Council: Issues on Aging Call for Presidential Panel

BY JOYCE FRIEDEN Associate Editor, Practice Trends

WASHINGTON — The issues of aging, dementia, and long-term care merit formation of a presidential commission, the President's Council on Bioethics suggests in a new report.

At its recent meeting in Washington, the commission heard from Greg Sachs, M.D., chief of the section of geriatrics at the University of Chicago, who said that when it came to caring for dementia patients, he was "less worried about the advancing number of people and smaller numbers of caregivers ... and much more worried about the propensity to overtreat, to not provide good end-of-life care, and in fact, to have a health care system that is particularly ill-suited for the ongoing care of people with dementia."

Current financial incentives don't encourage the idea of letting dementia patients die peacefully at a nursing home, Dr. Sachs said. "When the [nursing home] patient has pneumonia and is getting close to dying, the nursing home has to provide more care ... but they are not reimbursed more. Depending on where they are and if the patient is on Medicaid, if they send the patient to the hospital they can actually be paid a 'bed-hold,' and they are actually making money while the patient is in the hospital, rather than losing money from having to provide additional care.'

BONIVA® (ibandronate sodium) TABLETS BRIEF SUMMARY CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

CONTRAINDICATIONS

M HAMUDIAI ION Known hypersensitivity to BONIVA or to any of its excipients Uncorrected hypocalcemia (see **PRECAUTIONS: General**) Inability to stand or sit upright for at least 60 minutes (see **DOSAGE AND ADMINISTRATION**)

WARNINGS BONIVA, like other bisphosphonates administered orally may cause upper gastrointestinal disorders such as dysphagia, esophagitis, and esophageal or gastric ulcer (see **PRECAUTIONS**).

gastric ulcer (see **PRECAUTIONS**). **PRECAUTIONS: General** Mineral Metabolism: Hypocalcemia and other disturbances of bone and mineral metabolism should be effectively treated before starting BONNA therapy. Adequate intake of calcium and vitamin D is important in all patients. Upper Gastrointestinal Effects: Bisphosphonates administered orally have been associated with dysphagia, esophagitis, and esophageal or gastric ulcers. This association has been reported for bisphosphonates administered orally have been thas not been found in most preapproval clinical trials, including those conducted with BONNA. Therefore, patients should be advised to pay particular attention to and be able to comply with the dosing instructions to minimize the risk of these effects (see DOSAGE AND ADMINISTRATION). Severe Renal Impairment (creatinine clearance -30 mL/min). Jaw Osteonecrosis: Osteonecrosis, primarily in the jaw, has been reported in patients treated with bisphosphonates intravenously but some have occurred in patients treated with bisphosphonates intravenously but some have been in cancer patients undergoing dental procedures, but some have occurred in patients with severe renal impairment (creatinine clearance -30 mL/min). Jaw Osteonecrosis: on clinic diagnoses. Known risk factors for osteonecrosis include a diagnosis of cancer, concomitant therapies (eg. chemotherapy, radiotherapy, corticosteroids, and co-motif disorders (eg. anemia, coagulopathy, infection, pre-existing dental disease). Most reported cases have been in patients treated with bisphosphonate intravenously but some have been in patients treated orally. For patients who develop osteonecrosis of the jaw (ONJ) while on bisphosphonate therapy, dental asympty out some have been in patients treated orally. For patients who develop osteonecrosis the jadients taking bisphosphonate hard procedures, there are no data available to suggest whether patients requiring dental procedures, there are no data available to suggest whether instructe

Information Leaflet carefully before taking DONIVA, to re-read it each time the prescription is rereved and to pay particular attention to the dosing instructions in order to maximize absorption and chincal benefit. =BONIVA should be taken at least 60 minutes before the first food or drink (other =BONIVA should be taken at least 60 minutes before the first food or drink (other =BONIVA should be taken at least 60 minutes before taking any oral medications containing multivalent cations (including antacids, supplements or vitamins). =To facilitate delivery to the stomach, and thus reduce the potential for esophageal irritation, BONIVA tablets should be swallowed whole with a full glass of plain water (6 to 8 c) while the patient is standing or sitting in an upright position. Patients should not lie down for 60 minutes after taking BONIVA.

