Trends in the Utilization of, Spending on, and Prices for Outpatient Antifungal Agents in US Medicaid Programs: 1991–2009

Vibha C. A. Desai, MS[1]; Teresa M. Cavanaugh, PharmD, MS[1]; Christina M. L. Kelton, PhD[2]; Jeff J. Guo, PhD[1]; and Pamela C. Heaton, PhD[1]

[1]James L. Winkle College of Pharmacy, Academic Health Center, University of Cincinnati, Cincinnati, Ohio; and [2]Carl H. Lindner College of Business, University of Cincinnati, Cincinnati, Ohio

ABSTRACT

Background: The incidence of invasive fungal infections (IFIs) has increased substantially in the recent past. Advances in medical technology, including broad-spectrum antibiotics, may increase the risk for fungal infections. Moreover, immunocompromised patients with cancer, HIV/AIDS, and/or transplants are susceptible to IFIs. Meanwhile, superficial fungal infections (SFIs) are common and can be difficult to cure.

Objective: To provide a historical perspective on a dynamic market with expensive medications, this study describes trends in the utilization of, spending on, and average per-prescription spending on outpatient antifungal medications individually, in classes (for IFIs or SFIs), and overall, by the US Medicaid programs from 1991 to 2009.

Methods: The publicly available Medicaid State Drug Utilization Data, maintained by the Centers for Medicare & Medicaid Services, were used. Annual prescription counts and reimbursement amounts were calculated for each of the antifungals reimbursed by Medicaid. Average per-prescription spending as a proxy for drug price was calculated by dividing reimbursement by the number of prescriptions.

Results: Overall utilization for Medicaid beneficiaries remained steady, with 4.56 million prescriptions in 1991 and 4.51 million in 2009. Expenditures rose from $93.87 million to $143.76 million (in current-year US$) over the same time period. The drop in the utilization of first-generation azoles over the last 5 years of the study period can be explained in part by the movement of dual-eligibles from Medicaid to Medicare Part D and in part to a rise in fungal infections better treated with second-generation azoles or echinocandins. Whereas the average per-prescription price for generic (oral) fluconazole was $8 in 2009, the price per prescription of branded (intravenous) voriconazole was $2178.

Conclusions: Overall spending by Medicaid on outpatient antifungal medications increased more slowly than did the growth of the Medicaid programs from 1991 to 2009. However, the utilization of antifungal agents for IFIs increased almost 10-fold over this period, far outpacing the rise in the number of Medicaid beneficiaries. (*Clin Ther*. 2012; 34:2118–2131)

Key words: antifungal agents, antifungal drug utilization, invasive fungal infections, Medicaid, superficial fungal infections.

INTRODUCTION

Fungi are microorganisms, ubiquitous in the environment, which, usually harmless, become opportunistic pathogens in certain individuals. Fungal infections can be classified broadly as life-threatening invasive fungal infections (IFIs) (eg, aspergillosis, candidiasis, histoplasmosis, cryptococcosis), which may affect the vital organs such as the heart, lungs, and brain, and superficial fungal infections (SFIs) (eg, tinea pedis, sporotrichosis, vulvovaginal candidiasis), which may affect the skin, hair, nails, genitalia, and mucosa.

The incidence of IFIs has increased substantially over the recent past.[1,2] Advances in medical technology, such as total parenteral nutrition, invasive moni-

The data in this article were presented in poster format at the Annual Meeting of the International Society for Pharmacoeconomics and Outcomes Research, Baltimore, Maryland, May 2011.

