INTERFERON/ PEG-INTERFERON

INDICATION (unlicensed)

Myeloproliferative Neoplasm (high risk essential thrombocythaemia, high risk polycythaemia vera or 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

Roferon-A and IntronA were discontinued by manufacturer in 2019.
Supply in the UK is expected to deplete by the end of 2019.
Peginterferon is recommended in this situation.

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
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.
DRUG REGIMEN / CYCLE FREQUENCY

Starting Dose

PEG-INTERFERON ALPHA-2a**  45 microgram subcutaneously weekly  
(Pegasys ®)  
**Peg-interferon alpha-2b is not recommended due to lack of experience.

INTERFERON ALPHA-2*  1.5 million units subcutaneously THREE times a week

*Interferon alpha-2 is available as Roferon-A (interferon alpha-2a) or IntronA (interferon alpha-2b). There is no comparison study available between the two preparation and can be chosen based on local formulary. Prescribe by BRAND NAME to avoid error.

DOSE MODIFICATIONS

Haematological Toxicity
Titrates interferon/peg-interferon dose every 4 weeks based on haematological response,

<table>
<thead>
<tr>
<th>Platelet &gt; 400 x 10⁹/L, or WBC &gt; 10 x 10⁹/L</th>
<th>Increase dose by 1 level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Platelet 100-400 x 10⁹/L, and WBC ≤10 x 10⁹/L</td>
<td>Maintain current dose</td>
</tr>
<tr>
<td>Platelet &lt;100 x 10⁹/L, or Neutrophil &lt;1.0 x 10⁹/L, or Development of new drug associated anaemia (Hb &lt;100g/L)</td>
<td>Reduce dose by 1 level</td>
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<tr>
<td>Any Grade 4 Haematological Events</td>
<td>Withhold dose until recovery</td>
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<table>
<thead>
<tr>
<th>Peg-interferon</th>
<th>Level</th>
<th>Dose</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
<td>45 microgram/ week*</td>
</tr>
<tr>
<td></td>
<td>0.5**</td>
<td>65 microgram/ week</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>90 microgram/ week</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>135 microgram/ week</td>
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<tr>
<td></td>
<td>3</td>
<td>180 microgram/ week</td>
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<table>
<thead>
<tr>
<th>Interferon</th>
<th>Level</th>
<th>Dose</th>
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<tbody>
<tr>
<td></td>
<td>0</td>
<td>1.5 million units three time per week</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>3 million units three time per week</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>4.5 million units three time per week</td>
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<tr>
<td></td>
<td>3</td>
<td>6 million units three time per week</td>
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</tbody>
</table>

The dose levels are NOT equivalent and patients should not be switched between interferon and peg-interferon.

*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. For fevers, flu-like symptoms and chills consider restricting this to grade 4. For grade 2 liver toxicity, monitor closely and stop interferon treatment if persistent. Once toxicity has recovered to grade 1 level, restart at 1 dose level lower.
PACK SIZE

**Pegasys (Peginterferon alpha-2b)**
90microgram, 135microgram, 180microgram single use pre-filled syringe

**Roferon-A (Interferon alpha-2a)**
3 million units, 4.5 million units, 6 million units, 9 million units single use pre-filled syringe

<table>
<thead>
<tr>
<th>IntronA (interferon alpha-2b)</th>
<th>Max. Single Dose</th>
<th>Expiry</th>
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<tbody>
<tr>
<td>18 million units multi-dose pen</td>
<td>1.5 – 6 million units</td>
<td>4 weeks after first dose</td>
</tr>
<tr>
<td>30 million units multi-dose pen</td>
<td>2.5 – 10 million units</td>
<td>4 weeks after first dose</td>
</tr>
<tr>
<td>60 million units multi-dose pen</td>
<td>5 – 20 million units</td>
<td>4 weeks after first dose</td>
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**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.
- Severe hepatic dysfunction
- Epilepsy
- Pre-existing, uncontrolled thyroid disease
- In patients with a history of psychiatric disorders interferon or 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)
- 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.

TREATMENT RELATED MORTALITY
Risk of treatment related mortality is very low.

REFERENCES

REVIEW

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<tr>
<td>Cheuk-kie Jackie Cheung, Haematology Pharmacist</td>
<td>New document</td>
<td>June 2017</td>
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<td>Cheuk-kie Jackie Cheung, Haematology Pharmacist</td>
<td>Formatting, minor correction</td>
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<td>Cheuk-kie Jackie Cheung, Haematology Pharmacist</td>
<td>Annual protocol meeting</td>
<td>Oct 2019</td>
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<td>Oct 2021</td>
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