

Consider Bisphosphonate Holiday After 5 Years

BY BRUCE JANCIN

ESTES PARK, COLO. — Many bone disease experts are recommending a 1- to 2-year bisphosphonate holiday after 5 years of treatment in response to a recent spate of reports of atypical fractures of the femoral diaphysis.

There are now more than 70 reports of these atypical transverse fractures of the femoral shaft occurring in patients on

bisphosphonates for longer than 5 years. Affected individuals have also had severely suppressed bone turnover markers, Dr. Michael T. McDermott said at a conference on internal medicine sponsored by the University of Colorado.

“This tells us that drugs that turn off a major process like bone remodeling may be very valuable for 3-5 years, but we have to ask, are they good for longer periods of time? We don’t know the an-

swer yet,” observed Dr. McDermott, professor of medicine and director of diabetes practice at University of Colorado Hospital, Aurora.

These distinctive fractures have been bilateral in two-thirds of cases. There is no associated history of trauma, just spontaneous thigh pain. Radiographically they look like nonhealing stress fractures that have completed through the bone shaft.

“Treatment holidays are not advised for high-risk patients,” he stressed. For such patients—those who have a T-score less than -2.5 and/or previous fractures—options include a switch to anabolic agent such as teriparatide (Forteo) or to a nonbisphosphonate antiresorptive agent such as raloxifene (Evista), estrogen, or calcitonin. Continuing the bisphosphonate in a high-risk patient also is a reasonable strategy, he said. ■

Important Safety Information (contd)

- EMBEDA® is contraindicated in patients with a known hypersensitivity to morphine, morphine salts, naltrexone, or in any situation where opioids are contraindicated
- EMBEDA® is contraindicated in patients with significant respiratory depression in unmonitored settings or the absence of resuscitative equipment
- EMBEDA® is contraindicated in patients with acute or severe bronchial asthma or hypercapnia in unmonitored settings or the absence of resuscitative equipment
- EMBEDA® is contraindicated in any patient who has or is suspected of having paralytic ileus
- EMBEDA® may be expected to have additive effects when used in conjunction with alcohol, other opioids, or illicit drugs that cause central nervous system depression because respiratory depression, hypotension, and profound sedation or coma may result
- Respiratory depression is the chief hazard of all morphine preparations such as EMBEDA®. Respiratory depression occurs more frequently and is more dangerous in elderly and debilitated patients, and those suffering from conditions accompanied by hypoxia, hypercapnia, or upper airway obstruction (when even moderate therapeutic doses may significantly decrease pulmonary ventilation)
- EMBEDA® should be used with extreme caution in patients with chronic obstructive pulmonary disease or cor pulmonale, and in patients having a substantially decreased respiratory reserve (e.g., severe kyphoscoliosis), hypoxia, hypercapnia, or pre-existing respiratory depression. In such patients, even usual therapeutic doses of morphine may increase airway resistance and decrease respiratory drive to the point of apnea. In these patients, alternative non-opioid analgesics should be considered, and opioids should be employed only under careful medical supervision at the lowest effective dose
- The respiratory depressant effects of morphine with carbon dioxide retention and secondary elevation of cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions, or a pre-existing increase in intracranial pressure. EMBEDA® can produce effects on pupillary response and consciousness, which may obscure neurologic signs of further increases in pressure in patients with head injuries. EMBEDA® should only be administered under such circumstances when considered essential and then with extreme care
- EMBEDA® may cause severe hypotension. There is an added risk to individuals whose ability to maintain blood pressure has already been compromised by a reduced blood volume or a concurrent administration of drugs such as phenothiazines or general anesthetics. EMBEDA® may produce orthostatic hypotension and syncope in ambulatory patients
- EMBEDA® should be administered with caution to patients in circulatory shock, as vasodilation produced by the drug may further reduce cardiac output and blood pressure
- EMBEDA® should be used with caution and in reduced dosage in patients who are concurrently receiving other central nervous system depressants including sedatives or hypnotics, general anesthetics, phenothiazines, other tranquilizers, and alcohol because respiratory depression, hypotension, and profound sedation or coma may result
- EMBEDA® should not be given to patients with gastrointestinal obstruction, particularly paralytic ileus, as there is a risk of the product remaining in the stomach for an extended period and the subsequent release of a bolus of morphine when normal gut motility is restored
- Patients taking EMBEDA® who are scheduled for cordotomy or other interruption of pain transmission pathways should have EMBEDA® ceased 24 hours prior to the procedure and the pain controlled by parenteral short-acting opioids. In addition, the post-procedure titration of analgesics for such patients should be individualized to avoid either oversedation or withdrawal syndromes
- EMBEDA® may cause spasm of the sphincter of Oddi and should be used with caution in patients with biliary tract disease, including acute pancreatitis
- Tolerance is the need for increasing doses of opioids to maintain a defined effect such as analgesia (in the absence of disease progression or other external factors). Physical dependence is manifested by withdrawal symptoms after abrupt discontinuation of a drug or upon administration of an antagonist. Physical dependence and tolerance are common during chronic opioid therapy
- EMBEDA® should be administered with caution and in reduced dosages in elderly or debilitated patients; patients with severe renal or hepatic insufficiency; Addison’s disease; myxedema; hypothyroidism; prostatic hypertrophy or urethral stricture
- Caution should also be exercised in the administration of EMBEDA® to patients with CNS depression, toxic psychosis, acute alcoholism, and delirium tremens
- All opioids may aggravate convulsions in patients with convulsive disorders, and all opioids may induce or aggravate seizures in some clinical settings

Please see additional Important Safety Information and Brief Summary of full Prescribing Information, including boxed warning, on the following pages.