Systemic Anti Cancer Treatment Protocol

CYCLOPHOSPHAMIDE
Gynaecological Cancer

PROCTOCOL REF: MPHAGYNCYC
(Version No: 1.1)

Approved for use in:

- Second-line (or subsequent) treatment only for those women with platinum-refractory or platinum-resistant advanced ovarian cancer.

Dosage

Drug	Dose	Route	Frequency
Cyclophosphamide	50 to 150mg daily	Oral	Every 28 days until progression.

Supportive treatments:

Domperidone 10mg oral tablets three times a day when required

Interactions

Substances that delay activation of cyclophosphamide and thus reduce its efficacy include: Aprepitant, antifungals e.g. fluconazole, itraconazole**,** and sulfonamides

An increase of the concentration of cytotoxic metabolites may occur with: Allopurinol, protease inhibitors**,** enzyme inducers e.g. rifampin, phenobarbital, carbamazepine, phenytoin, St. John's wort, and corticosteroids.

Drugs that can enhance the toxic effects of cyclophosphamide include: Haematotoxicity and/or immunosuppression ACE inhibitors, thiazide diuretics, zidovudine, clozapine

Pulmonary toxicity: Amiodarone

Administration

- Dose: 50 to 150mg once daily, preferably in the morning, as tolerated.
- Cyclophosphamide tablets are available in 50mg strength.
- Swallow whole with a full glass of water.

Main Toxicities

Cardiac Disorders	Myocarditis and myopericarditis
Gastrointestinal	Nausea, vomiting, oral mucositis and metallic taste
General disorders and administration site conditions	Fever, asthenia, mucosal inflammation, chest pain, headache, dizziness, blurred vision, visual impairment, which could affect the ability to drive or use machines. Hyponatremia, fluid retention, and a syndrome resembling SIADH
Haematological	Neutropenia, thrombocytopenia, anaemia
Hepatobiliary	Abnormal hepatic function, veno-occlusive liver disease
Respiratory	Pneumonitis and pulmonary fibrosis
Skin and subcutaneous tissue disorders	Alopecia Cyclophosphamide may interfere with normal wound healing
Urological	Haemorrhagic cystitis, pyelitis, ureteritis, haematuria and nephrotoxicity, including renal tubular necrosis. Patients should be encouraged to increase oral fluid intake to at least 2 litres per day to reduce the time that the drug remains in the bladder. Mesna can be added to the supportive treatment if required as a daily oral dose

Investigations

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5	Cycle 6	Cycle 7	Ongoing
Medical Assessment	X				X			X	Every 3 cycles
SACT Assessment	X	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	X	Every cycle
U&E & LFT	X	X	X	X	X	X	X	X	Every cycle
CA125	X	X	X	X	X	X	X	X	Every cycle
CT scan	X				X			X	Every 3 cycles
Informed Consent	X								
PS recorded	X	X	X	X	X	X	X	X	Every cycle
Toxicities documented	X	X	X	X	X	X	X	X	Every cycle
Weight recorded	X	X	X	X	X	X	X	X	Every cycle

Dose Modifications and Toxicity Management:

Haematological toxicity

Proceed on day 1 if:-

Platelets ≥ 100 x 10^9/L	ANC ≥ 1.0 x 10^9/L

Delay 1 week on day 1 if:-

Platelets ≤ 99 x 10^9/L	ANC ≤ 0.9 x 10^9/L

Non-Haematological toxicity

Grading and Management of Toxicity

Toxicity should be grading according to the CTCAE v4.0 criteria. Following assessment treatment should be withheld for any toxicity until resolved to grade 0/1. For dose modification, follow the general guidance below and discuss with treating clinician.

	Grade 2	Grade 3	Grade 4
1st appearance	Interrupt treatment until resolved to grade 0/1, then continue at 100% of original dose with prophylaxis where possible	Interrupt treatment until resolved to grade 0/1, then continue at 75-80% of original dose with prophylaxis where possible	Discontinue treatment
2nd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 75-80% of original dose	Interrupt treatment until resolved to grade0/1, then continue at 50% of original dose	
3rd appearance	Interrupt treatment until resolved to grade 0/1, then continue at 50% of original dose	Discontinue treatment	
4th appearance	Discontinue treatment		

Hepatic Impairment

Severe hepatic impairment may be associated with a decreased effect of cyclophosphamide. The dose must be reduced in patients with severe hepatic impairment. A dose reduction of 25 % is recommended in patients with serum bilirubin concentrations of 53 – 86 µmol/L.

Renal Impairment

GFR (mL/min)	Dose
>20	100% dose
10 to 20	75% dose
<10	50% dose

References

1. Dosage Adjustment for Cytotoxics in Hepatic Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Hepatic Impairment (Version 3 - updated January 2009)

2. Dosage Adjustment for Cytotoxics in Renal Impairment. January 2009 UCLH - Dosage Adjustment for Cytotoxics in Renal Impairment (Version 3 - updated January 2009)

3. Stockley's drug interactions. Ninth edition. Edited K. Baxter. Pharmaceutical press. London. 2010

4. **www.medicines.org.uk**