-Plain water is the only drink that should be taken with BONIVA. Please note that some mineral waters may have a higher concentration of calcium and therefore should not be used. Patients should not chew or suck the tablet because of a potential for

BONIVA 150-mg tablet should be taken on the same date each month (ie, the tt's BONIVA day).

patient's BONIVA day). If the once-monthly dose is missed, and the patient's next scheduled BONIVA day is more than 7 days away, the patient should be instructed to take one BONIVA 150-mg tablet in the morning following the date that it is remembered (see **DOSAGE AND ADMINISTRATION)**. The patient should then return to taking one BONIVA 150-mg tablet every month in the morning of their chosen day, according to their original schedule.

original schedule. -The patient must not take two 150-mg tablets within the same week. If the patient's next scheduled BONIVA day is only 1 to 7 days away, the patient must wait until their next scheduled BONIVA day to take their tablet. The patient should then return to taking one BONIVA 150-mg tablet every month in the moring of their chosen day, according to their original schedule.

Patients should receive supplemental calcium and vitamin D if dietary intake is inadequate. Intake of supplemental calcium and vitamin D should be defayed for at least 60 minutes following oral administration of BONVA in order to maximize absorption of BONVA.

reast ou minutes rollowing oral administration of BONVA in order to maximize absorption of BONVA. Physicians should be alert to signs or symptoms signaling a possible esophageal reaction during therapy, and patients should be instructed to discontinue BONVA and seek medical attention if they develop symptoms of esophageal irritation such as new or worsening dysphagia, pain on swallowing, retrosternal pain, or heartburn. Drug Interactions

seek medical attention if they develop symptoms of esophageal irritation such as new or worsening dysphagia, pain on swallowing, retrosternal pain, or heartburn. **Drug Interactions** *Calcium Supplements/Antacids:* Products containing calcium and other multivalent cations (such as aluminum, magnesium, iron) are likely to interfere with absorption of BONIVA BONIVA bould be taken at least 60 minutes before any oral medicatons (such as aluminum, magnesium, torio) are likely to interfere with absorption of BONIVA BONIVA bould be taken at least 60 minutes before any oral medicatons (such as aluminum, magnesium, torio) are likely to interfere with absorption of BONIVA BONIVA bould be taken at least 60 minutes before any oral medicatons (such and Proton Pump Inhibitos (PPS): Of over 3500 patients enrolled in the BONIVA osteoporosis Treatment and Prevention Studies, 15% used anti-peptic agents (primality H2 blockers and PPts). Among these patients, the incidence of upper gastrointestinal adverse experiences in the patients treated with BONIVA 150 mg once monthly with daily dosing regimens of bandronate, 14% of patients used anti-peptic agents, brimal adverse experiences in the patients, the incidence of upper gastrointestinal adverse experiences in the patients treated with BONIVA 150 mg once monthly comes (INSAID): In the large, placebo-controlled osteoporosis Treatment Study, aspirin and nonsteroidal artifinammatory Drugs (INSAID): In the large, placebo-controlled osteoporosis Treatment Study, aspirin and nonsteroidal artifinammatory drugs were taken by 62% of the 2446 patients. Among aspirin or NSAID users, the incidence of upper gastrointestinal adverse experience of upper gastrointestinal events in patients concontinally taking aspirin on NSAID was similar to that in patients treated with bollowAI (S0-7%). Similari, In the 1-year monthly comparison study, aspirin and nonsteroidal artifinammatory drugs were taken by 3% of the 1602 patients. The incidence of upper gastrointestinal events in patients concontinally

rerrormed. **logenesis, Mutagenesis, Impairment of Fertility:** *Carcinogenesis*: In a 104-carcinogenicity study, doses of 3, 7, or 15 mg/kg/day were administered javage to male and female Wistar rats (systemic exposures up to 12 and 7

