Post-marketing study to assess the safety, tolerability and effectiveness of Fungisome™: An Indian Liposomal amphotericin B Preparation

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ABSTRACT
Background: In May 2003, an indigenously developed liposomal amphotericin B (Fungisome™) was introduced in the Indian market for the treatment of systemic fungal infections and visceral leishmaniasis. The present post marketing study assessed the safety and effectiveness of Fungisome™ in actual clinical practice.

Methods: The present study was carried out for a period of 6 months (Jun-Nov 2004), a year after the introduction of the drug. A list of doctors who had prescribed and procured the drug was obtained from the distributor. Consent to participate and scrutinize the patients’ source notes were obtained from the concerned doctors. All patients who had received Fungisome™ treatment were included. Data was collected from the patient’s source notes on a predesigned proforma. They were then analyzed by descriptive statistics. Cost of Fungisome™ was calculated on the basis of dose used and number of days of treatment.

Results: Data were available for 109/144 patients from 35/40 physicians. Fungisome™ was administered at 1–3 mg/kg/day for 7–76 days. No serious adverse events related to the drug were observed in the study. Mild infusion-related adverse events were reported in 40 (36%), moderate in 11 (10%) of patients and severe in 2 (1.8%). None of the adverse events were certain to Fungisome™ exposure. 28 (25%) were possible, and 13 (11.9%) were unlikely. Of the 91 assessable patients (received at least eight doses of Fungisome™) for efficacy complete response was observed in 67 (73.6%), 16 (17.5%) had partial responses, and 8 (8.7%) of patients had no response. The acquisition cost per day and per course treatment of different fungal infections ranged from (apprx) Rs 4500-8000 and 0.9 -2.1 lakh respectively.

Conclusion: This postmarketing study documents the safety, tolerability, effectiveness and cost advantage of indigenously developed liposomal amphotericin B in the treatment of systemic fungal infections and febrile neutropenia in actual clinical practice.

KEY WORDS: Post marketing, Liposomal amphotericin B, Systemic fungal infections, Fungisome™

Incorporation of amphotericin B into liposomes alters the pharmacokinetic properties of the drug, but it allows to retain significant in vitro and in vivo activity against fungal species, including Candida, Aspergillus, Cryptococcus, Mucormycosis, and Leishmania donavani. Fungisome™ is an intravenous liposomal preparation of amphotericin B developed by the Department of Clinical Pharmacology, Seth GS medical college and KEM Hospital, Mumbai, in collaboration with the Department of Biochemistry, Delhi University, with funding from Department of Biotechnology, Government of India, in the early 1990s in an effort to decrease the toxicity of conventional amphotericin B. Pharmaceutical, pre-clinical, and clinical studies were submitted to the Drugs Controller General of India (DCGI) and this led to the approval for manufacture and marketing of this drug. On 21 May 2003, Fungisome™ was introduced by Life care Innovations Pvt. Ltd., Gurgaon, Haryana, India, in Indian market for the treatment of systemic fungal infections and visceral leishmaniasis. The drug was introduced as 10, 25, and 50 mg amphotericin B/vial. Our experience in premarketing prospective clinical trials with Fungisome™ in adult and pediatric patients having systemic fungal infections has shown that this formulation both safe and effective. However the safety, effectiveness, and pattern of use of drug in postmarketing may be different from as assessed in clinical trials due to differences in prescribing physicians and patients. Key differences between clinical trials and the real world are the limited patient numbers and heterogenous patient population (e.g., pregnant women, children, elderly, and those predisposed to develop adverse events are frequently excluded). Effectiveness and safety when used for indications or in dosages other than initially tested remain unknown and knowledge about interactions with concomitantly used drugs is not always complete. Moreover, physicians prescribing habits are often unknown at the time of market entry and may vary over time due to commercial promotions, cost containment measures,
changing attitudes, and changing guidelines. Thus, it is necessary to undertake a continuous surveillance of newly introduced drugs under field conditions for a defined period of time after granting the marketing authorization. The present study was carried out for a period of 6 months (Jun 2004-Nov 2004), a year after the introduction of Fungisome™ into the market.

