FDA Panel Backs Avalide as First-Line HT Therapy

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ROCKVILLE, MD. — A Food and Drug Administration advisory panel unanimously recommended that the combination antihypertensive product irbesartan and hydrochlorothiazide be approved as a first-line treatment for hypertension.

The Cardiovascular and Renal Drugs Advisory Committee voted 7-0 in favor of approving the fixed-dose angiotensin receptor blocker–diuretic combination product as initial therapy.

The company has proposed that Avalide be indicated as initial treatment of severe hypertension. The panel was asked to comment on the wording of the indication statement that would be included in the label. Several were supportive of wording that Avalide can be considered as initial treatment when control of blood pressure is not likely to be achieved with one drug, or for moderate to severe hypertension.

The product, marketed as Avalide by Bristol-Myers Squibb (BMS), was approved in 1997 for treating hypertension, with a statement in its label that says the combination therapy should not be used until a patient has failed to achieve the desired effect with monotherapy.

The FDA usually follows the recommendations of its advisory panels, which are not binding.

The combination antihypertensives that have previously been approved as first-line treatments are Capozide (captopril and hydrochlorothiazide, or HCTZ), Ziac (bisoprolol/HCTZ), and Hyzaar (losartan/HCTZ).

At the meeting on Avalide, BMS provided the results of two studies. The first, a pivotal trial of 695 patients (mean age 52 years) with severe hypertension (an untreated diastolic blood pressure of at least 110 mm Hg or on monotherapy with a diastolic blood pressure of at least 100 mm Hg), compared Avalide with irbesartan monotherapy as initial therapy. The second, a supportive trial, compared Avalide with irbesartan and HCTZ monotherapies in patients with moderate hypertension. The studies used forced titration to 300 mg/25 mg of Avalide, 300 mg of irbesartan, or 25 mg of HCTZ.

In one study, Avalide was more effective in reducing blood pressure than either irbesartan or HCTZ alone, and had a comparable safety profile.

In the pivotal trial, 47% of patients on Avalide had achieved a diastolic blood pressure below 90 mm Hg at 5 weeks, the primary end point, compared with 33% of patients on irbesartan monotherapy, which was a highly significant difference.

Among black subjects (about 14% of the subjects), 40% of those on Avalide had achieved a diastolic blood pressure below 90 mm Hg at 5 weeks, compared with nearly 15% of those on irbesartan. In diabetic subjects, 33% had achieved blood pressure below 140/90 mm Hg, compared with 23% of those on irbesartan, at 5 weeks.

Overall, Avalide was safe and well tolerated, and was comparable to irbesartan, with no increase in dizziness or syncope and no serious adverse events related to treatment. No deaths were reported, according to BMS.

About 4% of patients in each group experienced dizziness, and headache was reported in 4% of those on Avalide and 6% of those on irbesartan. Hypotension was reported in 0.6% of those on Avalide and none of those on monotherapy. About 2% in each group discontinued treatment for an adverse event.

Among the 92 patients aged 65 and older, Avalide was well tolerated, there were no cases of hypotension or syncope, and dizziness was not more common than in younger patients.

In the supportive study of about 500 patients with moderate hypertension, Avalide was more effective in reducing blood pressure than either irbesartan or HCTZ alone, had a comparable safety profile, and was well tolerated in the elderly, according to BMS.

Several panel members said the company should get more data on the combination as first-line treatment in elderly and renal dysfunction patients.

Approval as a first-line treatment would not affect Avalide's patent, which expires in 2012, a spokesperson for BMS said. ■