Further information - pegaspargase

The following information is a summary only. It is recommended to consult full prescribing information for more details.

Pegaspargase (and other asparaginase products) should only be administered to patients at haematological cancer centres with expertise in their use.

Considerations include:

- Considerations of age and comorbidities when choosing whether or not to use pegaspargase**.** There is limited data available for the use of pegaspargase in patients **65 years and older**. Strongly consider not using pegaspargase in patients aged 65 years and older.
- A baseline abdominal ultrasound scan, to examine the biliary tract, pancreas and hepatic echotexture is recommended for all patients being considered for possible pegaspargase treatment.
- Dosing of pegaspargase.
- Systemic hypersensitivity reactions and approaches to management.
- Pharmacokinetic and pharmacodynamic interactions with other medicines.
- Monitoring and identification of toxicities.
- Therapeutic drug monitoring and switching to from pegaspargase to crisantaspase.

Note: To reduce the risk of hypersensitivity to pegaspargase avoid using other pegylated products e.g., pegFILGRASTIM if there is a suitable non-pegylated form.

Contraindications to pegaspargase:

- History of anaphylactic or severe hypersensitivity reactions to the active substance or to any of the excipients.
- History of serious thrombosis during previous asparaginase therapy.
- History of serious haemorrhagic events during previous asparaginase therapy.
- History of pancreatitis including pancreatitis related to previous asparaginase therapy.
- History of significant hepatic impairment, including alcoholic liver disease, autoimmune or viral hepatitis, and steatohepatitis/NASH.

pegaspargase - Monitoring parameters From eviQ "Management of asparaginase therapy" and Oncaspar® NZ Datasheet			
Clinical effect	**Monitoring parameters**	**Frequency**	**Oncaspar® NZ Datasheet synopsis**
Bone marrow suppression	Peripheral blood counts and bone marrow	Baseline and regularly throughout treatment.	The peripheral blood count and the patient's overall bone marrow status should be monitored closely.
Coagulation abnormalities (thrombotic and haemorrhagic)	INR, APTT, PT, fibrinogen, Anti-Thrombin (ATIII)	Baseline, prior to each cycle and at least twice a week throughout treatment until four weeks after each dose or more frequently if clinically indicated.	A baseline coagulation profile should be established and then periodically monitored during and after treatment. An increased prothrombin time (PT), increased activated partial thromboplastin time (APTT), and hypofibrinogenaemia may occur in patients receiving ONCASPAR®. When there is a marked decrease in fibrinogen or Antithrombin III (ATIII) levels, consider appropriate replacement therapy, in accordance with local protocols.
Pancreas and Hepatic toxicity	Abdominal ultrasound scan	Baseline abdominal ultrasound scan, to examine the biliary tract, pancreas and hepatic echotexture is recommended for **all** patients. If, as treatment progresses, there is increasing evidence of significant liver dysfunction (e.g., LFTs > 2 x ULN) or active liver disease, a repeat ultrasound scan of the liver should be performed.	Contraindications to ONCASPAR®: include a history of pancreatitis including pancreatitis related to previous asparaginase therapy, and significant hepatic impairment. Monitor the patient for changes in liver function tests.
Pancreatitis	Serum amylase and lipase levels	Baseline, prior to each cycle and at least twice a week throughout treatment until at least four weeks after therapy or more frequently if clinically indicated.	Serum amylase and/or lipase measurements should be performed frequently to identify early signs of pancreatic inflammation.
Hepatic toxicity	Liver function tests	Baseline, prior to each dose and at least twice a week throughout therapy, then at least weekly for four weeks after therapy or more frequently if clinically indicated.	Monitor the patient for changes in liver function tests.
Hyperuricaemia	Uric acid levels	Baseline and within induction treatment. If patient has a history of gout monitor regularly throughout treatment.	Monitoring details not specified.
Hyperglycaemia, and possible ketoacidosis	Blood glucose	Monitor regularly throughout treatment.	As hyperglycaemia may occur with the use of ONCASPAR® blood and urine glucose levels should be monitored.
Hyper-triglyceridaemia	Lipid levels	Baseline and then regularly throughout treatment.	Monitoring details not specified.
Anti-asparaginase antibodies	Asparaginase activity	If possible, periodic measurement of the asparaginase activity level in serum or plasma is recommended.	Development of anti-asparaginase antibodies may be associated with low asparaginase activity levels.

Guidance on use of crisantaspase (erwinia L-asparaginase, Erwinase®) in patients with hypersensitivity reactions to or silent inactivation of pegaspargase (pegylated-asparaginase, Oncaspar®)

Resuscitation equipment and medications should be readily on hand: antihistamine, adrenaline, oxygen, and IV corticosteroids. Observe patient for ONE hour after administration for signs of hypersensitivity reactions.

1. Re-challenge with pegaspargase may be possible when a previous infusion reaction was deemed not to be a systemic hypersensitivity reaction. Consider addition of hydrocortisone 100 mg IV to usual pegaspargase pre-medications.
2. Crisantaspase is NOT recommended as an alternative treatment for toxicities such as pancreatitis, hepatitis, coagulation abnormalities, or other non-hypersensitivity toxicities associated with pegaspargase.
3. Crisantaspase may be used in place of pegaspargase in the following circumstances:
    a. Systemic hypersensitivity reactions to pegaspargase. This includes patients with generalized rash with or without anaphylactic symptoms, but not those with only local pain or redness at the site of injection.
    b. Subclinical hypersensitivity reaction (silent inactivation) due to asparaginase antibody formation to pegaspargase with asparaginase inactivation. Silent inactivation may be difficult to detect so therapeutic drug monitoring of nadir systemic asparaginase activity of crisantaspase should be performed periodically.

    Patients with previously documented systemic reactions to pegaspargase should receive crisantaspase in any remaining asparaginase-containing courses.
4. In the event that a pegaspargase infusion is discontinued for an allergic reaction, regardless of the amount received, substitution with crisantaspase should begin approximately 48 to 72 hours after pegaspargase has been discontinued and preferably to coincide with the recommended Monday/Wednesday/Friday administration schedule detailed below in patients who are clinically stable.
5. Each dose of pegaspargase (≥ 1000 international units/m^2) should be replaced with 6 doses (number of doses as tolerated) of crisantaspase 25,000 units/m^2 given on Mondays, Wednesdays and Fridays. Alternatively, if preferred, administer once every 48 hours for 6 doses.
6. Prior to administration of crisantaspase administer the following pre-medications:
    a. paracetamol 1000 mg PO 30 minutes before crisantaspase
    b. loratadine 10 mg PO 30 minutes before crisantaspase
    c. famotidine 20 mg PO 30 minutes before crisantaspase

    Other H1 and H2 receptor antagonists may be substituted for loratadine or famotidine if necessary.
7. Crisantaspase may be administered by:
    a. intra-muscular injection. The individual dose may be split between two injection sites if the injection volume is more than 2 mL.
    b. intravenous infusion administered over 1 to 2 hours.

8. If a patient develops a Grade 2 allergic reaction, consider discontinuing the crisantaspase or undertaking a rechallenge with the addition of hydrocortisone 100 mg IV to the usual crisantaspase pre-medications.
9. If a patient develops a Grade 3 or higher anaphylaxis to crisantaspase, discontinue all future asparaginase therapy.

References

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