A PHARMACOECONOMIC ANALYSIS OF MONOTHERAPY VERSUS COMBINATION THERAPY IN THE TREATMENT OF PELVIC INFLAMMATORY DISEASE

Shamima Rashid

A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfillment of the requirements for the degree of
Master of Science in Medicine in Pharmacotherapy

Johannesburg, 2005

DECLARATION

I, Shamima Rashid, declare that this research report is my own work. It is being submitted for the Degree of Master of Science in Medicine in Pharmacotherapy in the University of the Witwatersrand, Johannesburg. It has not been submitted before for any degree or examination at this or any other University.

…….. (Signature of Candidate)

……11th …….day of……OCTOBER……(month), 2005

DEDICATION

To my parents, husband and daughter for their support and patience

ABSTRACT

Objective: To assess the relative cost effectiveness of moxifloxacin once-daily empirical monotherapy and ofloxacin/ metronidazole twice daily combination therapy for the treatment of uncomplicated pelvic inflammatory disease in adult female patients.

Design: This is a retrospective cost analysis using data from a clinical trial in order to perform the economic anlysis from a funder perspective. The cost analysis is based on the clinical results of the MAIDEN study which is a prospective, randomized, double-blind, multicentre, multinational Phase III study comparing the efficacy and safety of moxifloxacin 400 mg po od for 14 days with ofloxacin 400mg po bid plus metronidazole 400mg po bid for 14 days in patients with uncomplicated pelvic inflammatory disease. Decision analysis is used to characterise the economic outcomes between groups and provide a structure upon which to base the sensitivity analyses. Published 2004 cost values are used throughout. Cost values for moxifloxacin are based on the retail price of Avelon tablets in South Africa as appears on the Orderwise Retail Pharmacy Ordering System (September 2004). Cost values for the comparator, ofloxacin and metronidazole, are based on the cheapest available generics on the South African market i.e. Zanocin 400 and Metazol 400mg respectively.

Method: The cost analysis is based on the clinical results obtained from the MAIDEN study. Patients were enrolled in either the moxifloxacin treatment group (Group A) or the ofloxacin / metronidazole comparator group (Group B). Resource utilization included:

- cost for study antimicrobials (total number of doses for the study period)
- treatment for adverse events occurring up to 7 days after stopping the study medication
- treatment for failures (includes patients continued on antimicrobial therapy after the 14 day course of therapy)
- cost of additional physician visits to treat adverse events and treatment failures

The primary end-point is the overall cost of treatment per patient as determined by:

Clinical response 7 to 14 days after the last dose of study medication (Test-of-Cure visit)

Since the clinical findings from the MAIDEN study showed that moxifloxacin treatment was at least as efficacious as ofloxacin/metronidazole treatment, a cost-minimization analysis was performed and the results were analysed according to decision analysis. Decision analysis was used to characterise the economic outcomes between the groups and provided a structure upon which to base the sensitivity analyses. The outcomes were depicted on a decision tree which proportionately determined the cost of treatment per patient in the two treatment groups.

Results:

No significant differences in clinical success rates were detected. Differences were mainly due to the cost of treating adverse events in the two groups. Costs per patient in the monotherapy vs combination therapy comparisons were R10 847.00 for moxifloxacin and R16 630.00 for ofloxacin/metronidazole treatment. Sensitivity analyses revealed that moxifloxacin monotherapy can be cost effective compared with ofloxacin/metronidazole combination therapy in different situations.

Conclusion:

Per patient, the cost of drug treatment and treatment of adverse events and clinical relapses was R10 847.00 for treatment with moxifloxacin therapy and R16 630.00 for ofloxacin/metronidazole therapy . In comparison to ofloxacin/metronidazole combination therapy, moxifloxacin monotherapy was therefore cost saving.

