



19th October 2009

Important Safety Information:

Toxic epidermal necrolysis (TEN) and drug rash with eosinophilia and systemic symptoms (DRESS) syndrome associated with Intelence® ▼ (etravirine)

Dear Healthcare Professional,

In agreement with the European Medicines Agency (EMA), Janssen-Cilag International NV would like to inform you of cases of toxic epidermal necrolysis (TEN), one of which resulted in fatality and cases of drug rash with eosinophilia and systemic symptoms (DRESS) syndrome associated with the use of Intelence (etravirine).

Further information on the safety concern

Recently, cases of severe hypersensitivity syndromes, including drug rash with eosinophilia and systemic symptoms (DRESS) and TEN (toxic epidermal necrolysis), sometimes fatal, have been reported with the use of Intelence.

The DRESS syndrome is characterised by rash, fever, eosinophilia and systemic involvement (e.g. adenopathy, hepatitis, interstitial nephropathy, interstitial lung disease). Time to onset is usually around 3-6 weeks. The outcome in most of the cases is favourable upon discontinuation and after initiation of corticosteroid therapy.

Intelence must be immediately discontinued if severe rash or hypersensitivity reaction is suspected.

Delay in stopping Intelence treatment after the onset of severe rash may result in a life-threatening reaction.

Given the clinical relevance of these adverse reactions, the following information regarding severe skin and hypersensitivity reactions has been included in the Intelence SmPC:

4.4 Special warnings and precautions for use

Severe cutaneous and hypersensitivity reactions

Cutaneous reactions were most frequently mild to moderate, occurred in the second week of therapy, and were infrequent after week 4. Cutaneous reactions were mostly self-limiting and generally resolved within 1-2 weeks on continued therapy (see section 4.8).



Severe cutaneous adverse drug reactions have been reported with INTELENCE; Stevens-Johnson Syndrome and erythema multiforme have been rarely (< 0.1%) reported. Treatment with INTELENCE should be discontinued if a severe cutaneous reaction develops.

Cases of severe hypersensitivity syndromes, including DRESS (Drug Rash with Eosinophilia and Systemic Symptoms) and TEN (toxic epidermal necrolysis), sometimes fatal have been reported with the use of Intelence (see section 4.8). The DRESS syndrome is characterised by rash, fever, eosinophilia and systemic involvement (including, but not limited to, severe rash or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, hepatitis, eosinophilia). Time to onset is usually around 3-6 weeks and the outcome in most of the cases is favourable upon discontinuation and after initiation of corticosteroid therapy.

Patients should be informed to seek medical advice if severe rash or hypersensitivity reactions occur. Patients who are diagnosed with a hypersensitivity reaction whilst on therapy must discontinue Intelence immediately.

Delay in stopping Intelence treatment after the onset of severe rash may result in a life-threatening reaction.

Patients who have stopped treatment due to hypersensitivity reactions should not re-start therapy with Intelence.

4.8 Undesirable Effects

Adverse Drug Reactions from Clinical Trials

Additional ADRs of at least moderate intensity observed in other trials were acquired lipodystrophy, angioneurotic oedema, erythema multiforme and haemorrhagic stroke, each reported in no more than 0.5% of patients. Stevens-Johnson Syndrome (rare; < 0.1%) and toxic epidermal necrolysis (very rare; < 0.01%) have been reported during clinical development with Intelence.



Adverse drug reactions identified during post marketing experience with Intelence

Hypersensitivity reactions, including DRESS, have been reported with Intelence. These hypersensitivity reactions are characterised by rash, fever and sometimes organ involvement (including, but not limited to, severe rash or rash accompanied by fever, general malaise, fatigue, muscle or joint aches, blisters, oral lesions, conjunctivitis, hepatitis, eosinophilia) (see section 4.4).

Call for reporting

We remind you that any suspected adverse reaction should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA) and/or Janssen-Cilag Ltd. Suspected adverse reactions should be reported to the MHRA using a Yellow Card obtained either from the MHRA, CHM Freepost, London SW8 5BR or electronically via the website at www.yellowcard.gov.uk

Communication information

Should you require any further information, please contact Medical Information, Janssen-Cilag Ltd, on 0800 731 8450.

Yours faithfully,

PMF Barnes MBBS FFPM

Medical Director, Janssen-Cilag Ltd

Annex: Revised Product Information with changes highlighted

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