Access to Mepact® (Mifamurtide) in the United States

In the United States, current treatment for osteosarcoma typically follows a treatment protocol referred to as the “MAP” protocol: M = Methotrexate, A = Adriamycin (doxorubicin) and P = CisPlatin. However, oncologists may also decide on additional treatments. These may include Ifosomide and Etoposide, which are additional chemotherapies, or other targeted agents used as therapies after tumor removal.

In certain countries outside of the United States, a different type of therapy called Mepact® (mifamurtide) is commercially available. In Europe, for example, Mepact is approved for use in children, adolescents and young adults for the treatment of high-grade resectable, non-metastatic osteosarcoma, after macroscopically complete surgical resection in combination with post-operative multi-agent chemotherapy. According to the product labeling and information made available by the European Medicines Agency, Mepact activates two types of white blood cells, macrophages and monocytes, which in turn leads to increased production of several interleukins and other cytokines (small molecules which play a part in cell signaling in the immune system). This is believed to help the patient’s body kill cancer cells, but the exact mechanism by which Mepact leads to antitumor activity is not currently known.

In the United States, a multi-center clinical trial involving approximately 600 children and young adults with newly diagnosed, resectable, high grade osteosarcoma was conducted to assess, among other things, treatment with Mepact and the standard-of-care MAP protocol as compared to treatment with the MAP protocol alone. Based on the results of this study, a pharmaceutical company sought approval to sell mifamurtide in the United States. However, due to concerns regarding the study design and analysis, the product did not obtain approval from the U.S. Food and Drug Administration (FDA).

Nevertheless, some osteosarcoma patients have been able to obtain Mepact in the United States through the FDA’s compassionate use and personal importation programs. Although the process may take a fair amount of paperwork, and there can be no guarantee of success, obtaining the product in the United States has been streamlined by the number of children who have been successful in navigating FDA’s process to secure access. In addition, since 2017, there have been numerous children who received full coverage of Mepact by health insurance providers. The cost of Mepact if paid out of pocket has in past cases been negotiated to $100,000.00.

The following guidelines are intended to provide information regarding the possibility of obtaining Mepact in the United States in coordination with the FDA, and are meant to facilitate efforts by the families and oncologists of osteosarcoma patients to obtain Mepact with insurance coverage.

**Step 1:** Your oncologist must submit an Investigational New Drug application (IND) to the FDA for single patient use. This application seeks permission to obtain Mepact for compassionate use, which refers to the use of an unapproved therapy outside of a clinical trial. Your oncologist may also submit a request to charge for the investigational drug, which requires FDA authorization.
**Step 2:** The manufacturer of Mepact (Takeda Oncology) must send your oncologist a letter stating that the company agrees to supply Mepact to your oncologist and your child’s treating center. This effort is facilitated by the Clinigen Group plc. The Clinigen Group may be contacted at 215-944-8836 or 609-613-8384.

The FDA has a designated Patient Affairs Staff who may be helpful in navigating this process. The Patient Affairs Staff can be contacted at PatientAffairs@fda.hhs.gov or 301-796-8460. When contacting the Patient Affairs Staff, we recommend that you provide the following information, as applicable:

1. A statement that your child has osteosarcoma.
2. A statement that you would like to secure access to Mepact for your child’s personal use through the compassionate use program.
3. A short statement of other treatments that your child has already undergone.
4. A statement that you have a physician who plans to treat your child with the drug, along with the name and contact information for the physician (address, phone, email).

Like other medications, Mepact is associated with certain adverse events, and patients, their families and their doctors should be mindful of warnings, precautions and contraindications associated with Mepact’s use. In addition, even if Mepact’s manufacturer agrees to make Mepact available, and if FDA provides authorization, limitations in the supply of Mepact may result in delays accessing the therapy.

**Insurance Denials:**

Your insurance company may deny coverage for Mepact even after you have successfully completed all procedures with the FDA and drug manufacturer necessary to access Mepact. It is common for insurance companies to issue an initial coverage denial for drugs not approved by the FDA, but each insurance company has an appeals process. You can check your own insurance company’s policy to begin the appeal, or work with your case manager (if available).

**Recommendations for Supporting Your Appeal:**

1. If you have a case manager at your insurance company for your child’s oncology care, use their help in navigating the process for your particular insurance company.
2. Ask if you can have the name and title of the person in the insurance company that made the denial. This information will give you an idea of what documents may be most helpful to provide and whether you should request that the medical director or an oncologist review your petition.
3. Provide letters of medical necessity supporting the use of Mepact for your child. A letter should be provided by your treating oncologist, and if possible, another consulting oncologist.

4. We have provided a template appeal letter that can help inform your appeal. Be sure to adjust this letter to your own circumstances and needs.

5. Provide copies of supporting peer reviewed articles on the use and efficacy of Mepact.

6. E-mail and MAIL (with tracking) your appeal letter. Many insurance companies have faster review processes for appeals designated as priority or emergency. For certain BlueCross BlueShield plans, including the word “Priority” in the subject line may accelerate review time.