The primary objective was to assess safety, tolerability and efficacy of Fungisome™ and the secondary objective was to assess direct cost with its use (actual cost/patient).

**Methods**

The protocol for the study was approved by the institutional ethics committee. Confidentiality of data was maintained throughout the conduct of the study.

**Study design**

A retrospective analysis based on hospital source notes (patients’ records) and pharmacy records. The study is ongoing and the results of 109 patients are presented in this paper.

**Study procedure**

Fungisome™ is a prescription drug available only from a specific distributor in each city. A list of doctors from Mumbai, Delhi, Ahmedabad, and Pune, who had prescribed and procured Fungisome™ for their patients, was obtained from the distributor of the Life care Innovations Pvt Ltd. The doctors were contacted personally by the first author (S H). Their consent to participate in this study and permission to scrutinize the patients’ source notes without disclosing identity of the patient was obtained. Complete list of patients treated with Fungisome™ in large hospital was obtained from the doctor or from the hospital pharmacy. The doctor or his assistants then made the patients’ source notes available from the record section for retrieving of data as per study requirements. Inquiries were made with concerned doctors regarding any inconsistencies, incorrect or missing data in the source notes.

**Inclusion criteria**

All the patients, who received Fungisome™ irrespective of its indications, age of patient, comorbidity, and concomitant medications, were included in this study. No exclusion criteria were applied other than use of study drug so that maximum information could be captured.

**Data capture**

The study design comprised of retrieving of the data from the patients’ source notes by the first author. The following parameters were recorded viz. patients demographics, fungal disease, duration of fungal disease, site of fungal disease, organism causing the disease, microbiological diagnosis of fungal species (by either smear, culture, histology) imaging, clinical findings, and immunology, other associated/causative disease, characteristics and pattern of use of Fungisome™ viz. daily dose of Fungisome™ (if other than 1 mg/kg/day), duration of treatment, Fungisome™ treatment completed/stopped temporarily/permanently discontinued (reasons for temporarily/permanent discontinuation), reason to start Fungisome™ therapy, details of previous antifungal therapy and other concomitant treatment.

**Assessment of safety**

The adverse events were classified onto the following categories. Infusion-related adverse drug events such as chills, fever as well as other adverse drug events (e.g. headache, bodyache, nausea, rash, dizziness, anemia, tachyphoea, bronchospasm, thiorombophlebitis, anorexia, vomiting, and others).

Laboratory abnormalities consisting of haematological, serum electrolytes, liver function test, renal functions test, urine routine, and others. Biochemical parameters were recorded as abnormal if the deviation from pretreatment value was more than 10% and if the values were outside the normal range cited by that laboratory. If any unusual/unexpected or serious adverse event (SAE) not listed in product insert of Fungisome™ was noticed, then an additional reporting form for SAE was used, which gave a brief clinical history, relevant past history, description of unusual/SAE, onset, duration, severity, association with Fungisome™, action taken and management. The severity was graded as mild (not requiring treatment), moderate (requiring treatment), severe (requiring discontinuation of therapy),[5] and causality (cause-effect relationship) as certain, probable/likely, possible, and unlikely[5] and causality assessment in consultation with treating physician.

