Management of HIV Infection
The Potential Role of the Lamivudine/Zidovudine Combination Formulation

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Data Selection
Sources: Medical literature published in any language since 1966 on lamivudine and zidovudine, identified using AdisBase (a proprietary database of Adis International, Auckland, New Zealand), Medline and EMBASE. Additional references were identified from the reference lists of published articles. Bibliographical information, including contributory unpublished data, was also requested from the company developing the drug.


Selection: Studies in patients with HIV infection who received lamivudine and zidovudine. Inclusion of studies was based mainly on the methods section of the trials. When available, large, well controlled trials with appropriate statistical methodology were preferred. Relevant pharmacodynamic and pharmacokinetic data are also included.

Index terms: Lamivudine, zidovudine, HIV infection, acquired immune deficiency syndrome, pharmacokinetics, pharmacodynamics, pharmacoeconomics, therapeutic use.

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Abstract

HIV disease is a serious global health problem and a major cause of morbidity and mortality worldwide. It has recently been estimated that more than 30 million adults and 1.1 million children are infected with HIV; it is expected that 40 million people will have acquired the virus by the year 2000. The high costs of treating patients with HIV infection place a heavy burden on healthcare resources.

Primary aims of management of patients with HIV infection are decreased morbidity and improved survival via sustained suppression of HIV replication and the prevention of emergence of drug-resistant virus. Triple therapy with combinations of antiretroviral drugs is now regarded as optimal treatment and is the standard of care in most developed countries. Two nucleoside analogue reverse transcriptase inhibitors, such as lamivudine and zidovudine, plus a protease inhibitor or a non-nucleoside analogue reverse transcriptase inhibitor are among the combinations of drugs recommended for initial or second-line treatment.

A combination formulation of lamivudine and zidovudine has recently become available; it can be taken as a single tablet twice daily rather than as 8 tablets per day when the 2 drugs are given separately.

Combination therapy with lamivudine and zidovudine (as dual therapy or in combination with another nucleoside analogue reverse transcriptase inhibitor) decreases the rate of HIV disease progression in antiretroviral therapy-naive or -experienced patients. Dual therapy with lamivudine and zidovudine or triple therapy with lamivudine and zidovudine-containing regimens produces reductions in HIV RNA levels and improvements in CD4+ cell counts.

Lamivudine plus zidovudine therapy, alone or in combination with other drugs, is generally well tolerated. Gastrointestinal symptoms are the most common events reported during dual therapy with the 2 drugs. Neutropenia and anaemia may also occur during combination therapy with lamivudine and zidovudine and blood counts must be monitored regularly for signs of haematological toxicity.

Thus, the combination formulation of lamivudine and zidovudine has a potentially useful role as a component of initial or second-line treatment regimens for patients with HIV infection. Reducing the number of tablets that have to be taken each day simplifies the administration of lamivudine and zidovudine. The combination formulation is likely to be particularly beneficial in the management of patients who find it difficult to adhere to more complex treatment regimens.

At present, combinations of 2 nucleoside analogue reverse transcriptase inhibitors (such as lamivudine plus zidovudine) plus a protease inhibitor or a non-nucleoside reverse transcriptase inhibitor are recommended for the initial treatment of patients with HIV infection. Such regimens are usually complex, involving the daily administration of numerous tablets or capsules.

To simplify the administration of lamivudine and zidovudine and aid compliance, a combination formulation containing 150mg of lamivudine and 300mg of zidovudine per tablet[1] has been developed and is now available in the US, Europe, Australia, Thailand and Mexico. The recommended dosage of lamivudine is 150mg twice daily; zidovudine is usually administered at a dosage of 300mg twice daily or 200mg 3 times daily. The aim of this article is to identify the potential role of the combination