Peginterferon alfa-2a Therapy

INDICATIONS FOR USE:

INDICATION	ICD10	Regimen Code	HSE approved reimbursement status*
As monotherapy in adults for the treatment of polycythaemia vera.	D45	00883a	N/A
As monotherapy in adults for the treatment of essential thrombocythaemia.	D47	00883b	N/A
As monotherapy for the treatment of primary or secondary myelofibrosis (post-essential thrombocythemia or post -polycythemia vera.	D47	00883c	N/A

* This applies to post 2012 indications only

TREATMENT:

The starting dose of the drugs detailed below may be adjusted downward by the prescribing clinician, using their independent medical judgement, to consider each patient's individual clinical circumstances.

Admin. Order	Drug	Dose	Route	Cycle
1	Peginterferon alfa-2a (Pegasys®)	45 microgram gradually increased by a maximum of 45 micrograms per week to a max dose of 180 microgram	SC	Every 7 days
The dose at which haematological parameters are stabilised should be maintained. After that, the dose may be adapted and/or the administration interval prolonged as appropriate for the patient. The stabilisation of the haematological parameters is defined as • Polycythaemia vera: haematocrit (HCT) <45% without phlebotomy, platelets ≤400x10^9/L, leucocytes <10x10^9/L • Essential thrombocythaemia: platelets ≤400x10^9/L, leucocytes <10x10^9/L • Myelofibrosis: as per treating consultant haemato-oncologist. Peginterferon alfa-2a (Pegasys®) is administered subcutaneously in the abdomen or thigh.				

ELIGIBILITY:

- Indications as above

CAUTIONS:

- Existence of, or history of severe psychiatric disorders (based on risk benefit in consultation with treating consultant).
- Pre-existing thyroid disease should be controlled with conventional treatment
- History or presence of autoimmune disease (based on risk benefit in consultation with treating consultant)
- Pregnancy (based on risk benefit in consultation with treating consultant)
- Breastfeeding (based on risk benefit in consultation with treating consultant)
- Epilepsy

EXCLUSIONS:

- Hypersensitivity to the active substance or to any of the excipients
- 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
- Hepatitis B patients currently on treatment with telbivudine

PRESCRIPTIVE AUTHORITY:

The treatment plan must be initiated by a Consultant Haematologist working in the area of haematological malignancies

TESTS:

Baseline tests:

- Thyroid function test
- FBC, Renal and Liver profile
- LDH
- Coagulation screen
- Blood glucose, amylase
- Cardiac assessment
- Ophthalmological exam
- Dental examination
- Assess mental state and consider psychology referral if required

Regular tests:

- Thyroid function test
- FBC, Renal and liver profile
- LDH
- Blood glucose, amylase as clinically indicated
- Ophthalmological exam as clinically indicated
- Dental examination as clinically indicated
- Cardiac assessment (ECG as clinically indicated)
- Assess mental state and consider psychology referral if required

Disease monitoring:

Disease monitoring should be in line with the patient's treatment plan and any other test/s as directed by the supervising Consultant.

DOSE MODIFICATIONS:

- Any dose modification should be discussed with a Consultant.
- Titrate peg-interferon dose every 4 weeks based on haematological response

Table 1: Dose modification of peginterferon alfa-2a based on haematological response or toxicity

White Cell Count (WCC) or Absolute Neutrophil Count (ANC) ($x10^9$/L)		Platelets ($x10^9$/L)	Recommended Dose
WCC >10 $x10^9$	And /or	> 400 $x10^9$	Increase dose by 45 microgram
WCC < 10 $x10^9$	And	100 - 400 $x10^9$	Maintain current dose
ANC < 1.0 $x10^9$	And/or	< 400 $x10^9$ or New anaemia (Hb < 100g/L)	Decrease dose by 45 micrograms
Any grade 4 haematological event			Withhold dose until recovery

Renal and Hepatic Impairment:

Table 2: Dose modification of peginterferon alfa-2a in renal and hepatic impairment

Renal Impairment		Hepatic Impairment	
Mild or moderate	No dose adjustment is required.	**Child Pugh A**	No dose adjustment is required
Severe or end stage renal disease	A reduced dose of 135 mcg once weekly is recommended. Regardless of the starting dose or degree of renal impairment ,patients should be monitored and appropriate dose reductions of Pegasys during the course of therapy should be made in the event of adverse reactions.	**Child Pugh B or C**	Peginterferon alfa-2a has not been evaluated in patients with decompensated cirrhosis (e.g., Child-Pugh B or C or bleeding oesophageal varices)
Source – Pegasys SmPC			

