Date: 17 May 2006

For the attention of Dr Daniel BRASSEUR
European Medicines Agency (EMEA)
7 Westferry Circus, Canary Wharf
London, E14 4HB
United Kingdom

Ref: DPR/ARE/2006-223/JFDL/ADC

Subject: Withdrawal of SCINTIMUN, besilesomab, 1 mg, Kit for radiopharmaceutical preparation - EMEA/H/C/653

Dear Dr BRASSEUR,

I would like to inform you that, at this point of time, CIS bio international has taken the decision to withdraw the application for Marketing Authorisation of SCINTIMUN, besilesomab, 1 mg, kit for radiopharmaceutical preparation, which was intended to be used for:

- Scintigraphic imaging for determining the location of infectious/inflammatory lesions,
- Scintigraphic imaging of bone marrow involvement (detection and extent of carcinoma metastasis, as cold spots).

This withdrawal is based on the following reason:

In order to address issues on clinical safety and efficacy that have been raised by the CHMP in the Day 120 List of Questions, CIS bio international is currently conducting complementary clinical studies whose protocols were reviewed by the Rapporteur and co-Rapporteur and discussed during clarification meetings. Due to the time needed for completion of the studies, answering to the CHMP Day 120 List of Questions in the procedure timeframe is not possible. Based on this, CIS bio international has to withdraw the current application and will resubmit after completion of the two ongoing clinical studies.

Meanwhile, CIS bio international intends to continue the supply of this commercial product in the countries where national Marketing Authorisations have already been granted and in other countries that allow import for named/compassionate use.

I agree for this letter to be published on the EMEA website.

Yours sincerely,

Didier GARONNAT
Responsible Pharmacist

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CIS bio international
S.A. à Directoire et Conseil de Surveillance
au capital de 154 500 000 €

Siège social : SACLAY (Essonne) R.N. 306
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Appendix: further detailed comments

Clinical documentation submitted

- 5 clinical studies (phases I, II and III) including 1146 patients performed between 1987 and 1993,
- 2 bioequivalence studies to support a change in manufacturing process of the drug substance on 39 patients performed between 2000 and 2002,
- Literature references on more than 1200 cases,
- PSUR covering the period between January 1996 and May 2005 reporting a rate of adverse events of less than 0.004% in a total of 82 000 patients administered.

Ongoing clinical studies

In the Day 120 List of Questions, CHMP required additional data on clinical efficacy and safety using the nowadays standards.
Consequently, one clinical study and one observational study based on protocols reviewed by the Rapporteur and co-Rapporteur and discussed during clarification meetings are conducted:

- A multicenter, randomized, open-label, clinical study on the agreement of SCINTIMUN and labelled ^{99m}Tc-White Blood Cells in diagnosing infection/inflammation by immunoscintigraphy in peripheral bone and joints with suspected osteomyelitis. This trial is conducted in five EU countries (Czech Republic, France, Germany, Hungary and The Netherlands) and will include 130 patients.

- An observational study for collecting data on the occurrence of cardiovascular events in patients administered with SCINTIMUN in the approved indications and in routine practical use, under normal, non-study-like conditions and to compare the data with those obtained in patients administered with current radiopharmaceuticals in respective approved indications. Implementation of this study is ongoing in three European countries (Austria, France and Switzerland). It is intended to analyse 2,000 patients (1,000 patients administered with SCINTIMUN and 1,000 patients administered with another radioactive tracer in the same indication). These patients will be followed-up for one month after administration.

Information on the consequences of the withdrawal on ongoing clinical trials, current sales and compassionate use programme

CIS bio international confirms that the ongoing clinical studies will continue until completion.

Meanwhile, CIS bio international intends to supply this commercial product in the countries where national Marketing Authorisations have already been granted (Czech Republic, Hungary, Sweden and Switzerland) and to continue the compassionate use in countries allowing imports for named/compassionate use.

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