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Beirut-LEBANON

Malta

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Direct Healthcare Professional Communication
Management of severe cutaneous adverse reactions (SCAR) with Incivo (telaprevir)

Dear Healthcare Professional,

Janssen, in cooperation with the European Medicines Agency (EMA) and (*insert NCA*), would like to inform you of the following:

- Two cases of toxic epidermal necrolysis (TEN), including one fatal case, have been reported in association with the use of telaprevir.

- It is important to adhere to the recommendations for the monitoring and management of rash given in the product information, including immediate discontinuation of telaprevir if severe rash develops.

- Emerging data suggest that co-treatment with peginterferon and ribavirin can contribute to rash; these medications may also need to be stopped.

- Patients should be reminded to contact their doctor immediately if they develop a rash or have a rash that gets worse.

Further information on the safety concern and the recommendations

Incivo is a hepatitis C virus (HCV) NS3/4A protease inhibitor indicated, in combination with peginterferon alfa and ribavirin, for the treatment of genotype 1 chronic hepatitis C in adult patients with compensated liver disease.

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Recently, in post-marketing experience in Japan, there have been two cases of severe cutaneous adverse reactions (SCAR) reported as toxic epidermal necrolysis (TEN), including one fatal case. Severe rash including drug rash with eosinophilia and systemic symptoms (DRESS) and Stevens-Johnson syndrome (SJS) have been reported in clinical development at a rate of 0.4% and <0.1% respectively. TEN had not been previously reported.
Given the clinical relevance of this adverse reaction, the following information is added to the SmPC:

4.4 Special warnings and precautions for use
Severe rash
Severe, potentially life-threatening and fatal skin reactions have been reported with Incivo combination treatment. Toxic epidermal necrolysis (TEN) including fatal outcome has been observed in post-marketing experience (see section 4.8). Fatal cases have been reported in patients with progressive rash and systemic symptoms who continued to receive INCIVO combination treatment after a serious skin reaction was identified.

4.8 Undesirable effects
Skin and subcutaneous tissue disorders
Toxic epidermal necrolysis (TEN) and erythema multiforme have been added in Table 3 as rare (≥1/10,000 to<1/1,000) adverse drug reactions of Incivo, Peginterferon alfa and Ribavirin combination therapy.

There is specific guidance in the SmPC for the monitoring and management of cutaneous reactions, including severe rash, during combination therapy with Incivo which should be routinely adhered to. Key aspects of the **recommendations applicable for severe rash,** which require the immediate and permanent discontinuation of Incivo, are summarized below. The guidance now states that peginterferon and ribavirin should also be immediately discontinued if rash with accompanying systemic symptoms develops. This is based on emerging comparative data on telaprevir-associated rash when given with and without these products.

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Extent and features of Cutaneous Reactions	**Recommendations for Monitoring of Cutaneous Reactions and Discontinuation of Incivo, Ribavirin and Peginterferon alfa for Severe Rash**
Severe rash: Extent of rash > 50% of body surface area or associated with vesicles, bullae, ulcerations other than SJS	Permanently discontinue Incivo immediately. Consultation with a specialist in dermatology is recommended. Monitor for progression or systemic symptoms until the rash is resolved. Peginterferon alfa and ribavirin may be continued. If improvement is not observed within 7 days of Incivo discontinuation, sequential or simultaneous interruption or discontinuation of ribavirin and/or peginterferon alfa should be considered. If medically indicated, earlier interruption or discontinuation of peginterferon alfa and ribavirin may be needed.
Serious skin reactions including rash with systemic symptoms, progressive severe rash, suspicion or diagnosis of generalised bullous eruption, DRESS, SJS/TEN, acute generalized exanthematous pustulosis, erythema multiforme	Permanent and immediate discontinuation of Incivo, peginterferon alfa, and ribavirin. Consult with a specialist in dermatology.

Patients should be instructed to contact their healthcare provider immediately if they experience:

- skin rash
- if rash worsens
- if they develop other symptoms with a rash such as:
  - fever
  - tiredness
  - swelling of the face
  - swelling of lymph glands
- if they have a wide-spread rash with peeling skin which may be accompanied by fever, flu-like symptoms, painful skin blisters, and blisters in the mouth, eyes and/or genitals.

Call for reporting
We remind you that any suspected adverse reaction should be reported according to the national spontaneous reporting system. **Any suspected adverse drug reactions can be reported to:**
Medicines Authority Post-Licensing Directorate, 203 Level 3, Rue D'Argens,Gzira GZR 1368, Malta, or at: http://www.medicinesauthority.gov.mt/adrportal

Alternatively, adverse events may be reported to the address representing the Marketing Authorisation Holder below:

Communication information

Should you have any questions please contact:

Janssen Regional office:

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Dr. Tony Bou Khalil, Medical Affairs Manager
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Or

The responsible contact persons in Malta
Mr. Alan Mulligan, Regulatory Affairs Coordinator
Tel: + 356 2397 6000

Yours faithfully,

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