



15<sup>th</sup> February, 2008

**Direct Healthcare Professional Communication**

**SEBIVO® (TELBIVUDINE) IN THE TREATMENT OF CHRONIC HEPATITIS B**

**ADVERSE EVENT "PERIPHERAL NEUROPATHY"**

Dear Healthcare Professional,

Novartis in agreement with the Committee for Medicinal Products for Human Use (CHMP)\* wishes to inform you of an increased risk of "*Peripheral neuropathy*" in chronic hepatitis B patients treated with Sebivo® (telbivudine).

**Summary**

- Peripheral neuropathy has been uncommonly reported in telbivudine-treated patients when used as monotherapy.
- The risk of peripheral neuropathy is increased when telbivudine and pegylated interferon alfa-2a are combined. Such increased risk cannot be excluded for other interferons alfa (pegylated or standard).
- If peripheral neuropathy is suspected, treatment with telbivudine should be reconsidered.
- The benefit of telbivudine in combination with interferon alfa (pegylated or standard) is not currently established.
- Sebivo® is indicated for the treatment of chronic hepatitis B in adult patients with compensated liver disease and evidence of viral replication, persistently elevated serum alanine aminotransferase (ALT) levels and histological evidence of active inflammation and/or fibrosis **as monotherapy only**.
- The product information has been updated to reflect the risk of peripheral neuropathy with telbivudine with or without pegylated interferon alfa-2a.

**Further information on the safety concern**

Peripheral neuropathy has been reported as an uncommon adverse event in telbivudine-treated patients (0.3%) (NV 02B 007 GLOBE Phase III registration study).

This risk of peripheral neuropathy is increased when telbivudine and pegylated interferon alfa-2a are combined, as observed in a clinical trial (study CLDT600A2406) investigating the combination therapy of telbivudine 600 mg daily with pegylated interferon alfa-2a 180 µg once weekly. Eight cases of peripheral neuropathy (5 serious) were reported out of 48 patients treated with telbivudine and a standard dose of pegylated interferon alfa-2a (i.e with

a frequency of 16.6%). The time to onset for this event was approximately 2 to 6 months. All patients were taken off study medication and are being monitored. The clinical outcomes are currently unknown.

**Further information on recommendations to healthcare professionals**

Novartis has decided, based on the review of these data and in conjunction with the Data Safety Monitoring Board (DSMB) of the study, to discontinue the current combination arm whilst patients in the monotherapy arms are continuing treatment.

**Call for reporting**

Please contact Novartis if you have any questions about this information or the safe and effective use of Sebivo®.

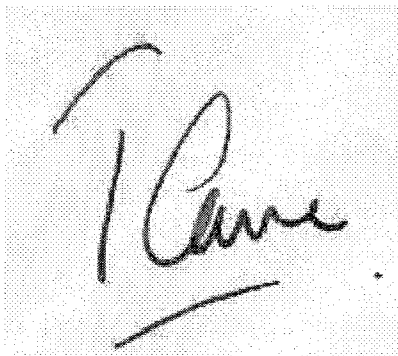
**Reporting suspected adverse reactions/ Call for Reporting**

As Sebivo® is a black triangle drug, please report all suspected adverse drug reactions via Yellow Card ([www.yellowcard.org.uk](http://www.yellowcard.org.uk)). Adverse drug reactions should also be reported to Novartis.

If you require any further information, or wish to report an adverse drug reaction please call Novartis' Medical Information Service on 01276 698370.

*A copy of the draft SmPC adopted by the CHMP on 24 January 2008 and awaiting European Commission decision is enclosed*

Yours sincerely,

A handwritten signature in black ink, appearing to read 'T Cave', is centered on a light gray, textured rectangular background.

Dr Tim Cave  
Novartis Medical Director UK

*\*This is the scientific decision-making committee under the direction of the European Medicines Agency (EMA)*