

Q&A
Thromboembolic Adverse Events (TEEs) Related to octagam®

1. What are TEEs?

In TEEs, a blood vessel gets (partially) blocked and the tissue supplied by this blood level is (partially) cut off from the blood flow. If the blood flow is reduced or blocked, ischemia may lead to tissue damage which results in reduced function or death of the tissue concerned. In the case of the heart, e.g., this may lead to transient reduced function or myocardial infarction.

2. Which types of TEEs happened with octagam?

The TEEs seen with octagam mainly include myocardial infarction, transient ischemic attack, cerebral infarction, pulmonary embolism, and deep vein thromboses. It is important to know that TEEs happen with any IVIG brand and that in IVIG therapy in general a TEE may be considered as an expected adverse event.

3. What causes TEEs in general?

In general there are many potential causes such as:

- Increased blood viscosity e.g. due to dehydration of a patient
- Abnormalities of the vessel wall (injuries, pre-existing blood clots on the vessel wall)
- Increased blood level of certain substances such as coagulation factors or lack of thrombolytic factors

4. What are the known general risk factors for developing TEEs?

In humans, there are known risk factors for TEEs which include:

- History of atherosclerosis, hypertension, diabetes mellitus, cardiovascular risk factors, advanced age, obesity, hyperlipidaemia, coagulation disorders, prolonged periods of immobilization, and known or suspected hyperviscosity.
- Contributing to the risk of developing a TEEs may be risk factors for hyperviscosity, including those with cryoglobulins, fasting chylomicronemia/markedly high triacylglycerols (triglycerides), or monoclonal gammopathies.

5. Which octagam concentration is concerned?

TEEs were mainly reported for octagam® 5% but a few also occurred with octagam®10%. Octagam 10% is not currently distributed in Australia.

6. How many cases occurred?

It is important to know that TEEs may be observed with any IVIG brand. Also with octagam cases of TEE have occasionally been reported in the past.

In Q3/2010 (July – September), however, a clear increase in the spontaneous reporting frequency of TEEs occurred. Initially about 30 cases were reported in Q3/2010 from the US, Germany, Austria, France, Spain, Portugal. Octapharma has not received any case reports of TEEs in Australia during this time.

7. How were the TEEs discovered?

Octapharma entertains a worldwide pharmacovigilance system. The system detects and documents spontaneous reports from the worldwide markets in a reliable and timely fashion.

In the framework of routine pharmacovigilance activities, a drug safety analysis was performed which noted the increased reporting frequency of thromboembolic events (TEEs) in Q3/2010.

8. What actions are Octapharma taking?

Octapharma Australia has voluntarily quarantined a number of batches from the Australian market, and we are working collaboratively with all Australian stakeholders, including the Therapeutic Goods Administration and National Blood Authority, to ensure the ongoing safety of our Australian patients

9. What was the baseline frequency of TEEs for Octagam prior to Q3 2010?

2008: 19 (worldwide)

2009: 21 (worldwide)

2010 Q1: 2

2010 Q2: 9

2010 Q3: 59 (worldwide, many of these reports were triggered by the recall measures thus the Q3 figure is no longer just "voluntary" reporting)

10. What is the new rate of TEEs for Q3 2010?

See answer to Q9 above.

11. What was the temporal relationship between the administration of octagam and the TEEs?

The time of onset of TEEs was found to be variable. Data showed that many patients (52%) exhibited thrombotic complications during or immediately after the infusion; another 11% experienced the event the same day and 11% during 1–3 days post-infusion; the remaining patients (14%) developed thrombotic manifestations after 3 days following Octagam therapy.

The majority (70%) of arterial thrombosis events occurred within the first 24 hours post Octagam infusion with declining frequency over time; venous thrombosis events seemed to occur slightly later.

12. Was any particular type of patient more predisposed to the TEEs?

Octapharma's analysis showed that the most common coexisting illnesses (risk factors) were as follows: obesity (24%), hypertension (23%), hyperlipidaemia (8%), coronary artery disease (7%), diabetes mellitus (6%), and history of arterial or venous thrombosis (5%).

13. My patient has been receiving octagam. What do I need to do?

None of the batches of octagam distributed in Australia have been associated with reports of thromboembolic episodes at an incidence beyond that expected. For this reason, there is no formal requirement to trace and notify patients who have previously received octagam. Octapharma also advise that it is not necessary to treat patients that have previously received octagam, prophylactically with anti-coagulants.

Clinicians, however, should use their own professional judgement to determine whether individual patients, who may be at an increased risk of developing thromboembolic complications as a result of their underlying medical condition(s), require closer follow-up and monitoring.