REGIMEN TITLE: **CVD (Cisplatin, Vinblastine, Dacarbazine)**  
Ambulatory, 3-day regimen

**Indication:**  
Advanced, unresectable *Melanoma*

**Regimen details:**  
- **Vinblastine**: 2.5mg/m² IV D1 to D3 (inclusive)
- **Dacarbazine**: 250 mg/m² IV D1 to D3 (inclusive)
- **Cisplatin**: 30mg/m² IV D1 to D3 (inclusive)

**Administration:**  
Days 1-3.  
- **Furosemide**: 40mg PO  
- **Vinblastine**: in 50 ml 0.9% Sodium Chloride over 5-10 minutes  
- **Dacarbazine**: in 500ml 0.9% Sodium Chloride over 60 min (see notes)  
- **Cisplatin**: in 1 litre 0.9% Sodium Chloride IV over 60 min  
  1 litre 0.9% Sodium Chloride + 20 mmol KCl + 1g MgSO4 IV over 60 minutes  
  Then *either* 500ml Sodium Chloride 0.9% IV over 60 minutes *or* 500ml drinking water  
*Follow guidance protocol for Hydration schedules & fluid balance monitoring for outpatient cisplatin regimens*

**Notes:**  
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, protect the infusion bag from light. Solution turns pink on exposure to light.

**Frequency:**  
3 weekly cycle, maximum 6 cycles

**Extravasation:**  
Vinblastine is Vesicant  
Dacarbazine is Vesicant

**Anti-emetics:**  
Severe emetogenicity. Uncontrolled vomiting may exacerbate cisplatin-induced fluid and electrolyte; [Mg²⁺] and [K⁺] imbalance

**Regular investigations:**  
- **FBC**: D1  
- **LFTs**: D1  
- **U&E**: D1  
- **Audiometric testing if clinically indicated**

**Dose Modifications**

**Haematological Toxicity**  
If at the start of any treatment cycle the neutrophils < 1.0 x 10⁹/L or PLT < 100 x 10⁹/L delay treatment for 1 week. If low counts persists, reduce all doses by 25%, maintain for subsequent cycles. In extended neutropenia, consider prophylactic pegfilgrastim for subsequent cycles, discuss with consultant.
Renal Impairment

In grade 1 renal toxicity (WHO Cr 1.25-2.0 x ULN), delay cycle for one week.

### GFR

<table>
<thead>
<tr>
<th>GFR</th>
<th>Cisplatin dose</th>
<th>Dacarbazine dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 60ml/min</td>
<td>100% dose</td>
<td>100% dose</td>
</tr>
<tr>
<td>50-60ml/min</td>
<td>75% dose</td>
<td>80% dose</td>
</tr>
<tr>
<td>40-50ml/min</td>
<td>50% dose</td>
<td>75% dose</td>
</tr>
<tr>
<td>&lt;40ml/min</td>
<td>Omit cisplatin, consider carboplatin</td>
<td>70% dose</td>
</tr>
<tr>
<td>&lt;30ml/min</td>
<td>Omit</td>
<td>Clinical decision</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

In grade 2 hepatic toxicity (WHO Bili 2.6-5.0 x ULN), delay course for 1 week.

**Cisplatin**

No dose adjustment is necessary in liver impairment

**Dacarbazine**

Activated and metabolised by the liver, Can be hepatotoxic- Clinical consideration for dose reductions

### Liver function tests

<table>
<thead>
<tr>
<th>Liver function tests</th>
<th>Vinblastine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bil 26-51 mcmol/L or AST/ALT 60-180 units/L</td>
<td>50% dose</td>
</tr>
<tr>
<td>Bil&gt;51 mcmol/L and AST/ALT normal</td>
<td>50% dose</td>
</tr>
<tr>
<td>Bil&gt;51 mcmol/L and AST/ALT &gt; 180 units/L</td>
<td>Omit</td>
</tr>
</tbody>
</table>

### Toxicities:

Other toxicities Total Alopecia, Thrombocytopenia, GI symptoms, Anorexia, Mucositis, Cardiovascular, Hypotension, Infertility, Ototoxicity, Neurotoxicity, CNS symptoms with Dacarbazine, hepato-toxicity (dacarbazine)

Drug interactions:

- Anti-epileptics: Cisplatin and Dacarbazine - reduced absorption of phenytoin
- Nephrotoxic drugs: Additive nephrotoxic effect with Cisplatin
- Furosemide: Additive ototoxicity with Cisplatin
- Erythromycin: Vinblastine toxicity may be increased

References:

- [www.medicines.org.uk](http://www.medicines.org.uk) (accessed Jan08)
- ASWCS Chemotherapy handbook Jan 2005 update
- SELCN Cytotoxic extravasation guidelines, issued May 2009