

Original article

# Antifungal stewardship: Implementation in a French teaching hospital

## *Expérience de la prescription raisonnée des antifongiques*

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### Abstract

**Context.** – Invasive fungal infections are responsible for severe morbidity and mortality in immunocompromised patients. New, more effective antifungal drugs have been available for more than a decade but are extremely expensive suggesting the need for judicious prescribing.

**Intervention.** – Infectious diseases physicians had been closely collaborating with hematologists on antimicrobial use since 2000. In 2002, an antifungal stewardship program (ASP) was implemented. It included discussing antifungal prescriptions with a dedicated infectious diseases physician twice weekly, telephone counseling 5 days a week from 9 A.M. to 7 P.M., and training meetings for junior/senior prescribers organized at least once yearly. The same year, a multidisciplinary group drafted evidence-based local guidelines on the use of antifungals in the hematology unit, which were published in 2004. These guidelines included decision algorithms and preprinted prescription forms that allowed only guideline-recommended drugs for a given indication. These guidelines have been updated and simplified at least every 2 years (current version 7.0; 2012).

**Results.** – Between 2003 and 2012, in the 20-bed isolated hematology sector (allograft and acute leukemia induction chemotherapy patients), antifungal consumption decreased by 40% (from approximately 1000 to 620 defined daily doses per 1000 hospitalization days). Invasive fungal infections (IFI) remained stable in the whole 51-bed department, during the study period, with 1 to 2 IFI per month. In 2005, the 12-week survival rate for 29 cases of invasive aspergillosis was 72%. Early IFI related mortality has decreased recently.

**Conclusion.** – A permanent collaboration between hematologists and an infectious diseases physician can improve antifungal prescribing.  
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**Keywords:** Antifungal stewardship; Invasive fungal infection; Pharmaco-economics

### Résumé

**Contexte.** – Les infections fongiques invasives ont une morbidité et une mortalité élevée chez les patients immunodéprimés. Les nouveaux antifongiques, efficaces, disponibles depuis une décennie ont un coût très élevé nécessitant une prescription raisonnée.

**Intervention.** – Une collaboration entre infectiologues et hématologues existait depuis 2000. En 2002, une action spécifique a été lancée sur les antifongiques avec : une discussion des prescriptions d'antifongiques lors des 2 vacations par semaine de l'infectiologue, un avis téléphonique disponible 5 j/7 de 9 à 19 h, une réunion de formation au moins annuelle pour internes et séniors. La même année, un groupe multidisciplinaire a rédigé en 2004 des recommandations sur l'usage des antifongiques au CHRU de Lille, dans le service d'hématologie. Elles comportaient des algorithmes décisionnels et des ordonnances préimprimées ne permettant que l'utilisation des antifongiques autorisés pour l'indication choisie. Ces recommandations ont été revues et simplifiées, au moins tous les 2 ans (version en cours : n° 7.0, 2012).

**Résultats.** – Entre 2003 et 2012, la consommation du secteur protégé (20 lits d'allogreffe/leucémie aiguë) a diminué de 40 % (100 à 620 DDJ/1000 JH). Le nombre d'infections fongiques diagnostiquées dans l'ensemble du service (51 lits) est resté stable avec 1 à 2 cas par mois. La survie de 29 aspergilloses, évaluée en 2005 était de 72 % à 12 semaines. La mortalité précoce liée à l'infection fongique a diminué ces dernières années.

**Conclusion.** – Une concertation permanente entre infectiologue et hématologue permet d'améliorer la prescription des antifongiques.  
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**Mots clés :** Antifungal stewardship ; Infections fongiques invasives ; Pharmacoéconomie

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## 1. Introduction

Invasive fungal infections (IFI) are severe complications occurring in hematology patients, especially in patients presenting with acute myeloid leukemia, and/or having undergone allogeneic hematopoietic stem cell transplantation. The diagnosis is difficult, and even if the therapeutic armamentarium has considerably increased in recent years, the optimal treatment strategy is complex and remains a matter of controversy.

Antifungal treatments account for an important and increasing part of the cost of drugs for hematology patients.

This is why the concept of antifungal stewardship has been developed in some units, like what has been implemented for antibiotics by mobile teams of infectious diseases specialists and referents in antibiotic therapy.

