New drugs

Rilpivirine

**Approved indication:** HIV

**Endurent (Janssen-Cilag)**
25 mg film-coated tablets

**Australian Medicines Handbook section 5.4.2**

Rilpivirine is a new antiretroviral for HIV. Like other non-nucleoside reverse transcriptase inhibitors – efavirenz (Aust Prescr 1999;22:147-51), etravirine (Aust Prescr 2009;32:51-5) and nevirapine – rilpivirine reduces viral DNA synthesis by inhibiting HIV-1 reverse transcriptase. It is indicated in combination with other antiretroviral drugs for treatment-naive patients with a viral load less than 100 000 copies/mL.

Following a dose-finding study,1 two phase III trials compared the efficacy of once-daily rilpivirine (25 mg) and efavirenz (600 mg) added to different antiretroviral regimens.2,3 At enrolment, patients had to have a viral load of at least 5000 copies/mL and be sensitive to the background drug regimen. There were three background regimens in the THRIVE trial2 (tenofovir disoproxil fumarate/emtricitabine, zidovudine/lamivudine or abacavir/lamivudine) and one regimen in the ECHO trial2 (tenofovir disoproxil fumarate/emtricitabine). Rilpivirine was non-inferior to efavirenz in both trials. Overall, 84% of patients who added rilpivirine had a viral load of 50 copies/mL or less after 48 weeks compared to 82% of those who added efavirenz. Increases in CD4 T cell counts were noted with both treatments.4

Not all patients responded to treatment in the trials, and virological failure was more common with rilpivirine than with efavirenz – 10% (72 of 686 patients) vs 6% (39 of 682 patients). The majority of treatment failures with rilpivirine (53 cases) occurred in patients with a high baseline viral load (>100 000 copies/mL).5 Cross-resistance to other non-nucleoside reverse transcriptase inhibitors is likely when the virus has become resistant to rilpivirine.

Rilpivirine seemed to be better tolerated than efavirenz with fewer adverse events leading to discontinuation (1.6% vs 4%). In the trials, the most common adverse effects (grade 2 or more) with rilpivirine were depression (3.5%), insomnia (2.9%), headache (2.6%), rash (2.2%), abnormal dreams (1.5%), nausea (1.2%) and dizziness (0.7%).4 There have been two attempted suicides and one suicide ideation with rilpivirine.

Rilpivirine should be taken with a meal as absorption is increased. Maximum plasma concentrations are reached after 4–5 hours. The elimination half-life is 50 hours with most of the drug and its metabolites being excreted in faeces.

Rilpivirine is metabolised by the cytochrome P450 3A system so drugs that induce this may reduce concentrations of rilpivirine and lead to treatment failure. Drugs that are contraindicated include carbamazepine, phenobarbitone, phenytoin, rifampicin, other non-nucleoside reverse transcriptase inhibitors, systemic dexamethasone (multiple doses) and St John’s wort. Drugs that increase gastric pH such as proton pump inhibitors may also reduce plasma concentrations and are contraindicated.

Rilpivirine is a pregnancy category B1 drug. It should only be used in pregnancy if the maternal benefit outweighs the risk to the fetus.

Most patients in the trials responded to rilpivirine. However, response rates in the real world may be lower as patients with resistance to the background antiretrovirals were excluded from the trials. Although rilpivirine appears to be better tolerated than efavirenz, viral resistance is more common.

**REFERENCES**


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The T-score \(T\) is explained in ‘New drugs: T-score for transparency’, Aust Prescr 2011;34:26-7.

* At the time the comment was prepared, information about this drug was available on the website of the Food and Drug Administration in the USA (www.fda.gov).