Mifamurtide

**INDICATIONS FOR USE:**

<table>
<thead>
<tr>
<th>INDICATION</th>
<th>ICD10</th>
<th>Protocol Code</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mifamurtide can be used in combination with post-operative multi-agent chemotherapy for the treatment of high-grade resectable non-metastatic osteosarcoma after macroscopically complete surgical resection, in children, adolescents and young adults. This treatment is an option to be discussed with the patient (or parent of a child).</td>
<td>C41</td>
<td>00100a</td>
</tr>
</tbody>
</table>

**ELIGIBILITY:**

- Indication as above.
- Patients aged from 2 to 30 years of age.
- Adequate haematological, hepatic and renal function.

**EXCLUSIONS:**

- Hypersensitivity to mifamurtide or any of the excipients.
- Metastatic disease at presentation.
- Incomplete surgical resection.
- Prior chemotherapy or radiotherapy other than pre-operative multiagent chemotherapy.

**TESTS:**

**Baseline tests:** FBC, U&Es, LFTs.

**Regular tests:**

- Prior to each cycle: FBC, U&Es, LFTs.
- Echocardiogram: annually or according to local practice.

**Disease monitoring:**

Disease monitoring should be in line with the patient’s treatment plan and any other test/s as directed by the supervising Consultant.
NCCP Chemotherapy Protocol

TREATMENT:
The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient’s individual clinical circumstances.

The recommended dose of mifamurtide for all patients is 2 mg/m² body surface area.

It should be administered as adjuvant therapy, combination with post-operative multi-agent chemotherapy, following resection and recovery from surgery (usually +/- 3 weeks post operatively): twice weekly at least 3 days apart for 12 weeks, followed by once-weekly treatments for an additional 24 weeks for a total of 48 infusions in 36 weeks.

Treatment should continue to completion or until unacceptable toxicity occurs.

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
<th>Route</th>
<th>Diluent &amp; Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-12</td>
<td>1 and 4</td>
<td>Mifamurtide</td>
<td>2mg/m²</td>
<td>IV</td>
<td>50ml* 0.9% NaCl over 60 minutes</td>
</tr>
<tr>
<td>13-36</td>
<td>1</td>
<td>Mifamurtide</td>
<td>2mg/m²</td>
<td>IV</td>
<td>50ml* 0.9% NaCl over 60 minutes</td>
</tr>
</tbody>
</table>

*The final volume will be greater than 50 ml as the required dose is added to 50 ml 0.9% NaCl giving a total volume between 50 ml - 100 ml.

DOSE MODIFICATIONS:
- Any dose modification should be discussed with a Consultant.

<table>
<thead>
<tr>
<th>Renal Impairment</th>
<th>Hepatic Impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr Cl (ml/min)</td>
<td>Dose</td>
</tr>
<tr>
<td>&lt;30</td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>≥30</td>
<td>No dose adjustment necessary</td>
</tr>
<tr>
<td>*Severe</td>
<td>No data available Exercise caution</td>
</tr>
</tbody>
</table>

Continued monitoring of the kidney and liver function is recommended if mifamurtide is used beyond completion of chemotherapy until all therapy is completed.

SUPPORTIVE CARE:
EMETOGENIC POTENTIAL: Moderate (Refer to local policy).
PREMEDICATIONS:
Paracetamol and chlorphenamine may be utilised as a premedication, to prevent fevers and chills. Corticosteroids, including dexamethasone, should be avoided (see Drug Interactions).

TAKE HOME MEDICATIONS: None.

OTHER SUPPORTIVE CARE:
No specific recommendations.

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS
The adverse effects listed are not exhaustive. Please refer to the relevant Summary of Product Characteristics for full details.

- **Respiratory distress:** In patients with a history of asthma or other chronic obstructive pulmonary disease, consideration should be given to administration of bronchodilators on a prophylactic basis. If a severe respiratory reaction occurs, administration of mifamurtide should be discontinued and appropriate treatment initiated.

- **Neutropenia:** Episodes of neutropenic fever should be monitored and managed appropriately. Mifamurtide may be given during periods of neutropenia, but subsequent fever attributed to the treatment should be monitored closely. Fever or chills persisting for more than 8 hours after mifamurtide administration should be evaluated for sepsis.

- **Inflammatory response:** Mifamurtide should be used with caution in patients with a history of autoimmune, inflammatory or other collagen diseases. During administration, patients should be monitored for unusual signs or symptoms, such as arthritis or synovitis, suggestive of uncontrolled inflammatory reactions.

- **Cardiovascular disorders:** Patients with a history of venous thrombosis, vasculitis or unstable cardiovascular disorders should be closely monitored during administration. If symptoms are persistent and worsening, administration should be delayed or discontinued.

- **Gastrointestinal toxicity:** Nausea, vomiting and loss of appetite are very common adverse reactions to mifamurtide. Gastrointestinal toxicity may be exacerbated when mifamurtide is used in combination with high dose, multi-agent chemotherapy and was associated with an increased use of parenteral nutrition.
DRUG INTERACTIONS:
- Mifamurtide is **contraindicated** with concurrent use of:
  - Cyclosporin or other calcineurin inhibitors.
  - High-dose non-steroidal anti-inflammatory drugs (NSAIDs, cyclooxygenase inhibitors).
- The administration of mifamurtide should be separate from the administration times of doxorubicin or other lipophilic medicinal products if used in the same chemotherapy regimen.
- Because mifamurtide acts through stimulation of the immune system, the chronic or routine use of corticosteroids should be avoided during treatment with mifamurtide.
- Current drug interaction databases should be consulted for more information.

ATC CODE:
Mifamurtide – L03AX15

REIMBURSEMENT CATEGORY:
Mifamurtide is available for use in public hospitals and is currently available for reimbursement through the Oncology Hospital Drugs Management System (hosted by PCRS January 2015).

PRESCRIPTIVE AUTHORITY:
The treatment plan must be initiated by a Consultant Medical oncologist.

REFERENCES:
Version | Date       | Amendment                                      | Approved By                  |
---------|------------|-----------------------------------------------|------------------------------|
1        | 5/3/2013   |                                               | Dr Michael Capra             |
          |            |                                               | Dr Deirdre O’Mahony          |
2        | 3/3/2015   | Updated Tests section                        | Dr Maccon Keane              |
3        | 1/3/2017   | Reviewed - Clarified dosing in renal and hepatic impairment | Dr Michael Capra             |
          |            |                                               | Prof Maccon Keane            |

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.

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