**Assessment of efficacy**

Assessment of effectiveness of Fungisome™ therapy was based on the clinical, radiological and microbiological cure.[1] Clinical efficacy was recorded in all patients treated for at least 8 days with Fungisome™. Those receiving less than eight maintenance doses were considered non-evaluable or non-assessable. The response in evaluable patients was then classified as:

- **Complete response:** When two consecutive fungal cultures done at 7 days interval were negative and a complete resolution of disease as confirmed on clinical, radiological and or microbiological criteria occurred for more than 8 weeks after stopping the treatment. In case the subject died due to causes other than the drug or fungal infection before completion of the treatment of amphotericin B (liposomal), if weekly culture or histopathology revealed no fungus then such patients were considered to be responded completely provided the postmortem (if done) in these patients showed no evidence of fungal elements. In case of febrile neutropenia complete response was defined as resolution of fever during neutropenic period, absence of emergent fungal infection and subjects’ survival for at least 7 days post-Fungisome™ therapy.[8]

- **Partial response:** When only partial resolution of disease occurred or recurrence of disease is observed during follow up or lost to follow up.

- **Failure of response:** When no response to drug therapy is observed within 2 weeks or after increasing the dose to the maximum tolerated level (up to 3 mg/kg/day).

**Statistical methods**

Descriptive statistics were used and percentage of patients with adverse events and percentage of patients who were responders out of the total subjects enrolled were calculated. The direct cost/patient/course with Fungisome was also calculated.

**Results**

At the time of writing this paper, 40 physicians had used Fungisome™ in 144 patients across four cities. Complete data were available for 109/144 patients from 55 physicians. Of these 109 patients, 91 were assessable and 18 were nonassessable patients for efficacy. Follow up data until 8 weeks were available in 67/109 patients, 13 patients succumbed to their underlying disease and the remaining 29 patients were lost to follow up. Of the 18 nonassessable, 16 patients did not complete eight doses of intravenous Fungisome™ and the remaining two patients received Fungisome™ gurgles thrice daily for 10 days as local application for mucositis of the oral cavity. There were 74 males (67.9%) and 35 females (32.1%) and the mean age
was 30 years (Mean ± SD is 30.88 ± 22.59). The mean weight of the patients was 36 kg (36.49 ± 22.82 kg). Of the 91 evaluable patients 45 (49.5%) patients had proven fungal infections and remaining 46 (50.5%) were treated empirically with Fungisome™ for febrile neutropenia (these patients were suspected to have fungal infections, in the presence neutropenia). Those patients who were febrile for at least 96 h after therapy with broad spectrum antibacterial agents or showed the presence of symptoms or signs consistent with invasive fungal infection, excluding superficial mucocutaneous infection, while on antibacterial therapy(9) were also included).

Safety

For the analysis of safety, all 109 patients enrolled in this study were included. Fungisome™ in the dose of 1, 2 and 3 mg/kg/d were used in 86, 9 and 14 patients respectively. A total of 2776 infusions of Fungisome™ with dose ranging between 1 and 3 mg/kg/day were administered in this study. Of 2776 infusions, mild-infusion-related adverse events were observed in 40 (36%) subjects who did not require any treatment. Moderate adverse events were treated with pheniramine and hydrocortisone injection in 10% (11) of patients and severe adverse events warrant discontinuation of therapy in 1.8% (n = 2). None of the adverse events was certain (n = 0) to Fungisome™ exposure and 11% were probable (n = 12), 25% were possible (n = 28), and 11.9% were unlikely (n = 13) [Table 1]. No SAEs related to the drug were observed in this present study. Apnea and mild bronchospasm were reported in one patient of bronchial asthma after 4 h of Fungisome™ administration. This patient was treated with pheniramine and hydrocortisone injection. However, this patient did not warrant discontinuation of therapy and Fungisome™ administered (rechallenge) on the subsequent day did not cause apnea and bronchospasm.

