# Lack of injectable anti-HIV therapies in the Japanese market limits treatment options for dysphagic patients

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The human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) pandemic is considered to be one of the most significant health crises of a generation. According to the Joint United Nations Programme on HIV and AIDS (UNAIDS), an estimated 75 million people have been infected with HIV since 1981, and AIDS has claimed the lives of more than 32 million people. In some countries, AIDS is the leading cause of death. HIV infects and causes the death of immune cells, resulting in eventual immunosuppression and depletion of T-helper cells that express cluster of differentiation 4 (CD4), which is a glycoprotein also found on the surface of cells such as macrophages, monocytes, and dendritic cells. The destruction of these cells impairs the immune system and leaves patients vulnerable to opportunistic infections that do not typically affect people who are not immunocompromised. Examples of opportunistic infections include Kaposi's sarcoma, extrapulmonary cryptococcosis, and cytomegalovirus retinitis.

The goal of highly active antiretroviral therapy (HAART) is to prolong life, suppress viral replication, and fortify the immune system, which is responsible not only for protecting the body from pathogenic agents but also for antitumor activity and preservation of structures such as the blood-brain barrier. Currently, the overwhelming majority of treatment options are administered orally. Although this is considered to be convenient for most HIV-infected patients, there are some individuals who are unable to adhere to an oral treatment regimen. For some patients, the first noticeable sign of an infection is the presence of lesions or ulcers in the mouth. These patients may have difficulty swallowing and have suboptimal adherence to a regimen that consists only of oral therapies.

The infection is incurable and eventually fatal, so patients must continue to take their medication once treatment is initiated. Poor compliance is a risk factor for a shortened life expectancy and a greater chance of contracting opportunistic infections. As such, drug developers have launched injectable therapies that can be used to suppress viral replication. The marketed injectable antiretroviral drugs, Roche's Fuzeon (enfuvirtide) and TaiMed's Trogarzo (ibalizumab), have launched in countries such as the US and Germany. However, no injectable anti-HIV drugs have been approved for use in Japan.

This is not the first time that the Japan HAART market has lagged behind other countries with sizeable HIV-infected populations. A similar pattern of delayed approvals can be observed with oral antiretroviral drugs. Gilead Sciences/Bristol-Myers Squibb's Atripla (efavirenz/emtricitabine/tenofovir disoproxil fumarate) was the first once-daily, single-tablet regimen (STR) to launch in the HIV therapeutics market. It became available in the US in 2006, but has still not launched in Japan. The first STR in the Japan market was Stribild (elvitegravir/cobicistat/ tenofovir disoproxil fumarate/emtricitabine), which launched in 2013. Other STRs such as Merck's Delstrigo (doravirine/lamivudine/tenofovir disoproxil fumarate) and Mylan's Symfi (efavirenz/lamivudine/tenofovir disoproxil fumarate) are also not available in Japan. One of the main reasons for these delays is the fact that drug developers seeking marketing authorization for therapeutics in Japan are usually required to run clinical trials in the country, which can be costly and time-consuming. Conversely, drugs can gain approval in Australia based on findings from clinical trials conducted in Europe or the US.

Although there is an understandable need to ensure that drugs entering the market are safe, effective, and affordable, HIV-infected patients in Japan could be severely disadvantaged by the persisting lack of injectable treatment options. Since the ongoing coronavirus (COVID-19) pandemic poses a significant threat to immunosuppressed individuals, it may be beneficial for the drug approval process in Japan to be reviewed so that the system can efficiently provide vulnerable patients with the opportunity to live long, uninhibited lives.