (EMA) concluded that manidipine is associated with a cloudy peritoneal effluent in patients undergoing peritoneal dialysis. Therefore, the EMA recommended that the Summary of Product Characteristics (SmPC) and Package Leaflet (PIL) of manidipine

medicinal products should be updated to include this risk as an adverse reaction with unknown frequency and the corresponding warnings about the importance of considering this association for differential diagnosis.

It is an association that should be recognised as a cloudy peritoneal effluent could be confused with infectious peritonitis, which could lead to unnecessary hospitalisation and the administration of empirical antibiotic therapy.

The cloudiness is due to an increase in the concentration of triglycerides in the peritoneal effluent and tends to resolve after stopping the manidipine.

Invitation for reporting

Health professionals are expected to report adverse reactions in patients taking manidipine to the Italian Medicines Agency in accordance with the national spontaneous reporting system https://www.aifa.gov.it/content/segnalazioni-reazioni-avverse

The Italian Medicines Agency (AIFA) would like to take this opportunity to remind all healthcare professionals of the importance of reporting suspected adverse drug reactions as an indispensable tool for confirming a favourable benefit-risk relationship under actual conditions of use. Reports of suspected adverse reactions should be sent to the pharmacovigilance officer of the Facility which the professional belongs to. This notice is also published on the AIFA website (www.aifa.gov.it), and it is recommended that the website be regularly checked for the best professional information and service to citizens.