times, respectively, human exposure at the recommended daily oral dose of 2.5 mg, and cumulative exposures up to 3.5 and 2 times, respectively, human exposure at the recommended once-monthly oral dose of 150 mg, based on AUC comparison). There were no significant drug-related tumor findings in male or female rats. In a 78-week carcinogenicity study, doses of 5.20, or 40 on/kyd/day were administred by oral gavage to male and female NMRI mice (exposures up to 475 and 70 times, respectively, human exposure at the recommended daily oral dose of 2.5 mg and cumulative exposures up to 135 and 20 times, respectively, human exposure at the recommended once-monthly oral dose of 150 mg, based on AUC comparison). There were no significant drug-related tumor findings in male or female ince. In 90-week carcinogenicity study, doses of 5.20, or 80 mg/kg/day were administered in the drinking water to NMRI mice (cumulative monthly exposure) at the recommended dose of 150 mg, based on AUC comparison). A dose-related increased incidence of adrenal subcapsular adenoma/carcinoma was observed in female mice, which was statiscially significant at 80 mg/kg/day 220 to 400 times human exposure at the recommended daily oral dose of 150 mg, based on AUC comparison). The relevance of these findings to humans is unknown. *Mutagenesis*. There was no evidence for a mutagenic or clastogenic potential of bandronate in the following sassys: in vito bacterial mutagenesis sassy in *Salimonella typhirmurum* and *Escherichia coli* (Ames test), mammalian cell mutagenesis sasy in Chines hamster V79 cells, and chronosomal aberration test in human peripheral lymphocytes, each with and without metabolic activation. Handronate was not genotoxic in the in vivo mouse micronucleus tests for chromosomal damage. Impairment of Fertility: In female rats treated from 14 days prior to mating through gestation, decreases in fertility, corpora lutea, and implantation sites were observed

chromosomal damage. Impairment of Fartility: In female rats treated from 14 days prior to mating through gestation, decreases in fertility, corpora lutea, and implantation sites were observed at an oral dose of 16 mg/kg/day (45 times human exposure at the recommended daily oral dose of 2.5 mg and 13 times human exposure at the recommended once-monthly oral dose of 150 mg, based on AUC comparison).

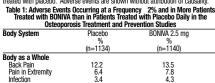
gestation, decreases in fertility, corpora lutez, and implantation sites were observed at an oral dose of 15 mg/kg/day (45 times human exposure at the recommended daily oral dose of 150 mg, based on AUC comparison). **Pregnancy:** *Pregnancy:* Category *C*: In female rats given oral doses of 1, 4, or 16 mg/kg/day beginning 14 days before mating and continuing through lactation, maternal details were observed at the time of delivery in all dose groups (3 times human exposure at the recommended daily oral dose of 2.5 mg or 1 times human exposure at the recommended once-monthly oral dose of 150 mg, based on AUC comparison). Perinatal pup loss in dams given 16 mg/kg/day (45 times human exposure at the recommended once-monthly oral dose of 150 mg, based on AUC comparison). Perinatal pup loss in dams given 16 mg/kg/day (45 times human exposure at the recommended oxer-monthly oral dose of 150 mg, based on AUC comparison). Vasi likely related to maternal dystocia. In pregnant rats given oral doses of 6, 20, or 60 mg/kg/day during gestation, calcium supplementation (32 mg/kg/day by subcutaneous nijection from gestation day 18 to parturition) did not complexely prevent dystocia and periparturient motality in any of the treated groups (16 times human exposure at the recommended daily oral dose of 2.5 mg ad 4.6 times human exposure at the recommended daily oral dose of 150 mg, based on AUC comparison). A low incidence of postimplication loss was observed in rats treated from 14 days before mating through tactation or during gestation, only at doses causing maternal dystocia and periparturient motality, in regomant task tosed oraly with 1, 5, or 20 mg/kg/da y mg sostation day 17 through lactation day 21 (following closure of the fard palate through weaning), maternal dystocity, including dystocia and periparturent motality. In recommended daily oral dose of 2.5 mg ad 4 times human exposure at the recommended daily oral dose of 2.5 mg ad 4 times human exposure at the recommended daily oral dose of 2.5 mg ad 4 times human expos