Effects on biochemical parameters: Of 109 patients treated with Fungisome™ none showed increase in serum creatinine by more than twice the baseline value. Data of the 4 patients with preexisting renal dysfunction, who had received more than 40 doses (each received 40, 56, 57 and other 76 infusions respectively) of Fungisome™ was specially analyzed for the effect on creatinine (Baseline serum creatinine 2.5 mg/dl). Patient who received lower than 40 doses also did not have any significant alteration in creatinine. Serum potassium decreased from pretreatment normal value to value below normal during treatment in 8 (16.3%) of the 26 neonates and pediatric patients. These were restored to normal by treatment with oral potassium chloride supplement. However, hypokalemia was not seen in any of the adult patients treated with Fungisome™. Thrombocytopenia was reported in two neonates with candidiasis after 7 and 9 doses of Fungisome™ therapy, respectively. These patients were subsequently treated with platelet transfusion. Decrease in hemoglobin by 1.7g% was seen in one patient with mucormycosis after 25 days of Fungisome™ therapy. This patient’s hemoglobin returned to normal after withholding the drug for 1 week and treatment with hematinics. Subsequent reintroduction of Fungisome™ 1 mg/kg/day for 32 days did not cause any decrease in haemoglobin concentration.

Efficacy assessment: Overall 67/91 (73.6 %) patients had complete response and 16 (17.5%) had partial response (Table 1). In all the patients Fungisome™ was started in the dose of 1-3 mg/kg/day and duration of treatment ranged from 7-57 days for complete response. Of the 45 proven fungal infections 23 were candidiasis, 11 mucormycosis, 9 aspergillosis, 2 cryptococcal meningitis. Complete response was produced in 19/23 (82.6%) candidiasis, 4/9 (44.4%) aspergillosis, 1/2 (50%) cryptococcal, and 8/11 (72.7%) mucormycosis patients. 16 (17.7%) patients had partial response. Of the 46 suspected fungal infections, in the presence neutropenia complete response was produced in 35 / 46 (76.08%) of patients in the dose range of 1-3 mg/kg/day and duration of treatment ranged

Table 1: Safety and efficacy of Fungisome in observational post marketing study

<table>
<thead>
<tr>
<th>Efficacy (n=91)</th>
<th>Febrile neutropenia</th>
<th>Candidiasis</th>
<th>Mucormycosis</th>
<th>Cryptococcosis</th>
<th>Aspergillosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of Rx (Days)</td>
<td>7-76</td>
<td>7-30</td>
<td>10-57</td>
<td>13-40</td>
<td>9-56</td>
<td>91</td>
</tr>
<tr>
<td>Complete Response</td>
<td>35 (76.08)</td>
<td>19 (82.6)</td>
<td>8 (72.7)</td>
<td>1 (50)</td>
<td>4 (44.4)</td>
<td>67 (73.6)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>6 (13)</td>
<td>3 (13.0)</td>
<td>3 (27.3)</td>
<td>1 (50)</td>
<td>3 (33.3)</td>
<td>16 (17.5)</td>
</tr>
<tr>
<td>No Response</td>
<td>5</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>8 (8.7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ADRs (n=109)</th>
<th>Febrile neutropenia</th>
<th>Candidiasis</th>
<th>Mucormycosis</th>
<th>Cryptococcosis</th>
<th>Aspergillosis</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage</td>
<td>Mild</td>
<td>28</td>
<td>8</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Severe</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>35</td>
<td>11</td>
<td>2</td>
<td>2</td>
<td>11</td>
</tr>
</tbody>
</table>

| Causality | Certain | 0 | 0 | 0 | 0 | 0 (0.0) |
| | Probable | 6 | 4 | 1 | 0 | 1 | 12 (11) |
| | Possible | 22 | 5 | 0 | 0 | 1 | 28 (25.68) |
| | Unlikely | 7 | 2 | 1 | 1 | 2 | 13 (11.9) |

Figures in paranthesis indicate percentages.
The total cost of FungisomeTM was calculated for each patient on the basis of dose used and number of days of treatment. In the present study 54 patients had used formulation of 50mg vial, 31 patients had used 25mg vial and 24 patients had used 10mg vial. The mean acquisition cost (in Rs) per patient per course with FungisomeTM treatment ranged from Rs 0.9-2.1 lakhs (US$ 2045 - 4773) (Rs 94,976 for candidiasis, 2,10,963 for mucormycosis, 1,03,370 for cryptococcosis, 1,45,038 for aspergillosis and 91,442 for febrile neutropenia respectively). The mean acquisition cost per day treatment ranged from Rs 4,500-8,000 (US$ 102 - 182) (Rs 6,104 for candidiasis, 8,045 mucormycosis, cryptococcosis 4,575, aspergillosis 6,649 and febrile neutropenia was 6,017 respectively) (Table 2). 6/109 patients could not afford FungisomeTM and had discontinuation of treatment.