Table 3: Peginterferon alfa-2a dose modifications for non-haematological adverse effects during treatment

Severity of toxicity	Recommended dose modification
Grade 2 hepatotoxicity	Monitor closely and stop interferon treatment if persistent. Once toxicity has recovered to Grade 1, restart with the dose reduced by 45 micrograms.
Grade 3 non-haematological toxicity	Hold treatment • For fevers, flu-like symptoms and rigors consider restricting this to Grade 4.

SUPPORTIVE CARE:

EMETOGENIC POTENTIAL:

As outlined in NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting Available on the NCCP website

Peg-interferon – Minimal **(Refer to local policy).For information:**

Within NCIS regimens, antiemetics have been standardised by the Medical Oncologists and Haemato-oncologists and information is available in the following documents:

- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Medical Oncology) - Available on the NCCP website
- NCCP Supportive Care Antiemetic Medicines for **Inclusion in NCIS** (Haemato-oncology) - Available on the NCCP website

PREMEDICATIONS:

- 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 (consider addition of gastro-protection where appropriate)

OTHER SUPPORTIVE CARE:

- VTE prophylaxis **(Refer to local policy)**
- Mouth / oral care **(Refer to local policy)**

ADVERSE EFFECTS:

- Please refer to the relevant Summary of Product Characteristics (SmPC) for details.

REGIMEN SPECIFIC COMPLICATIONS

- **Fever, flu-like symptoms** such as headache, dizziness, diarrhoea, nausea, abdominal pain are commonly associated in the first 48 hours. This may be managed by continuing paracetamol following discussion with the treating consultant.
- **Psychiatric and Central Nervous System (CNS):** Severe CNS effects, particularly depression, suicidal ideation and attempted suicide have been observed in some patients during Pegasys therapy, and even after treatment discontinuation mainly during the 6-month follow-up period. Other CNS effects including aggressive behaviour (sometimes directed against others such as homicidal ideation), bipolar disorders, mania, confusion and alterations of mental status have been observed with alfa interferons. All patients should be closely monitored for any signs or symptoms of psychiatric disorders. If symptoms of psychiatric disorders appear, the potential seriousness of these undesirable effects must be borne in mind by the prescribing physician and the need for adequate therapeutic management should be considered. If psychiatric symptoms persist or worsen, or suicidal ideation is identified, it is recommended that treatment with Pegasys be discontinued, and the patient followed, with psychiatric intervention as appropriate. Patients with existence of, or history of severe psychiatric conditions: If treatment with Pegasys is judged necessary in patients with existence or history of severe psychiatric conditions, this should only be initiated after having ensured appropriate individualised diagnostic and therapeutic management of the psychiatric condition. The use of Pegasys in children and adolescents with existence of or history of severe psychiatric conditions is contraindicated

DRUG INTERACTIONS:

- Current SmPC and drug interaction databases should be consulted for information.

REFERENCES:

1. Pegylated interferon alfa-2a for polycythemia vera or essential thrombocythemia resistant or intolerant to hydroxyurea. Blood. 2019 Oct 31;134(18):1498-1509. doi: 10.1182/blood.2019000428. PMID: 31515250; PMCID: PMC6839950.
2. A randomized phase 3 trial of interferon-α vs hydroxyurea in polycythemia vera and essential thrombocythemia. Blood. 2022 May 12;139(19):2931-2941. doi: 10.1182/blood.2021012743. PMID: 35007321; PMCID: PMC9101248.
3. NCCP Classification Document for Systemic Anti-Cancer Therapy (SACT) Induced Nausea and Vomiting. V6 2025. Available at:https://www.hse.ie/eng/services/list/5/cancer/profinfo/chemoprotocols/nccp-classification-document-for-systemic-anti-cancer-therapy-sact-induced-nausea-and-vomiting.pdf
4. Peginterferon alfa-2a (Pegasys®) SmPC. Accessed October 2024. Available at: https://www.ema.europa.eu/en/medicines/human/EPAR/pegasys

Version	Date	Amendment	Approved By
1	05/03/2025		Dr. Claire Andrews

Comments and feedback welcome at oncologydrugs@cancercontrol.ie.