Platinum derivatives

Cisplatin, carboplatin, and oxaliplatin

These are widely used chemotherapeutic agents for many decades and are applied in numerous regimens.
Mode of action: They cause irreparable DNA damage (cross-linking) in the cell, leading to cell death (apoptosis). Because they affect all rapidly dividing cells (not just cancer cells), they can sometimes cause significant side effects.

Common side effects of platinum derivatives are listed according to the individual active ingredients:

1. Cisplatin

1.1 Nausea and vomiting – not only spontaneous, but also delayed. Cisplatin is classified as highly emetogenic.
1.2 Nephrotoxicity – this is often dose-limiting; the patient must be well hydrated during treatment and should also drink plenty of fluids after the infusion. Fluid excretion should be monitored (weight control).
1.3 Ototoxicity – hearing tests should be performed regularly; this also limits the dose; existing damage can be exacerbated.
1.4 Peripheral neuropathy – especially with prolonged use.
1.5 Allergic reactions are possible with prolonged use.

2. Carboplatin – less toxic than cisplatin
2.1 Dosage is usually based on AUC due to nephrotoxicity (lower than with cisplatin)
2.2 Less ototoxicity than cisplatin
2.3 Emetogenicity classified as moderately emetogenic
2.4 Myelosuppressive – dose-limiting
2.5 Allergic reactions are possible with prolonged administration

3. Oxaliplatin
3.1 Neurotoxicity – Neuropathies of the hands and feet, both acute and chronic – dose-limiting
3.2 Moderately emetogenic
3.3 Myelosuppressive
3.4 Allergic reactions are possible with prolonged administration

Use of platinum derivatives in various treatment regimens:

Cisplatin as monotherapy or in combination with other cytotoxic drugs.
Examples: ovarian cancer, bladder cancer, NSCLC, head and neck cancer, testicular cancer, gastric cancer, and others in various regimens.

Carboplatin often in combination with other cytotoxic drugs.
Examples: ovarian cancer, NSCLC, bladder cancer, renal cancer.

Oxaliplatin in combination with other cytotoxic drugs.
Examples: predominantly in colorectal therapies.

Special instructions for preparation:

Cisplatin:
Always prepare in 0.9% saline solution.
Use as large a volume as possible.
Provide a light-protective bag.
Protect from light for longer durations.
Stability of the patient-specific preparation – country- and pharmacy-specific; the same applies to opened vials.
(Expiration dates can also be viewed at stabilis.org)
Look at product information SmPC.

Carboplatin:
Prepare in 5% glucose solution if possible, as its shelf life is longer than when using 0.9% saline (expiration dates can also be found at stabilis.org). Otherwise, follow country- and pharmacy-specific regulations.
When prepared in 0.9% saline, prolonged storage (over 24 hours) will result in conversion to cisplatin.
Look at the product information SmPC

Oxaliplatin:
Always prepare in 5% glucose, as it is incompatible with 0.9% saline (yellowing and precipitation may occur). (Expiry dates can also be found at stabilis.org.) Otherwise, follow country- and pharmacy-specific regulations. Look at the Summary of Product Characteristics (SmPC).

Supportive measures for platinum derivatives:

Cisplatin – highly emetogenic
Antiemetic: Triple combination of dexamethasone, 5HT3 antagonist, and neurokinin-1 receptor antagonist. Due to possible delayed emesis, continue on days 2 and 3 after treatment.
(look at Mascc.org guideline)
Insufficient fluid excretion: Furosemide

Carboplatin – moderately emetogenic
Antiemetic: Dexamethasone with 5HT3 antagonists, depending on the combination, switch to the triple combination as with cisplatin
(look at Mascc.org guideline)

Oxaliplatin – slightly emetogenic on its own
Antiemetic: at least metoclopramide or alizapride, in combination therapies dexamethasone and 5HT3 antagonists
(look at Mascc.org guideline)
Neuropathy: do not drink cold drinks from the refrigerator or, in combination therapies with 5FU, do not suck on ice cubes during the 5FU infusion/bolus administration. Wear comfortable shoes and gloves to prevent injury.

To avoid confusion and potentially uncontrollable or unforeseeable complications, it is recommended that **Carboplatin** and **Oxaliplatin** always be prepared in **5% glucose**

Cisplatin should always be prepared in **0.9% sodium chloride**.

The following regimens are examples:

Cisplatin:
Endoetrial cancer: PAC – Paciltaxel / Doxorubicin / Cisplatin
Testicular cancer: PEB – Cisplatin / Etoposod / Bleomycin
Melanoma: CVD – Dacarbazine / Vinorelbine / Cisplatin

Carboplatin:
Small cell lung cancer SCLC: Carboplatin / Etoposide
Non-small cell lung cancer NSCLC: Gemcitabine / Carboplatin
Esophageal cancer: 5FU / Carboplatin
Cervical cancer: Carboplatin / Ifosfamide

Oxaliplatin:
Gastric cancer: EOX – Epirubin / Oxaliplatin / 5-FU
Small bowel cancer: FolFox6 – Oxaliplatin / Folinic acid / 5-FU
Pancreatic cancer: FOLFIRINOX – Oxaliplatin / Irinotecan / Folinic acid / 5-FU

Insert examples of therapy regimens