**Discussion**

FungisomeTM is a liposomal amphotericin B developed and marketed in India and is approved for use in systemic fungal infection and visceral leishmaniasis. The present postmarketing study (PMIS) was carried out to assess the safety and ‘effectiveness’ in the real world situations. Despite the experience from controlled clinical studies, it is important to carry out the PMIS as some adverse events can be seen only after the use of drug in clinical practice. Apart from providing data on the safety, tolerability and efficacy, an added benefit of this (PMIS) is that it provides a effectiveness and safety when used for off label indications other than initially tested. The strength of PMIS lies in providing real-world clinical evidence of the potential benefits of therapy in patients with multiple concomitant illnesses who are receiving a variety of other medications.

The present study was carried out in 109/144 patients treated with FungisomeTM, 12 months post marketing. Data of 35 patients was not available because of inability to access the patient’s source notes in few hospitals. Efforts are made to get access to these patients’ source notes as well. FungisomeTM was shown to be well tolerated in the present study, with only a small number of patients reporting adverse events. FungisomeTM was not permanently discontinued due to toxicity in any of these patients in this study. No serious adverse events related to the drug were observed in this present study. Pulmonary adverse events (Apnea and mild bronchospasm) were reported in one patient of bronchial asthma after 4 h of FungisomeTM administration. This patient was treated with pheniramine and hydrocortisone injection. This patient did not warrant discontinuation of therapy and FungisomeTM administered (rechallenge) on the subsequent day did not cause apnea and or bronchospasm. Data of the four patients with preexisting renal dysfunction, who had received more than 40 doses (each received 40, 56, 57 and 76 infusions, respectively) of FungisomeTM were specially analyzed for the effect on creatinine. Serum creatinine level decreased significantly from baseline during the course of FungisomeTM therapy and renal function improved significantly from week 1 to week 12 among these four patients. Patients who received lower than 40 doses also did not have any significant alteration in creatinine. This reveals that FungisomeTM can be given safely to patients with preexisting renal impairment. Thrombocytopenia was considered possibly related to the FungisomeTM occurred in 2 patients. They recovered completely following temporary discontinuation of the therapy and treatment with platelet transfusion. The influence of underlying disease in one patient and concomitant administration of Ibuprofen known to cause thrombocytopenia on rare occasions cannot be disregarded.

The effectiveness of FungisomeTM is similar to those in the previously reported phase II and Phase III study 2,3,5. In phase II study, complete response was observed 32/33 cases of Candida, 6/7 cases of Cryptococcal meningitis, 4/7 cases of Aspergillosis and 1/1 case of Cladosporiosis in the dose of 1mg/kg/day. In phase III clinical trial out of 17 assessable in FungisomeTM group all showed complete response. The duration of treatment in Candidiasis ranged from 22-30 doses, 59-62 doses in Aspergillosis, 58-136 doses in Mucormycosis, 3-58 in Cryptococcal meningitis. In the present study complete response was produced in 19/23 (82.6%) Candidiasis, 4/7 (44.4%) Aspergillosis, 1/2 (50%) Cryptococcal, and 8/11 (72.7%) Mucormycosis patients. The duration of treatment in the