We report the antifungal stewardship program (ASP) that was developed with hematologists at the Lille Regional Teaching Hospital.

A literature review proved that this concept remained much less developed than for antibiotics, and that, according to the authors of published articles, the primary objective of these programs seemed to be the mastery of costs, the ecological concern being a secondary objective.

## 2. Monitoring of antifungals at the Lille Regional Teaching Hospital

### 2.1. History

The collaboration between the 2 specialties began in 2000, when, during an outbreak of aspergillosis, hematologists asked infectious disease specialists for their expertise and support. This led to drafting the first formal recommendations for the prescription of antifungal at the Lille Regional Teaching Hospital in 2002. They were elaborated according to a structured method, based on creating multidisciplinary work groups, systematic literature reviews, critical reviewing by experts not belonging to the work groups, and grading of recommendations according to evidence-based medicine. Updates have been made frequently, along with the evolution of knowledge. The fourth version of the recommendations, the largest one, was drafted in November 2004 and published the following year [1]. It took into account both the approval labeling modifications of some agents and the synthesis drafted after to the consensus conference on candidosis and aspergillosis grouping the French Society of Anesthesiology and Intensive Care, the French Society of Infectious Diseases, and French Society of Intensive Care in May 2004, with the participation of the French Society of Hematology, the French Society of Medical Mycology, and French Society of Bone Marrow Graft ([www.infectiologie.com/site/medias/\\_documents/consensus/antifongiques-court-04.pdf](http://www.infectiologie.com/site/medias/_documents/consensus/antifongiques-court-04.pdf)) [2]. These recommendations were put on-line on the Nord-Pas-de-Calais Infectious Diseases site ([www.infectio-lille.com](http://www.infectio-lille.com))

where they are still available as archives ([www.infectio-lille.com/Antibiotiques/referentiel-antifongiques-chru-lille2004.pdf](http://www.infectio-lille.com/Antibiotiques/referentiel-antifongiques-chru-lille2004.pdf)).

The 2004 recommendations included a decision tree (Fig. 1) to help the clinician choose the adequate therapy. Models of individual prescription forms had also been developed on which the clinician had to choose a clinical case (prophylaxis, empirical treatment, documented treatment, etc.). The prescription of various antifungal agents was open or not, according to the indication, thanks to a system of white boxes (prescription possible) or black boxes (prescription not possible). The duration of treatment was also strictly limited to 7 days, compelling the clinician to renew the prescription for the treatment.

This prescription system, effective when it was implemented, was sometimes circumvented by a diagnosis made to obtain the wanted agent. It was abandoned in 2011 to come back to a system of prefilled prescriptions agent by agent, mentioning the indications, the precautions for administration, and the contraindications.

The successive recommendations versions were progressively simplified and clarified. The current 7th version is only 3 pages long with 2 additional pages of references and the decision tree was removed. The current version may be downloaded on [www.infectio-lille.com/index.php/anti-infectieux.html](http://www.infectio-lille.com/index.php/anti-infectieux.html).

We estimated that the simplest and easiest way for clinicians to use these was to consider successively the various possible cases: primary or secondary prophylaxis, empirical treatment, preemptive treatment or treatment of a proven or probable fungal infection.

Besides treatments, the recommendations strongly bear on diagnostic elements, and especially on performing an early thoracic CT scan, and on the systematic research, during the neutropenia periods, of *Aspergillus* antigenemia (and, more recently, beta-D-glucan, and serum dosages of triazoles antifungals). The recommendations were sent to all physicians, including residents.

The results of discussion on antifungal prescription were also directly integrated in the decision trees for the antibiotic therapy of febrile neutropenia. These 2 page-long recommendations are reviewed every year and adapted to the evolution of local ecology.

### 2.2. Means implemented

The referent infectious disease specialist comes to the hematology unit twice a week to discuss patient files, and is available by phone at any time. During this bi-weekly meeting, all the patients of the isolated sector with a suspected infection are systematically reviewed, whereas patients of the conventional sector are reviewed case by case at the physician's request. The "supervising" infectious disease specialist helps train residents and regularly organizes case discussions or more informal or convivial meetings, including in the evening.

The prescription guide is updated at least every 2 years in close collaboration with the hematologists.

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