Indication: Patients with essential thrombocythaemia (ET), polycythaemia vera (PV), myelofibrosis (PMF) at high risk of thrombosis. Intermediate risk ET patients on the basis of PT1 amended trial.

Treatment intent: To normalise blood count i.e. platelets < 400 x 10⁹/L and PCV <0.45
To reduce risk of thrombosis

Regimen details: Hydroxycarbamide *15-20mg/kg orally once daily

* If urgent cytoreduction is needed up to 3g/day doses may be used, but more frequent monitoring is needed

Hydroxycarbamide is available as 500mg capsules. The dose need not be divided through the day.

Can also be used in combination with anagrelide in patients who are refractory/intolerant to hydroxyurea (see Barosi 2007)

Administration: Orally

Premedication: None required

Frequency: Continuous

Extravasation: Not applicable

Anti-emetics: Not usually required

Supportive medication: Consider the use of allopurinol especially when rapid control of blood counts is desired and in those patients with raised serum urate and/or history of gout.

Regular investigations: FBC at every visit, initially monitor every 1 to 2 weeks when titrating dose. Thereafter in stable patients review may gradually be extended to 3 months. LFTs and renal function every 3 months

Dose Modifications

Haematological Toxicity Hydroxycarbamide causes macrocytic red cell indices and may mask iron, B12 or folic acid deficiency. The dose should be reduced if the patient develops neutropenia <1.5 x 10⁹/L, and titrated against the Hb and platelet count, stop the drug if the platelet count is less than 100 x 10⁹/L

Renal Impairment

<table>
<thead>
<tr>
<th>GFR (mL/min)</th>
<th>% usual dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50</td>
<td>100%</td>
</tr>
<tr>
<td>10-50</td>
<td>50%</td>
</tr>
<tr>
<td>&lt;10</td>
<td>discontinue</td>
</tr>
</tbody>
</table>

Reason for Update: Network Protocol Development
Version: 1
Supersedes: All other versions
Prepared by: Laura Cameron
Approved by SELCN DTAC Chair: Nic Ketley
Approved by Chair Haem TWG: Anil Lakhani
Prepared by: Laura Cameron
Date: 3rd July 2008
Approved by SELCN DTAC Chair: Nic Ketley
Date: 3rd July 2008
Approved by Chair Haem TWG: Anil Lakhani
Hydroxycarbamide (Hydroxyurea) (HU) for essential thrombocythemia, polycythaemia vera, myelofibosis.

Hepatic Impairment: No dose modification necessary

Toxicities: Drowsiness – dose reduction or consider dosing at night only

Hydroxycarbamide in contraindicated in patients with marked bone marrow depression, or severe anemia; or in patients who have demonstrated a previous hypersensitivity to hydroxycarbamide or any other component or its formulation.

Hydroxycarbamide is genotoxic, fetotoxic, teratogenic in animals and has the potential to be mutagenic. It should not be used in pregnancy; its effects on fertility have not been established.

Breast feeding is not recommended due to the secretion into breast milk.

Elderly patients and patients with extensive prior radiation or chemotherapy may be more sensitive to the effects of hydroxycarbamide.

Drug interactions:

<table>
<thead>
<tr>
<th>AGENT</th>
<th>EFFECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytarabine</td>
<td>increased cytarabine toxicity</td>
</tr>
<tr>
<td>Didanosine</td>
<td>increased incidence of pancreatitis and neurotoxicity, avoid concomitant use</td>
</tr>
<tr>
<td>Clozapine</td>
<td>increased risk of agranulocytosis, avoid concomitant use</td>
</tr>
<tr>
<td>Stavudine</td>
<td>increased risk of toxicity, avoid concomitant use</td>
</tr>
<tr>
<td>RADIOTHERAPY</td>
<td>increased toxicity</td>
</tr>
</tbody>
</table>

Comments: Do not use during pregnancy
Care in the elderly may be more susceptible to toxicity
Significantly increased risk of acute myeloid leukaemia when given with other leukaemogenic drugs in particular hydroxy carbamide.

References:

