Jur’s Out on Weekly vs. Monthly Bisphosphonates

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WASHINGTON — With billions of dollars at stake and the number of osteoporosis patients expected to grow, the battle for market share among osteoporosis drugs is heating up. New data are emerging all the time, including results from several studies presented at an international symposium sponsored by the National Osteoporosis Foundation.

For the oral bisphosphonates, the question is whether women are more likely to stick with weekly formulations, like alendronate (Fosamax) and risedronate (Actonel), or monthly formulations, like ibandronate (Boniva). And the answer depends on whom you ask, judging from four poster presentations.

Two studies involving researchers from Roche Laboratories Inc. (codeveloper of Boniva, along with GlaxoSmithKline) suggested that not only did women prefer once-monthly alendronate but they were also more likely to persist with the drug than were those on weekly alendronate or risedronate.

In the first study, Dr. John A. Sunnyce of Laurel Highlands OB.Gyn. in Hopwood, Pa., and his colleagues assessed data from the HealthCare Integrated Research database, which contains claims data for roughly 17.5 million patients. Persistence was estimated as the proportion of patients who remained on therapy with no refill gaps based on a grace period, determined by the dosing window for weekly bisphosphonates (30-day gap) and monthly ibandronate (45-day gap).

Data collection began in April 2003 and is ongoing. Researchers identified women at least 45 years old with at least one claim for a monthly (ibandronate) or weekly (alendronate or risedronate) bisphosphonate. A total of 4,335 women were identified on alendronate or risedronate and 213 on ibandronate.

The unadjusted 9-month persistence rate was 41% for patients receiving monthly ibandronate and 33% for those on weekly bisphosphonates. The median time to discontinuation was 145 days for those on ibandronate and 115 days for those on weekly therapy.

Monthly ibandronate users were 16% more likely to be persistent with therapy, compared with those on weekly alendronate or risedronate, after controlling for demographic variables, and persisters were 38% more likely to report adherence and 30% less likely to report side effects by 30 days after starting therapy.

The results included 84,399 treated patients. All of the women were included if they filled a new prescription for bisphosphonates as their biggest problem. And 37% of patients on ibandronate were advised to take the drug at least 60 minutes before the first food or drink in the morning and before taking any oral medications or supplements, including calcium, antacids, and vitamins. These patients should not lie down for 30 minutes after taking either of these drugs.

Persistence was confirmed using the interview process. The researchers used a telephone interview to assess reasons for persistence with bisphosphonate therapy. The final sample included 377 patients who persisted on weekly alendronate and 190 who persisted on monthly ibandronate.

Belief in the efficacy of osteoporosis drugs and the absence of side effects were strong determinants of persistence with bisphosphonate therapy. In all, 93% of weekly persisters reported belief in the drug’s effectiveness, compared with 88% of monthly persisters. In both groups, 83% reported an absence of side effects.

However, weekly persisters reported fewer side effects, more positive beliefs about drug safety and efficacy, and fewer osteoporosis concerns than monthly persisters did. Weekly and monthly persisters reported higher absence of side effects costs being a problem. And 37% of weekly persisters and 35% of monthly persisters reported that remembering to take the bisphosphonate was a problem.

Dosing frequency was not cited as a problem by many in either group—15% of weekly persisters and 7% of monthly persisters. “The DASH study suggests that the major drivers of persistence with bisphosphonates are belief in the effectiveness of the therapy and the lack of side effects and drug interactions, not dosing frequency,” the researchers wrote.

Compliance is key to successful treatment with these drugs because bioavailability is notoriously poor.

Under optimal conditions—if patients follow dosing instructions perfectly—bioavailability of oral bisphosphonates is minimal relative to a reference intravenous dose, the mean oral bioavailability of alendronate in women is 0.64% for doses administered 30 mg of risedronate when administered after an overnight fast and 2 hours before breakfast. Mean oral bioavailability is 0.63% for 30 mg of risedronate.

But optimal conditions are demanding for a patient. Patients on alendronate and risedronate should take the drugs with plain water first thing in the morning and at least 30 minutes before food, drinks, and taking any oral medications or supplements, including calcium, antacids, and vitamins. The patients should not lie down for 30 minutes after taking either of these drugs.

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For risedronate, the extent of absorption of a 30 mg dose when administered 30 minutes before breakfast is reduced by 55%, compared with dosing in the fasting state. Dosing 1 hour before breakfast reduces the extent of absorption by 40%, compared with dosing in the fasting state. Dosing either 1 hour after breakfast or 3 hours after dinner results in a similar extent of absorption.

For ibandronate, the oral bioavailability is reduced by about 37% when administered 30 minutes before breakfast, in comparison with that observed in fasted patients. Both bioavailability and the effect of food on absorption are reduced when food or beverages are taken less than 60 minutes after an ibandronate dose.