NEW DRUGS

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Bictegravir/emtricitabine/tenofovir alafenamide

Approved indication: HIV infection

Biktarvy (Gilead)
50 mg (with 200 mg and 25 mg) film-coated tablets
Australian Medicines Handbook section 5.6, Antiretrovirals

The current approach to previously untreated patients with HIV infection is to prescribe a regimen of at least three antiretroviral drugs from two or more different classes. An integrase inhibitor, such as dolutegravir or elvitegravir, is usually included in these regimens. The new product is a fixed-dose combination of bictegravir (an integrase inhibitor) with emtricitabine (a nucleoside reverse transcriptase inhibitor) and tenofovir alafenamide (a nucleotide analogue).

Like other integrase inhibitors, bictegravir blocks the integration of viral DNA into cellular DNA. This step is essential for viral replication.

The combination product is taken once a day. The bictegravir component has a half-life of 17 hours and it is mainly cleared by metabolism. As this pathway includes cytochrome P450 3A there is a potential for interaction with other drugs metabolised by this enzyme. Co-administration with rifampicin is contraindicated. As the product also contains emtricitabine and tenofovir, there are many potential drug interactions. The combination is not recommended if the patient's creatinine clearance is below 30 mL/min. It has not been studied in severe liver impairment.

There have been two main trials of the combination in untreated patients. These were non-inferiority studies comparing the combination with other three-drug regimens.

In one of these trials the comparative regimen also included emtricitabine and tenofovir alafenamide, but used dolutegravir for integrase inhibition. This trial randomised 657 patients who had at least 500 copies of viral RNA/mL of plasma. They were to be treated for 144 weeks, but the response to therapy was assessed at 48 weeks. At this time point, viral RNA concentrations were below 50 copies/mL for 89.4% of the patients taking the bictegravir combination and for 92.9% of those taking the comparison regimen.[1]

The other trial compared the combination with a regimen containing dolutegravir, abacavir and lamivudine. In this trial 631 patients, with viral RNA of at least 500 copies/mL, were randomised to 144 weeks of treatment. After 48 weeks the viral RNA was below 50 copies/mL in 92.4% of the patients taking the combination and 93% of those taking the other regimen.[2]

Having established that the combination is non-inferior to other regimens for initial treatment, there has been research into switching patients, taking other regimens, to the new combination. These patients already had viral RNA below 50 copies/mL. One study of 567 patients taking dolutegravir, abacavir and lamivudine switched 284 of them to the new combination. After 48 weeks viral RNA remained below 50 copies/mL in 94% of those who switched and in 95% of those who did not.[3]

An open-label study assessed the combination in 578 patients treated with regimens containing a protease inhibitor. There were 290 patients who switched to the combination and after 48 weeks the virus remained suppressed in 92% compared with 89% of the patients who did not switch treatment.[4]

Few patients had to discontinue treatment because of adverse events. In one of the studies of previously untreated patients 2% withdrew,[1] while in the other study there were no withdrawals.[2] Treatment-related events were less frequent with bictegravir than they were with a similar regimen using dolutegravir (18% vs 26%).[1] Common adverse events include headache, diarrhoea and nausea. In one of the switching studies treatment-related adverse events were more frequent in the patients who changed to the bictegravir product (19% vs 2%). The main differences were in the frequency of headache, flatulence and diarrhoea.[4] Although the combination can increase serum creatinine and bilirubin, no patients had to stop treatment because of renal or hepatic adverse effects. There is limited information about the safety of the combination in patients co-infected with hepatitis B. There is a possibility that the hepatitis may flare up if treatment with the combination is stopped. The safety in pregnancy is uncertain as women who became pregnant in the trials stopped the combination.[1-3] There was no evidence of teratogenicity in animal studies.

Adhering to treatment is vital in the management of HIV infection. A single daily tablet should help to achieve and maintain viral suppression. There were no cases of treatment-emergent resistance during the trials.[1-4]

T manufacturer provided the product information

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Some of the views expressed in the following notes on newly approved products should be regarded as preliminary, as there may be limited published data at the time of publication, and little experience in Australia of their safety or efficacy. However, the Editorial Executive Committee believes that comments made in good faith at an early stage may still be of value. Before new drugs are prescribed, the Committee believes it is important that more detailed information is obtained from the manufacturer's approved product information, a drug information centre or some other appropriate source.

REFERENCES

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The Transparency Score is explained in New drugs: transparency, Vol 37 No 1, Aust Prescr 2014;37:27.

At the time the comment was prepared, information about this drug was available on the websites of the Food and Drug Administration in the USA, the European Medicines Agency and the Therapeutic Goods Administration.