**Table 2: Direct cost associated Fungisome treatment in post marketing study**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Duration of treatment(Days)</th>
<th>Mean Acquisition Cost / dose/day(Rs)</th>
<th>Total Cost Of Fungisome RX(Rs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidiasis</td>
<td>7-30</td>
<td>6,104.2</td>
<td>94,976.43</td>
</tr>
<tr>
<td>Mucormycosis</td>
<td>10-57</td>
<td>8,045.4</td>
<td>2,10,963.6</td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>13-40</td>
<td>4,575.5</td>
<td>1,03,370</td>
</tr>
<tr>
<td>Aspergillosis</td>
<td>9-56</td>
<td>6,649.8</td>
<td>1,45,038.3</td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>7-76</td>
<td>6,017.8</td>
<td>91,442.30</td>
</tr>
</tbody>
</table>

**Table 3: Cost comparisons of different lipid preparations of Amphotericin B for a 50 kg person**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Duration</th>
<th>Cost per vial (Rs) (50mg)</th>
<th>Cost /per day (Rs)</th>
<th>Total Cost of Rx(Rs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambisome</td>
<td>3mg/kg</td>
<td>4 weeks</td>
<td>10,400</td>
<td>31,200</td>
</tr>
<tr>
<td>Abelcet (ABLC)/Ampholip</td>
<td>5mg/kg</td>
<td>4 weeks</td>
<td>3675</td>
<td>18,375</td>
</tr>
<tr>
<td>Amphocil(ABCD)</td>
<td>4mg/kg</td>
<td>4 weeks</td>
<td>8590</td>
<td>34,360</td>
</tr>
<tr>
<td>Fungisome</td>
<td>1mg/kg</td>
<td>4 weeks</td>
<td>5900</td>
<td>5,900</td>
</tr>
<tr>
<td>Conventional Amp B</td>
<td>1mg/kg</td>
<td>4 weeks</td>
<td>280</td>
<td>280</td>
</tr>
</tbody>
</table>
The present study was 7-30 doses in Candidiasis, 9-56 doses in Aspergillosis, 13-40 doses in Cryptococcus and 10-57 doses in Mucormycosis (Table 2). Mucosal and oesophageal candida infection was cured in 2 patients who had received liposomal amphotericin B gargas thrice daily for 10 days. Thus the effectiveness of Fungisome™ against proven fungal infections is similar to other marketed liposomal preparations which produced clinical cure or improvement in 20-80% in most studies.

Prophylaxis with systemic antifungal drugs in immunocompromised patients may reduce or delay the development of fungal infections. In the present study empirical use of liposomal amphotericin B for suspected fungal infections in immunocompromised patients produced complete clinical resolution (complete response) in 35/46 (76.08%) of patients. Fungisome™ was administered with dose range of 1-3 mg/kg/day for 7-76 days. The predominant underlying medical condition in this study was neutropenia secondary to hematological malignancy. The empirical use of other marketed liposomal amphotericin B for suspected fungal infections in immunocompromised patients produced complete clinical resolution (complete response) or significant clinical improvement in 50-87% of patients in non comparative studies. However the definitions of clinical response and proven fungal infections varied widely in these studies as did patient inclusion criteria. In several other studies liposomal amphotericin B was at least as efficacious as conventional amphotericin B in treatment of neutropenic patients with pyrexia of unknown origin. Combined efficacy data from two comparative studies which included 134 adults and 204 children who received liposomal amphotericin B or conventional amphotericin B showed successful outcome in 58.64% and 49% of patients. Although this study provided effectiveness and safety when used for Febrile neutropenia (off label indication), a randomized comparative trial evaluating the safety and efficacy Fungisome™ versus conventional Amphotericin B in the empirical treatment of febrile neutropenia is planned. The patent application for the extended use of Fungisome™ for febrile neutropenic patients is pending.

