The Christie NHS
NHS Foundation Trust

GUIDELINES FOR THE USE OF G-CSF & PEGFILGRASTIM (NEULASTA)

Document Reference:	*N/A*	**Version:**	V1.1
Document Owner:	Dr Andrew Sykes Chair Drugs & Therapeutics Committee	**Document Author:**	June So Director of Pharmacy
Accountable Committee:	Drugs & Therapeutics Committee	**Date Approved:**	7th July 2011
Ratified by:	Document Ratification Committee	**Date Ratified:**	N/A
Date issued:	Jan 2012	**Review date:**	July 2013
Target audience:	All prescribers involved with chemotherapy	**Equality Impact Assessment:**	N/A

1.0 Purpose

The purpose of these guidelines is to provide clarity about the indications for the use of growth factors including pegfilgrastim.

2.0 Clinical indications for growth factors

The indications can be summarised as:

- Primary or secondary prophylaxis
- Reducing the duration of severe neutropenic sepsis
- Peripheral blood stem cell mobilisation
- Clinical trial use as stated in the trial protocol

Further detail is provided in section 5

3.0 Choice of daily G-CSF

The daily G-CSF preparations, lenograstim and filgrastim are clinically equivalent plus there has been the recent introduction of the daily biosimilar agents eg zarzio which replaced ratiograstim on the North West regional contract following a recent tendering exercise (March 2011).

The DTC at their meeting on June 2011 approved the following recommendation (after consideration of the published data):

- Zarzio is the daily G-CSF of choice for all indications (whenever a daily preparation is indicated)
- Exception: Filgrastim (neupogen) for peripheral blood stem cell mobilisation

4.0 Cost of growth factors

The comparative cost of these preparations is shown below.
(Apr 2011 prices)

G-CSF	Unit Price	7 Days
Zarzio 300mcg	£14.40	£100.80
Zarzio 480mcg	£22.80	£159.60
(Filgrastim biosimilar)		
Lenograstim 263mcg	£24	£168.00
Filgrastim 300mcg	£43.20	£302.40
Filgrastim 480mcg	£69.12	£483.84
(Neupogen)		
Neulasta	£360	

5.0 Criteria for G-CSF prescribing

5.1 Primary prophylaxis

This is in chemo-naïve patients where the risk of neutropenia is felt to be 'high'.
The current guidelines produced by the British Committee for Standards in Haematology indicate that the febrile neutropenic (FN) risk has to be 40% or greater to be regarded as 'high'. Other groups notably ASCO and the EORTC put a trigger level for G-CSF use at 20% risk (ref. 2). It is recommended that this be adopted.
The regimens in the Trust policy when Neulasta may be considered has been integrated with a fuller list of regimens taken from reference 2 to produce a table with a % FN risk category (table 1).

The % FN risk has been categorised as follows:

Green	% FN risk more than 20%	Primary prophylaxis recommended	Prescribe daily G-CSF or neulasta
Amber	% FN risk 10-20%	Primary prophylaxis not recommended unless there are other patient factors (see ref 3)	Prescribe daily G-CSF if clinically reqd
Red	% FN risk less than 10%	Primary prophylaxis not recommended	Prescribe daily G-CSF if clinically reqd

Other patient factors to consider (ref 3) for primary prophylaxis are:

- Extensive prior chemotherapy
- Previous irradiation to the pelvis or other areas containing large amounts of bone marrow
- Co-morbidity considered to increase the risk of sepsis or consequences of sepsis

Recommendations for amber/red regimens when % FN risk is less than 20%:

1. If clinically required, prescribe the daily G-CSF zarzio for 7 days
2. Dose the patient on daily G-CSF according to patient weight (zarzio is available in 30mu and 48mu presentations)
3. Consider neulasta only in psychosocial situations that make daily G-CSF difficult or impractical

5.2 Secondary prophylaxis

Secondary prophylaxis is used to maintain dose intensity following an episode of sepsis or to prevent treatment delays.

Recommendation:
Consider neulasta in lymphoma, adjuvant breast cancer, germ cell cancer treatment where chemotherapy is given with curative intent. Also in some sarcomas (particularly teenage and young adolescents) where scheduling intensive programmes of treatment.

