

# Magistral preparation of fumagillin for the treatment of Enterocytozoon bieneusi microsporidiosis: between active pharmaceutical ingredient shortage and major therapeutic need

S. Filali<sup>1</sup>, C. Dupuis<sup>1</sup>, A. Louguet<sup>1</sup>, M. Rabodonirina<sup>2</sup>, N. Laverdure<sup>3</sup>, Ph. Poirier<sup>4</sup>, A. Von Kanel<sup>4</sup>, B. Lapras<sup>1</sup>, C. Pivot<sup>1</sup>, C. Paillet<sup>1</sup>, **C. Merienne<sup>1</sup>**, F. Pirot<sup>1</sup>

<sup>1</sup>Preparation and Control of Medicines Unit, FRIPHARM platform, Pharmacy, Edouard Herriot Hospital - Hospices Civils de Lyon ; <sup>2</sup>Parasitology and Medical Mycology Department, Croix-Rousse Hospital - Hospices Civils de Lyon ; <sup>3</sup>Pediatric gastroenterology, hepatology and nutrition department, Femme Mère Enfant Hospital - Hospices Civils de Lyon ; <sup>4</sup>Parasitology and mycology department, Clermont-Ferrand University Hospital - Gabriel Montpied Hospital.

## BACKGROUND

### EBM

Severe and potentially fatale diarrhea  
**Life-threatening patients**

### API

- Shortage
- Chemically unstable

**Fumagillin**  
Hematotoxic antimicrobial

**Discontinuation of the only commercial product shown to be effective**

## MATERIALS & METHODS

A resquest for fumagillin sample, addressed to the former marketing authorization holder with information to ANSM, was granted with an API transfer (-80°C)

Upon receipt, API analysis :

- Infrared (IR)
- UV spectrometry
- High performance liquid chromatography coupled to mass spectrometry (HPLC-MS)

Formulation :

Suspension of fumagillin (20 mg/ml) dispersed in propylene glycol dicaprylate/dicaprate (oil carrier)

Suspension analysis :

- Fumagillin content
- UV spectrometry
- HPLC-MS

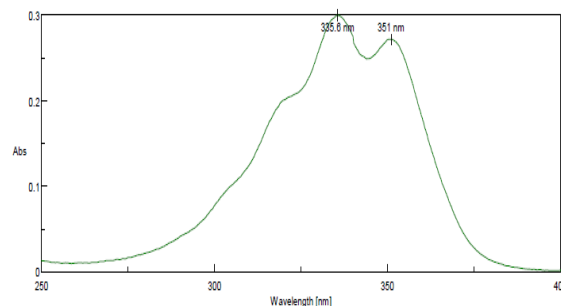
Waiver request to treat, three patients with EBM to the Commission du Médicament et des Dispositifs Médicaux Stériles (COMEDIMS) and four other patients to the ARS

## OBJECTIVES

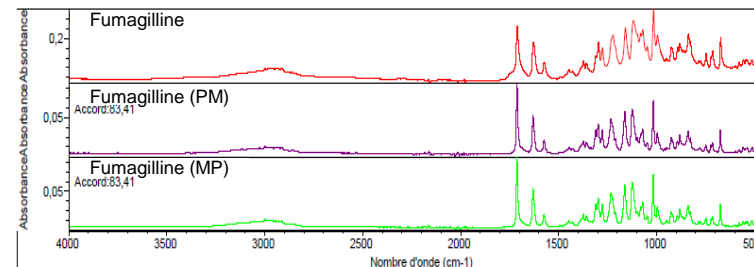
We report a **translational approach** that made available a treatment for EBM in immunocomprised patients.

## RESULTS & DISCUSSION

- Analyses of API and fumagillin content of MP were within physicochemical specifications under strict adherence to storage conditions limiting hydrolysis and photodegradation of the API
- Waiver request granted by COMEDIMS and ARS



Graph 1. UV spectrum fumagillin (MP)



Graph 2. IR spectrum fumagillin (API and MP)



## CONCLUSION

Despite context of API shortage, we developed a fumagillin magistral preparation (MP), which highlights the importance of developing a **network of national and European API providers**. Developing this fumagillin MP is a concrete and translational pharmaceutical solution to a **major therapeutic need**.