Skin Pathway Group – CVD (Cisplatin, Vinblastine, Dacarbazine) in Melanoma

**Indication:** Advanced, unresectable melanoma

**Regimen details:**
- **Vinblastine** 2.5mg/m² IV Day 1 to Day 3 (inclusive)
- **Dacarbazine** 250 mg/m² IV Day 1 to Day 3 (inclusive)
- **Cisplatin** 30mg/m² IV Day 1 to Day 3 (inclusive)

**Administration:** Suggested hydration schedule (for days 1 to 3):

Furosemide 40mg PO
**Vinblastine** in 50 ml Sodium Chloride 0.9% over 5-10 minutes
**Dacarbazine** in 500ml Sodium Chloride 0.9% over 60 min (see notes)
**Cisplatin** in 1 litre Sodium Chloride 0.9% IV over 60 min
1 litre Sodium Chloride 0.9% + 20 mmol KCl + 1g MgSO₄ IV over 60 minutes

Then either 500ml Sodium Chloride 0.9% IV over 60 minutes or 500ml drinking water

Aluminium containing equipment should not be used during preparation and administration of cisplatin.

Anaphylactic-like reactions to cisplatin have been reported. Facial oedema, bronchoconstriction, tachycardia, and hypotension may occur within minutes of administration. Adrenaline, corticosteroids, and antihistamines have been effectively employed to alleviate symptoms.

Dacarbazine infusion rate can be decreased and volume can be increased to avoid venous pain during infusion.

Dacarbazine is light-sensitive. It is likely that pain during the infusion may be caused by degradation products on exposure to light. Use light protective giving set or cover the line with aluminium foil.

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protect the infusion bag from light. Solution turns pink on exposure to light.

Frequency: 3 weekly cycle, maximum 6 cycles

Pre-medication: Not routinely required

Anti-emetics: Very High emetogenicity
Follow Local Anti-emetic Policy

Supportive medication: Not routinely required

Extravasation: Vesicant
Vinblastine and Dacarbazine should be administered with appropriate precautions to prevent extravasation.
If there is any possibility that extravasation has occurred, contact a senior member of the medical team and follow local protocol for dealing with cytotoxic extravasation
Cisplatin is not a vesicant

Regular investigation:

Prior to Cycle 1:

FBC Day 1 (within 14 days)
LFTs Day 1 (within 14 days)
U&Es Day 1 (within 14 days)

Audiometric testing if clinically indicated

Prior to Day 1 (cycle 2 onwards):

FBC Day 1 (within 72 hours)
LFTs Day 1 (within 72 hours)
U&Es Day 1 (within 72 hours)

Toxicities:

Total alopecia, thrombocytopenia, GI symptoms, anorexia, mucositis, cardiovascular, hypotension, infertility, ototoxicity, neurotoxicity, CNS symptoms with Dacarbazine, hepatotoxicity (dacarbazine)
DOSE MODIFICATIONS

Haematological Toxicity

<table>
<thead>
<tr>
<th>Neutrophils (x 10^9/L)</th>
<th>Platelets x (x 10^9/L)</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 1.0 &amp; ≥ 100</td>
<td></td>
<td>Give 100% dose</td>
</tr>
<tr>
<td>&lt; 1.0 or &lt; 100</td>
<td></td>
<td>Delay for 1 week. Repeat FBC, if recovered to above these levels, give 100% dose.</td>
</tr>
</tbody>
</table>

If low counts persists after delay of 1 week, reduce all doses by 25%. Maintain 25% dose reduction for subsequent cycles.

Non-haematological Toxicities

Renal Impairment

<table>
<thead>
<tr>
<th>Creatinine Clearance (ml/min)</th>
<th>Cisplatin Dose</th>
<th>Dacarbazine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>45-59</td>
<td>75%</td>
<td>80%</td>
</tr>
<tr>
<td>30-45</td>
<td>Omit cisplatin, consider carboplatin</td>
<td>75%</td>
</tr>
<tr>
<td>&lt;30</td>
<td>Omit cisplatin, consider carboplatin</td>
<td>70%</td>
</tr>
</tbody>
</table>

Cisplatin-induced nephrotoxicity is dose-related and cumulative. It manifests early by elevations in blood urea, creatinine, and wasting of potassium and magnesium. Renal toxicity may be irreversible and is more prolonged and severe with repeated courses.

Hepatic Impairment

Cisplatin

No dose adjustment is necessary in liver impairment

Dacarbazine

Activated and metabolised by the liver, can be hepatotoxic—consider dose reductions

<table>
<thead>
<tr>
<th>Bilirubin (micromol/L)</th>
<th>AST / ALT (units/L)</th>
<th>Vinblastine Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>26-51</td>
<td>or 60-180</td>
<td>50% dose</td>
</tr>
<tr>
<td>&gt;51</td>
<td>&amp; within reference range</td>
<td>50% dose</td>
</tr>
<tr>
<td>&gt;51</td>
<td>&amp; &gt; 180</td>
<td>Omit</td>
</tr>
</tbody>
</table>

Location of regimen: Day case setting delivery
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Drug interactions:

- Anti-epileptics: Cisplatin and Dacarbazine - reduced absorption of phenytoin
- Nephrotoxic drugs: additive nephrotoxic effect with Cisplatin
- Erythromycin: Vinblastine toxicity may be increased
- Dacarbazine is metabolised by cytochrome P450, therefore the co-administration of other drugs which are metabolised by the same hepatic enzymes can present a theoretical interaction

References:

- www.medicines.org.uk,