In postmarketing studies information on patients exposed to drug in ‘real life situation’ is obtained. However it has its limitations. First, it may not be possible to cover all the patients exposed. Second, inconsistencies may exist in the data. In the present study, patients were identified and selected in a systematic manner, since the drug is marketed from single distributor in each city and list of all doctors prescribing the drug and all patients receiving the medication was available. However still data of 35 patients could not be obtained. Second, follow data was not available in the source notes and cure was assessed in 67/91 patients as per predefined criteria and remaining 24 patients it was assessed by clinical criteria only (clinically asymptomatic and fungal investigation negative during discharge). Third, occurrence of adverse events might be less frequently reported in the source notes and causality assessment was not mentioned in 28 patients. Causality assessment was done in consultation with concerned doctor. Overall majority of the data from source notes were consistent and reliable and thus the results confirms the safety, tolerability and efficacy of this liposomal preparation.

Judgment about the preferred formulation for the treatment of systemic fungal infections is made on the basis of several factors including the clinical characteristics of the patient, morbidity and costs associated with therapeutic option. Cost of any drug is important, especially in developing countries. The mean acquisition cost (in Rs) per patient per course with Fungisome™ treatment ranged from Rs 0.9 - 2.1 lakhs. The mean acquisition cost per day treatment of different systemic fungal infections ranged from Rs 4,500-8,000. In the present study 24 patients had used 10 mg vial and 31 patients had used 25 mg vial. These formulations of 10 mg/vial and 25 mg/vial further reduced the cost of treatment. Using clinical data from published studies in immunocompromised patients with proven fungal infection, Tollemar and Ringden [10] calculated mean acquisition cost of liposomal amphotericin B (Ambisome) per course. Mean cost per patient per course in these studies ranged from US $3248 to US $20416 (Rs 1,55,900 - 10,00,380). In comparison to the acquisition cost of marketed liposomal preparations in India, the cost of Fungisome™ is 8-10 times less and thus a safe, effective and cost advantage option for Indian physicians. (Table 3).

Acknowledgments

The contributions of all doctors of the Mumbai, Delhi, Ahmedabad, and Pune city who had used Fungisome in their patients and permitting to access the patient’s source data were gratefully acknowledged. We thank the following physicians for contributing the patient’s data for this study. Dr Purvash Parikh, Dr Shripad D Banavali, Dr Sandeep Gupta, Dr Ajay Puri, Dr VR Pai, Dr PSRK Sastry, Dr Indrani Banerjee, Dr SK Pai, Tata Memorial Hospital, Dr SK Pandya, Dr Bhupendra V Gandhi, Dr MM Bahadur, Dr Fazal, Jaslok Hospital, Dr RP Mathur, Jagivanram Western Hospital, Dr DM Narulkar, Narulkar ENT Hospital, Dr Savitha M Gangurde, Dr Babasheb Ambekar Memorial Central Railway Hospital, Dr Devang K Shah, Dr Prashant Gandhi Neoplus Critical Care, Dr Prahal P Prabhusaday Gurumanak Hospital, Dr Bharrat Shah PD Hinduja Hospital, Dr Sharad M Sheth Nanavathi Hospital, Dr Dilip Kamdar, Dr Alen Ahmed, KEM hospital, Dr Bhupendra S Avasthi, Dr Khabra Surya Nursing home, Dr Uma Ali BJ Wadia Hospital, Dr Desilva, Dr Om Srivastava HN Hospital, Dr Keerthi Upadya, Leelavati Hospital, Dr Bhavane Parekh Bombay Hospital, Dr Pratibha Dileep Sterling Hospital, Ahmedabad, Dr Sonal Dalal Gujarat Kidney foundation Ahmedabad, Dr. Sandip A Shah GCRI Clinic, Ahmedabad, Dr RK Mani Apollo Hospital, New Delhi, Dr SK Chowdhry, Delhi Heart and Lung Hospital, New Delhi, Dr AK Gupta, Dr R Acharya Sir Ganga Ram Hospital New Delhi, Dr Atul Sharma IRCH, New Delhi. We also thank the Life care innovations for helping us to conduct this study. A detailed PMS all over the India is currently being carried out and the result will be published.

References

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- Medical management of disasters - V. Kvetan
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