SACT PROTOCOL

The Clatterbridge Cancer Centre NHS Foundation Trust

Systemic Anti Cancer Therapy Protocol

Cyclophosphamide Gynaecological cancer

PROTOCOL REF: MPHAGYNCYC
(Version No. 1.2

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	**50-150mg daily**	PO	Every 28 days until progression

Continuous treatment until progression or they can no longer tolerate treatment

Administration (+/- Counselling Points):

Women of childbearing potential should use effective contraception throughout treatment and for 6-12 months after the last dose of cyclophosphamide

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.

Emetogenic risk (if applicable):

Moderately Emetogenic

Supportive treatments:

Metoclopramide tablets 10mg three times a day for five days.

Dosing in renal and hepatic impairment:

	GFR (mL/min)	Dose
Renal	10 - 29	75% dose
	<10	50% dose

Hepatic	**Mild and moderate**: no need for dose adjustment is expected **Severe:** not recommended, due to risk of reduced efficacy

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

For more detailed interactions please refer to the SmPC

Main toxicities:

Cardiac disorders	Myocarditis, myopericarditis supraventricular arrhythmias (including atrial fibrillation and flutter) as well as ventricular arrhythmias (including severe QT prolongation associated with ventricular tachyarrhythmia.
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	Leukopenia, 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

For more detailed toxicities/adverse reactions please refer to the SmPC

Investigations and treatment plan:

	Pre	Cycle 1	Cycle 2	Cycle 3	Cycle 4	cycle 5	Cycle 6	Cycle 7	Ongoing
Informed Consent	X								
Clinical Assessment	X				X				Every 3 cycles
SACT Assessment (to include PS and toxicities)	X	X	X	X	X	X	X	X	Every cycle
FBC	X	X	X	X	X	X	X	X	Every cycle
U&E & LFTs & Magnesium	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				Every 3 cycles
Main observations (blood pressure, resp rate etc)	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-

ANC ≥ 1.0 x 10^9/L	Plt ≥ 100 x 10^9/L

Delay 1 week on day 1 if-

ANC ≤ 0.9 x 10^9/L	Plt ≤ 99 x 10^9/L

These haematological guidelines assume that patients are well with good performance status, that other acute toxicities have resolved and the patient has not had a previous episode of neutropenic sepsis.

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		
4th appearance	Discontinue treatment		

References:

1. Electronic Medicines Compendium (2016, December) *Cyclophosphamide tablets 50mg* https://www.medicines.org.uk/emc/product/1813/ emc
2. Joint Formulary Committee. *British National Formulary (onlin*e) London: BMJ Group and Pharmaceutical Press
3. Krens S D, Lassche, Jansman G F G A, et al. Dose recommendations for anticancer drugs in patients with renal or hepatic impairment. *Lancet Oncol* 2019; 20: e201–08.
4. Northern Cancer Alliance (2018) *Anti-emetic Guidelines for Chemotherapy Induced Nausea and Vomiting (CINV)* Newcastle Upon Tyne: NHS England

Circulation/Dissemination

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Date document posted on the Intranet	N/A

Version History

Date	Version	Author name and designation	Summary of main changes
		Anna Burke Advanced Pharmacist NMP	V1.1 Routine protocol update
		Sarah Craig Advanced Pharmacist Teacher Practitioner	V1.2 Slight changes to renal and hepatic section and interactions using most up to date references