In all other cases - following episodes of febrile neutropenia or prolonged neutropenia with previous cycles - particularly if chemotherapy is not being given with curative intent:

consider dose reduction or delay OR Secondary prophylaxis with growth factors.

If secondary prophylaxis is required, use daily G-CSF ie zarzio as recommended for amber/red regimens above.

5.3 Febrile neutropenic patients

Growth factors should not be used in:

- afebrile neutropenic patients.

- the treatment of uncomplicated fever and neutropenia as an adjunct to antibiotic therapy.

Daily G-CSF ie zarzio is recommended in patients with profound neutropenia (ANC < 0.1 x 10^9/L) and any one of the following prognostic factors that are predictive of poor clinical outcome:

- pneumonia
- multi-organ dysfunction
- hypotension
- invasive fungal infection
- Age >65 or those with post-treatment lymphopenia.

Table 1: Chemotherapy regimens and febrile neutropenia risk category (based on reference 2)

Malignancy	FN risk category (%)	Chemotherapy regimen
Breast cancer	>20	AC → Docetaxel
		Doxorubicin/Docetaxel
		FEC 100 (ref 4)
		FEC-T (ref 4)
	10–20	AC
		Docetaxel
		Capecitabine/Docetaxel
		Epi-CMF
	<10	Weekly paclitaxel/docetaxel
Head & neck	10-20	Docetaxel/platinum/5FU (TPF)
Small cell lung cancer	>20	Topotecan
	10–20	CAV
		Etoposide/Carboplatin
	<10	CAV → PE
		Paclitaxel/Carboplatin
Non-small cell lung cancer	>20	Etoposide/Cisplatin
	10-20	Docetaxel/Cisplatin
		Vinorelbine/Cisplatin
	<10	Gemcitabine/Cisplatin
		Gemcitabine/carboplatin

Malignancy	FN risk category (%)	Chemotherapy regimen
Non-Hodgkin's lymphoma & myeloma	>20	DHAP
		CHOP
		R-CHOP
		ESHAP DHAP
		VAPEC-B
		R-CVP
		GDCVP
		IVAC
		ChlVPP/EVA
		DTPACE
	10-20	Fludarabine/Mitoxantrone, FMC
	<10	ABVD (Hodgkin's lymphoma)
Ovarian cancer	>20	Paclitaxel
	10–20	Topotecan
	<10	Carboplatin/Paclitaxel
		Gemcitabine/Cisplatin Gemcitabine/carboplatin
		Carboplatin/caelyx
		Rotterdam
Sarcoma	>20	Doxorubicin 75/Ifosfamide 10
		VIDE
Urothelial cancer	>20	MVAC
		Paclitaxel/Carboplatin
Germ cell tumours	>20	BOP → VIP-B
		VeIP, TIP
		T-BEP
	10–20	Cisplatin/Etoposide
		BEP → EP

Malignancy	FN risk category (%)	Chemotherapy regimen
GI cancer	10–20	5-FU/leucovorin
		FOLFIRI IrMdG
	<10	FOLFOX OxMdG
		ECF/ECX
		MCF/MCX M-cap
		Irinotecan
		EOX

References

Cost-effectiveness of pegfilgrastim versus six days of filgrastim for preventing febrile neutropenia in breast cancer patients. Marco Danova, Silvia Chiroli, Giovanni Rosti, and Quan V Doan. Tumori, 95: 219-226, 2009.

EORTC guidelines for the use of granulocyte-colony stimulating factor to reduce the incidence of chemotherapy-induced febrile neutropenia in adult patients with lymphomas and solid tumours. M.S. Aapro et al, European Organisation for Research and Treatment of Cancer (EORTC) Granulocyte Colony-Stimulating Factor (G-CSF) Guidelines Working Party. European Journal of Cancer 42 (2006) 2433 – 2453.

GM&CCN guidelines on the use of growth factors Jan 2009

Christie audit May 2010 by Breast group

VERSION CONTROL SHEET

Version	Date	Author	Status	Comment
1.0	July 2009	June So	Closed	
1.1	July 2011	June So	Active	Change of biosimilar from ratiograstim to zarzio with price update
				Recommendation to use zarzio (daily gcsf) except filgrastim for PBSC mobilisation
				FEC-T and FEC100 in breast added to >20% FN risk category based on audit data (see references)