ACKNOWLEDGEMENTS

Bayer (Pty) Ltd
27 Wrench Road
Isando

Dr Gareth Lowndes
University of the Witwatersrand
Faculty of Health Sciences
Department of Pharmacy

Dr Neil Butkow
University of the Witwatersrand
Faculty of Health Sciences

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NOMENCLATURE

bid:	Twice daily
CI:	Confidence interval
Clinical Resolution	Disappearance of acute signs and symptoms of infection such that alternate antimicrobial therapy was not required or administered
Clinical Improvement	Improvement of acute signs and symptoms of infection such that alternate antimicrobial therapy was not required or administered
Clinical Failure	No apparent response to therapy, persistence of signs and symptoms of infection, or reappearance of signs and symptoms at or before the test-of-cure visit, or use of additional antimicrobial therapy for the current infection
Indeterminate	Patients in whom clinical assessment was not possible to determine
EDL:	Essential Drugs List
IV:	Intravenous
MAIDEN	Prospective, randomized, double-blind, multicentre, multinational study comparing efficacy and safety of moxifloxacin 400 mg po od for 14 days with ofloxacin 400 mg po bid plus metronidazole 400 mg po bid for 14 days in patients with uncomplicated pelvic inflammatory disease
od:	Once daily

Perspective	of the analysis is the viewpoint from which the analysis is conducted and costs are measured
PID:	Pelvic Inflammatory Disease
po:	per os
SEP:	Single Exit Price
TOC:	Test-of-Cure i.e. clinical response 7 to 14 days after last dose of study medication
WHO:	World Health Organisation

PREFACE

The government of South Africa clearly outlines its commitment to ensuring availability and accessibility of medicines for all people in the health objectives of the National Drug Policy. The criteria for selection of essential drugs for Primary Health Care in South Africa are based on the WHO guidelines for a national EDL (Essential Drugs List) which includes the following points :

- Sufficient proven scientific data regarding effectiveness must be available.
- Any drug included in the EDL should have a substantial safety and risk/benefit ratio
- Combination products, as an exception, will be included where patient compliance becomes an important factor, or two pharmacologically active ingredients are synergistically active in a product.
- Where drugs are clinically equally effective, the drugs will be compared on the following factors:
    - The best cost advantage.
    - The best researched.
    - The best pharmacokinetic properties.
    - The best patient compliance.
    - The most reliable local manufacturer.

In the context of the above principles, a pharmacoeconomic analysis is necessary for evaluating medicines in South Africa. Internationally, assessing new drug therapies for their cost effectiveness is becoming standard in an increasing number of countries. In addition to Australia, Canada and several other countries, the Netherlands and Finland have also recently taken steps in the direction of introducing pharmacoeconomic guidelines within a formal evidence-based decision making mechanism. A full cost-effectiveness analysis includes the following components:

1. All relevant costs and clinical outcomes are included in the analysis and valued.
2. The analysis is incremental in that it utilizes the difference in costs and difference in clinical outcomes between one specific pharmaceutical product as opposed to the other alternate therapy.
3. Costs and clinical outcomes may be discounted over time if the outcome is long-term.

4. The perspective of the decision-maker is clearly identified. The societal perspective that incorporates both direct and indirect costs and clinical outcomes should be presented.
5. All sources of data for the baseline analysis are clearly identified.
6. Sensitivity analyses are used to assess the robustness of the qualitative conclusions and identify areas where more research is needed to more precisely estimate the values of those variables to which the result is sensitive.
7. The incremental cost-effectiveness ratios are compared with each in order to determine the relative economic attractiveness of investing in this pharmaceutical product as opposed to other healthcare interventions. A cost-effectiveness analysis is indicated when there are differences in efficacy and safety between two drugs for a specified indication. A cost effectiveness analysis should first assess whether the proposed drug is superior to current best practice from the available clinical trials. There is little value in assessing the cost effectiveness of a new drug when superiority has not been established. Where there is no difference in clinical outcomes, cost minimisation is used as a cost analysis tool.

Pharmacoeconomics is therefore an integral part of formulary selection. The drug therapies used in this pharmacoeconomic analysis are those used in a clinical trial with its main focus on the private sector. They do not to date feature on the EDL. Within the framework of this pharmacoeconomic analysis, in order to establish the cost effectiveness of other drug therapies that do feature on the public sector's EDL, additional studies that reflect the societal perspective would need to be performed. Pharmacoeconomics can not be used in isolation. Various factors play a role in the final decision. We hope that this study assists in providing a clearer vision of the value of pharmacoeconomics within the South African health structure as outlined in the treatment of uncomplicated pelvic inflammatory disease in the private sector with a focus on the fluoroquinolones and their use as monotherapy and combination therapy.