ANTIVIRAL MARKET OVERVIEW

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1 INTRODUCTION

According to the latest figures published today in the UNAIDS/WHO 2006 AIDS Epidemic Update, an estimated 39.5 million people are living with the human immunodeficiency virus and 170 million people are thought to be infected with hepatitis C virus [1]. These figures just illustrate that the number of viral infections are rising and more and better antivirals are urgently required. Approximately 40 antiviral drugs have been officially approved for clinical use [1], and at least half of them are used in the treatment of human immunodeficiency virus (HIV) infections (acquired immuno deficiency syndrome; AIDS). The other antivirals that are readily available include those for the treatment of herpes simplex virus (HSV), varicella-zoster virus (VZV), cytomegalovirus (CMV), influenza virus, respiratory syncytial virus (RSV), and hepatitis B (HBV) and C virus (HCV) infections [2].

There are several other important virus infections for which no antiviral drugs have been developed; even for those infections for which antiviral drug therapy exists, there is still substantial room for advancement in terms of higher potency and/or increased selectivity or safety. The approaches toward the treatment of HIV, HBV, and HCV, herpesvirus, human papillomavirus (HPV), and poxvirus infections will be reviewed in this context.

2 ANTIVIRAL DRUGS FOR HUMAN IMMUNODEFICIENCY VIRUS INFECTIONS

Currently, there are over 20 antiretroviral drugs approved by the Food and Drug Administration (FDA) falling into 5 categories: nucleoside analogs (zidovudine, lamivudine, didanosine, zalcitabine, stavudine, abacavir, emtricitabine), nucleotide analogs (tenofovir), nonnucleoside analogs (nevirapine, delavirdine, efavirenz), protease inhibitors (saquinavir, indinavir, ritonavir, nelfinavir, amprenavir, fosamprenavir, atazanivir, lopinavir, tipranavir, darunavir), and fusion inhibitors (enfuvirtide). Five combination antiretrovirals exist to increase medication compliance: Combivir (zidovudine/lamivudine), Trizivir (zidovudine, lamivudine, abacavir), Truvada (tenofovir/emtricitabine), Epzicom (lamivudine/abacavir), and the latest approved (July 2006) Atripla (efavirenz, emtricitabine, tenofovir). Highlights of each class of drug will be described before development of new therapeutics agents is discussed further. The goals of using antiretroviral drugs are to reduce viral load for a prolonged period and delay disease progression. General guidelines for treatment initiation of antiretroviral therapy are reviewed in Table 1 and dosages are listed in Table 2.

2.1 Nucleoside Analogs

Nucleoside reverse transcriptase inhibitors (NRTIs) were the first family of antiretrovirals to be created against HIV. Zidovudine was the first FDA-approved (1987) drug for HIV infection. NRTIs are activated following intracellular phosphorylation. The triphosphorylated metabolites attach to viral reverse transcriptase and are integrated into the growing deoxyribonucleic and acid (DNA) chain where they bring about DNA termination. The end result is that they inhibit ribonucleic acid (RNA)-dependent DNA synthesis [3].

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