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

established. Geriatric Use: Of the patients receiving BONIVA 2.5 mg daily in postmenopausal osteoporosis studies, 52% were over 65 years of age, and 10% were over 75 years of age. Of the patients receiving BONIVA 150 mg once monthly in the postmenopausal osteoporosis 1-year study, 52% were over 65 years of age, and 9% were over 75 years of age. No overall differences in effectiveness or safety were observed between these patients and younger patients but greater sensitivity in some older individuals cannot be ruled out. ADVERSE FRACTIONS

AUVERSE HEACTIONS Daily Dosing: Daily treatment with oral BONIVA was studied in over 3900 patients in postmenopausal osteoporosis trials of up to 3 years duration. The overall adverse event profile of BONIVA 2.5 mg once daily in these studies was similar to that of placebo.

Field politie to boliver 2.5 ing once daily in trace studies was similar to that of placebo.
Treatment and Prevention of Postmenopausal Osteoporosis: Most adverse events were mild or moderate and did not lead to discontinuation. The incidence of serious adverse events was 20% in the placebo group and 23% in the BONIVA 2.5 mg daily group. The percentage of patients who withdrew from treatment due to diverse events was approximately 17% in both the BONIVA 2.5 mg daily group. The percentage of patients who withdrew from treatment due to diverse events was approximately 17% in both the BONIVA 2.5 mg daily group and the placebo group. Overall, and according to body system, there was no difference between BONIVA and placebo, with adverse events of the digestive system being the most common reason for withdrawal.
Table 1 diverse events and in more patients treated daily with BONIVA than patients treated with placebo. Adverse events are shown without attribution of causality.



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Patients with a previous history of gastrointestinal disease, including patients with Poptic ucer without recent bleeding or hospitalization and patients with dyspegsia or fewer and task of the task of t Distributed by

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In addition, the physician, instead of being paid at a lower rate and making less frequent visits, "hospitalizes the patient and makes more money by seeing the patient on a daily basis and gets reimbursed at a higher rate," he continued. And the hospital makes money because pneumonia is a disease for which the payment often exceeds the cost of care.

"All the financial incentives are aligned for this patient to be transferred to the hospital rather than being cared for in the nursing home and being allowed to die peacefully," he said.

Robert Friedlander, Ph.D., director of the Center for an Aging Society at Georgetown University, Washington, told the council that although most of the caregiving for elderly patients is provided at home-often by family membersthree-quarters of the money spent on caregiving is spent at institutions. This is partly because institutional long-term care is a mandated benefit under Medicaid, whereas home- and communitybased care is not.

But "there have been tremendous efforts on the part of states to move care out of the nursing home," especially since states think care is cheaper outside of institutions, he said. "This rebalancing has meant that in the period from 1991 to 2001, the expenditures in home- and communitybased care in Medicaid have more than tripled, from \$6.2 billion to \$22.2 billion.'

There has been movement toward changing the financing of long-term care. "The past 6-8 years, most of the focus has been on tax credits for caregivers and more public incentives for the purchase of long-term care insurance," Dr. Friedlander explained.

More fundamental changes need to be made to the long-term care financing system to ease the burden on caregivers than are currently in place, Dr. Friedlander said.

Further, things will only get worse as baby boomers live longer, and there are fewer children to support and care for them. "I would call these the best of times. I think when we get to the real crisis, these are going to look like the good old days.'

Peter Rabins, M.D., codirector of geriatric psychiatry and neuropsychiatry at Hopkins, said there was another element of the long-term care system that was worth considering. "Probably about 1 million or so people now live in assisted living, and studies just completed by [myself and colleagues] show that, just as in nursing homes, about two-thirds of individuals in assisted living have dementia," he said.

As a result, "all the relatively mild dementia cases are in assisted living and what has happened in nursing homes is that they now treat the very advanced patients," he said. "So nursing homes have changed very dramatically. I think that's very important to keep in mind."

Leon Kass, M.D., American Enterprise Institute, retired as council chair at the September meeting.

The council's report, "Taking Care: Ethical Caregiving in Our Aging Society," can be found online at www.bioethics.gov/ reports/taking_care/index.html.