PEG-INTERFERON

INDICATION (unlicensed)

Myeloproliferative Neoplasm (high risk essential thrombocythaemia, high risk polycythaemia vera pre-fibrotic myelofibrosis or overt myelofibrosis with proliferative features)

Local Funding Arrangement required for peg-interferon*- consider for:

- 1st line indication for younger patients with early disease presentation
- 2nd line indication for patients with resistance/intolerance to hydroxycarbamide

*available at OUH for patients with indications above

Available as 90microgram, 135microgram, 180microgram single use pre-filled syringe

Roferon-A and IntronA were discontinued by manufacturer in 2019 and are no longer available.

TREATMENT INTENT

Disease Modification
Refer to disease specific European LeukemiaNet (ELN) guidelines for disease monitoring.

PRE-ASSESSMENT

1. Investigations to include FBC, blood film and manual differential, coagulation screen, urea, creatinine, electrolytes, liver function tests, calcium, lipid profile, glucose, amylase, urate, consider erythropoietin level if anaemic. Thyroid function should be checked at baseline (TSH and T4) and anti-thyroid peroxidase antibodies
2. Ensure diagnosis is confirmed prior to commencing treatment by WHO or BSH criteria
3. Record performance status (WHO/ECOG).
4. Record height and weight.
5. Take careful history for any past psychiatric problems
6. Baseline eye examination (by optician)
7. ECG and consider echo in selected patients at risk of cardiac disease
8. Consent - ensure patient has received adequate verbal and written information regarding their disease, treatment and potential side effects. Document in medical notes all information that has been given. Obtain written consent on the day of treatment.
9. Treatment should be agreed in the relevant MDT.
10. Arrangements should be made for patient/carer training to self-administer peg-interferon.

DRUG REGIMEN / CYCLE FREQUENCY

Starting Dose

PEG-INTERFERON ALPHA-2a 45 microgram** subcutaneously **weekly**
(Pegasys®)

DOSE MODIFICATIONS

Dose modifications based on haematological response or toxicity

Titrate peg-interferon dose every 4 weeks based on haematological response,

Haematocrit > 0.45 (PV), **or** Platelet > 400 x 10^9/L (ET), **or** WBC > 10 x 10^9/L	Increase dose by 1 level
Haematocrit ≤ 0.45 (PV), **or** Platelet 100-400 x 10^9/L (ET), **and** WBC ≤10 x 10^9/L	Maintain current dose
Platelet <100 x 10^9/L, **or** Neutrophil <1.0 x 10^9/L, **or** Development of new drug associated anaemia (Hb <100g/L)	Reduce dose by 1 level
Any Grade 4 Haematological Events	Withhold dose until recovery

Dose Level	Dose
0	45 microgram/ week*
0.5**	65 microgram/ week
1	90 microgram/ week
2	135 microgram/ week
3	180 microgram/ week

*Frequency of Peg-interferon injection can be reduced to every 2 or 3 weeks in patients showing sustained haematological remission.

**Dose Level 0.5 (65 microgram/ week) may be used for dose titration in patients with concern about peg-interferon toxicity.

Treatment should be interrupted in the event of grade 3 non-haematological toxicity. Discontinue permanently if severe depression symptoms develop.
For fevers, flu-like symptoms and chills consider restricting this to grade 4.

Renal Impairment	Hepatic Impairment
GFR ≥ 30mL/min: Maximum dose 180mcg weekly GFR < 30mL/min: Maximum dose 135mcg weekly	Mild impairment (Child-Pugh Stage A): 100% dose Moderate/severe impairment (Child-Pugh Stage B or C): Limited information. Clinical decision For grade 2 liver toxicity, monitor closely and stop peg-interferon treatment if persistent. Once toxicity has recovered to grade 1 level, restart at 1 dose level lower.

CONTRAINDICATIONS

- History of unstable pre-existing cardiac disease in the last 6 months, e.g. uncontrolled congestive heart failure, recent myocardial infarction, severe arrhythmic disorder.
- Autoimmune hepatitis
- Severe hepatic dysfunction
- Pre-existing, uncontrolled thyroid disease
- In patients with a history of psychiatric disorders peg-interferon may cause deterioration and should only be used with caution and after careful consideration of risk versus benefit. Specific monitoring of psychiatric state should be in place.

INVESTIGATIONS

- FBC, U&E and LFTs at each clinic appointment (initially every 2 weeks)
- Lipids, glucose, amylase every 3-4 months
- Thyroid function every 6 months
- Eye examination yearly (optometry) due to risk of optic neuritis
- In patients with sustained haematological remission, repeat molecular testing should be considered to assess molecular response

CONCURRENT MEDICATION

Paracetamol 1000mg 30minutes prior to all doses during first 2 weeks, then as required.
Allopurinol 300mg OD if clinically appropriate
Aspirin 75mg OD if clinically appropriate

EMETIC RISK

Minimal

ADVERSE EFFECTS / REGIMEN SPECIFIC COMPLICATIONS

(Consult with pharmacist and refer to SPC for full details)

Very commonly reported:
Flu-like symptoms: headache, dizziness, diarrhoea, nausea, abdominal pain, anaemia,

neutropenia, thrombocytopenia, hyperthyroidism, hypothyroidism, anorexia, hypertriglyceridemia, depression, insomnia.

Pulmonary infiltrates, pneumonitis, and pneumonia, occasionally resulting in fatality, have been observed rarely with interferon treatment.

Worsening of pruritus is frequently observed in MPN patients and may require systemic relief.

Consider monitoring mental state and psychology referral in selected patients if required.

TREATMENT RELATED MORTALITY

Risk of treatment related mortality is very low.

REFERENCES

1. Roche. Pegasys. Summary of product characteristics. Updated 17/5/2021. Accessed on 5/11/2021 via http://www.medicines.org.uk/emc
2. Harrison et al (2010) Guideline for investigation and management of adults and children presenting with a thrombocytosis. BJH 149(3):352-375
3. Reilly et al (2012) Guideline for the diagnosis and management of myelofibrosis. BJH 158(4):453-471
4. Barosi et al (2013) Revised response criteria for polycythemia vera and essential thrombocythemia: an ELN and IWG-MRT consensus project. Blood 121(23):4778-4781.
5. Tefferi et al (2013) Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report. Blood 122(8):1395-1398
6. Myeloproliferative Disorders-Research Consortium (MPD-RC) MPD-RC 112 Randomized Trial of Pegylated Interferon Alfa-2a versus Hydroxyurea Therapy in the Treatment of High Risk Polycythemia Vera and High Risk Essential Thrombocythemia Mandatory Companion EudraCT trial ID: 2010-019501-41 v8 updated: 21/12/2015

REVIEW

Name	Revision	Date	Version	Review date
Cheuk-kie Jackie Cheung, Haematology Pharmacist	New document	June 2017	1.0	
Cheuk-kie Jackie Cheung, Haematology Pharmacist	Formatting, minor correction	June 2018	1.1	
Cheuk-kie Jackie Cheung, Haematology Pharmacist	Annual protocol meeting	Oct 2019	1.2	Oct 2021
Yen Lim, Haematology Pharmacist NSSG Myeloid Group	Removal of interferon as now discontinued. Annual protocol meeting	Nov 2021	1.3	Nov 2023