UNIVERSITI TEKNOLOGI MARA

A QUALITATIVE REVIEW OF OFF-LABEL MEDICATION REQUESTS

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ABSTRACT

The aim and objective of the study is to review the request for off-label use made to the Pharmaceutical Services Division, Ministry of Health Malaysia. A total of 125 requests for off-label use of medications were made from January to December 2009. The three most common drugs requested for off-label use was Tigecycline 50mg Injection (n=34; 27.2%), N-Acetylcysteine 600mg Tablet (n=12; 96%) and Mycophenolate mofetil 250mg and 500mg Capsule (n=11; 8.8%). The most common indications for which drugs were requested for off-label use were multidrug-resistant *Acinetobacter baunamii* infection (n=34; 27.2%), prevention of contrast-induced nephrotoxicity (n=12; 9.6%) and systemic lupus erythematous and idiopathic pulmonary arterial hypertension (n=9; 7.2%). The major therapeutic subgroups were antibacterials for systemic use (n=34; 27.2%), antineoplastic agents (n=30; 2.4%) and immunosuppressants (n=17; 13.6%). 59.2% of requests (n=74) did not state the reason for request (n=74; 59.2%). 40 requests (32%) were because of the alternative listed in the drug formulary was not effective. Patients also developed side effects with alternative (n=9; 7.2%) and there was no alternative in the drug formulary (n=2; 1.6%). Only 23 requests (18.4%) included scientific papers. Types of study design of scientific papers submitted included case-report with level of evidence 4 (n=6; 26.1%) cohort study with level of evidence 2b (n=4; 17.4%), case-control with level of evidence 3b and case-series with level of evidence 4 (n=1; 4.3%). The findings from this study are expected to highlight the pressing need for more evidence-based use of off-label use of medications.

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CHAPTER ONE

INTRODUCTION

Background of Research

The main objective of drug licensing is to control the production, distribution as well as marketing of pharmaceutical products. This is achieved through evaluation of all documentation produced by the pharmaceutical industry for the drugs to be registered, which is carried out by regulatory agencies. Then, the information is reviewed to determine a drug's safety and efficacy as well as to define the therapeutic indications and patient characteristics for which it will be used (Pandolfini, Impicciatore and Provasi et al., 2002). These evaluation and review processes of drug licensing and clinical trials help since drug licensing is important to ensure the use of safe, effective and high-quality medication (Lindell-Osuagwu, Korhonen, Helin-Tanninent et al., 2009).

Off-label prescribing refers to prescription of a registered medicine for use which is not indicated in the product information as approved by the authority (Gazarian, 2007). In this study, the term "off-label use of medications" refers to using a registered drug for use that is not included in the product information (PI) or that has not been approved by the Drug Control Authority (DCA) of Malaysia. Examples include use of the drug in a different indication, age group, dose, frequency or route to that which is approved by the DCA. After a pharmaceutical product has been