Accepted for publication September 6, 2012.
http://dx.doi.org/10.1016/j.clinthera.2012.09.003
0149-2918/$ - see front matter

toring devices, and broad-spectrum antibiotics, may increase the risk for fungal infections.[3] Adding to a growing population of susceptible hosts are immunocompromised individuals such as those with cancer, HIV/AIDS, and transplants, who, should they contract an IFI, have a mortality rate ranging from 40% to 85%.[4] Amphotericin B deoxycholate was the first drug approved by the US Food and Drug Administration (FDA) for the treatment of IFIs, in the 1950s.[5] It has a broad spectrum of activity and high efficacy and remained the mainstay of treatment for life-threatening IFIs for >30 years; however, it has been associated with high rates of nephrotoxicity and infusion-related reactions (50%–90%).[3] The introduction of the first azole antifungal agents, fluconazole in 1990 and itraconazole in 1992, substantially expanded the options for treatment.[6] Later, between 1996 and 2000, new lipid preparations of amphotericin B, associated with fewer adverse reactions than amphotericin B deoxycholate, became available.[7] In the last decade, echinocandins such as anidulafungin, caspofungin, and micafungin, as well as second-generation azoles such as posaconazole and voriconazole, with broad spectrums of activity and reduced adverse events, entered the antifungal market.[8–10] Flucytosine, first synthesized in 1957, is almost always used concurrently with another antifungal drug, usually amphotericin B deoxycholate, due to concerns over emerging resistance.[11] It is used primarily to treat cryptococcosis but is also valuable for some cases of severe invasive aspergillosis.[12]

SFIs are the more common form of fungal infections. In most cases, SFIs are more easily treatable, although they can be difficult to cure. Tinea pedis, or athlete's foot, affects ~70% of adults at least once in their lifetime.[13] Uncomplicated vulvovaginal candidiasis, which affects 75% of women at least once in their lifetime, has cure rates ranging from 70% to 95% when treated with azole antifungals or nystatin.[13] Complicated vulvovaginal candidiasis occurs in immunocompromised patients, and the cure rate in these patients ranges from 67% to 80%.[14] Onychomycosis, an SFI of the nails, is the most difficult type of SFI to treat, having high treatment failure and recurrence rates, ranging from 20% to 50%.[15,16] Oral terbinafine and itraconazole are the first-line agents for onychomycosis. Topical therapy includes ciclopirox nail lacquer.[17,18] Oropharyngeal and esophageal candidiasis occurring among HIV/AIDS patients requires frequent courses of antifungal treatment, primarily with topical or oral azoles.[19–21] Nystatin, a widely used antifungal medication for SFIs and of bacterial origin, was isolated from *Streptomyces noursei* in 1950 and was patented in 1957.[22] Cutaneous, vaginal, mucosal, and esophageal *Candida* are sensitive to nystatin[23]; however, due to the toxicity of nystatin, no intravenous formulations of nystatin have been approved for use in the United States.[13] Ketoconazole, approved by the FDA in the 1980s as the first oral treatment of non–life-threatening systemic fungal infections, is now little used for systemic infections but is often used to treat dermatophytosis (ringworm) and is used as well for histoplasmosis, chromoblastomycosis, and paracoccidioidomycosis.[24]

Limited pharmacoeconomic analysis exists in the antifungal therapeutic area.[25] One study reported that, in 2004, US $2 billion in annual hospital costs in the United States could be attributable to IFIs.[26] In terms of the total cost of treatment, more expensive antifungal agents may be more cost-effective than lower-cost agents that are less effective and/or more toxic.[27] Medicare and Medicaid are the 2 largest public payers for antifungal medications in the United States. Because Medicare Part D is relatively new (implemented in January 2006), a long-term trend in public spending on antifungals can be captured best by studying spending by Medicaid. Based on a literature search, no studies have reported the trends in the utilization and spending on antifungal agents. Accordingly, the aims of the present study were to assess the trends in utilization of, spending on, and prices for antifungal agents indicated for IFIs and SFIs in Medicaid beneficiaries. The results should be informative to health care providers and payers who must balance the efficacy, safety, and costs of antifungal medications on a daily basis.

METHODS

A descriptive, retrospective data analysis was conducted using the publicly available National Summary Files from the Medicaid State Drug Utilization Data maintained by the Centers for Medicare & Medicaid Services (CMS), as part of the Medicaid Rebate Program, for the years 1991 to 2009.[28] The database includes Medicaid beneficiaries from 49 states (all but Arizona), together with the District of Columbia. Each record in the database contains an 11-digit National Drug Code (NDC), drug name, year and quarter of Medicaid expenditure, number of pharmacy claims,