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P O S I T I O N P A P E R

VICTIMS' AND PATIENTS' ORGANISATIONS POSITION PAPER ON THE RISK MANAGEMENT PROGRAMME IN THE SCOPE OF A MARKETING AUTHORISATION FOR THALIDOMIDE TO TREAT MULTIPLE MYELOMA

APRIL 2004

Declaration of interests

We, the undersigned, declare no interests neither in the capital of the marketing authorisation applicants (MAA) "Pharmion Ltd., Cambrige, UK" and "Laphal Developpement, France" or in the capital of any local or international branch of the company. As individuals we did not work for the applicant, nor did we receive training. Any other financial interests (e.g. unconditional grants) received by our organisations from the pharmaceutical industry and contacts with MAA are listed at the end of this document.

Main consideration

1. Although cause of a major catastrophe for thousands of persons exposed during their intra-uterine development, thalidomide now has the potential to ensure long term remission in some patients for a severe life-threatening disease. Thalidomide does represent a major medical progress against multiple myeloma, a rare cancer affecting more than 20 000 additional people each year in Europe.

2. We, the thalidomide victims' and myeloma patients' organisations mutually recognise and are aware of the risks related to the use of thalidomide and also its need for the treatment of multiple myeloma.

3. We, thalidomide victims' and myeloma patients' organisations, support the need for a risk management programme run by health care professionals to ensure safest and most efficient thalidomide dispensation. This applies to all available forms of thalidomide on the European market, whether authorised for the indication of multiple myeloma or other indications by other manufacturers or distributors.

4. Even though any new exposure to thalidomide during pregnancy should be avoided, accidents will occur with very low incidence[1]. The marketing authorisation holder should make provision of funds to secure financial support to the affected family and the victim over his/her entire life. We recommend this provision to condition granting of the marketing authorisation and to be implemented by Member States as it is their competence.

5. We reject the proposed risk management programme as designed by the marketing authorisation applicant. Practical aspects of the risk management programme should comply with current laws and practices in member states. It should be well designed to respect multiple myeloma patients' quality of life, and be under the responsibility both of prescribing physician and delivering pharmacist. The risk management programme must be implemented and monitored independently from the product marketing authorisation holder. We hold this view even though there were no complaint from patients participating to the PRMP in the UK during the implementation phase, with reference to IMF UK.

6. Such a risk management programme should include:

   - Brand name must be Thalidomide®
   - A pregnancy test required 7 days before starting thalidomide (when appropriate)
   - One reliable form of birth control (when appropriate)
   - Start of treatment on 2nd or 3rd day of next menses (after negative pregnancy test) (when appropriate)
   - One month treatment supply delivered and renewed each month, using unit dosing (up to 2 months treatment could be delivered when appropriate, to respect patient quality of life)
   - Monthly pregnancy testing (when appropriate)
   - Monthly contraceptive counseling (when appropriate)
   - Appropriate information documents and consent forms for all parties involved
   - Picture of a thalidomide victim displayed on the inner side of the product package cover (avoiding the "Avoid pregnancy" logo that could be confounded with a contraceptive pill logo)
   - doctors can evaluate physical and mental condition of the patient and which part of the risk management programme is relevant/suitable for his/her patient. For some patients, oral information is the only option (e.g. elderly with relapsed MM) whereas confrontation with a video addressing contraception methods would be unethical.
   - After initial information and signing of consent form, either the pharmacy or the hospital dispenses tablets monthly in a dispenser package (clearly indicating which tablets are taken each day)
   - If the patient does not adhere to the relevant parts of the risk management programme, doctor must take appropriate steps and ultimately stop the prescription of thalidomide

7. Any foetal exposure, resulting in a live birth or not, must demand speedy and intensive investigation and review of the risk management programme.

8. It is the responsibility of the marketing authorisation holder to fulfil its post-authorisation commitments, to ensure quality of the product, and to report

[1] No pregnancy reported to the AFSSAPS in the ATU programme with more than 2000 women enrolled

adverse reactions as well as unexpected events to competent authorities, as provided for in the current EU legislation on pharmaceutical products.

a. drug-drug interactions should be better documented, in particular impact on oral contraceptive product efficacy should be measured

b. additional animal and human pharmacokinetic studies are needed to document on the risk of saliva or sperm transmission.

9. We will follow up on the implementation of the risk management programme in each member state and continue our participation to the working group on thalidomide risk management programme.

Organisations who have signed the Victims' and Patients' organisations position paper on the risk management programme in the scope of a marketing authorisation for thalidomide to treat multiple myeloma

Name of organization & address	*Person responsible*	*Declaration of interests*
PATIENTS ORGANISATIONS:		
Arbeitsgemeinschaft Multiples Myelom/Plasmozytom (APMM), Austria Freinbergstr. 12 4020 Linz, Austria	Ms Doris Mayerböck Deputy head of the AMA (Austrian Myeloma Association), affiliate to APMM, Germany for Austria	As far as I have been informed there are no interests in between APMM and Pharmion. On behalf of APMM Germany I am not authorized for any declaration. We did not receive financial support from any pharmaceutical company.
Arbeitsgemeinschaft Multiples Myelom/Plasmozytom (APMM), Germany c/o SHG NRW Hellweg 23 59514 Welver-Dinker, Germany	Dr Rolf Pelzing	APMM Germany is the umbrella organization of German self support groups of myeloma patients. It does not receive any kind of support from Pharmion or any other potential supplier of thalidomide, nor has it any other connection to Pharmion.
Austrian Myeloma Association Bürglsteinstr. 21-10 5020 Salzburg, Austria	Ilse Hein	AMA (Austrian Myeloma Association) is an independent organization. AMA does not receive funding from private industry.
CKP (Contactgroep Kahler- en Waldenstrompatienten) Postbus 197 2900 AD Capelle aan den IJssel The Netherlands.	Mr. S. Homminga, chairman of the board Dr. P.W. Wijermans, medical advisor Mrs. C.L.M. van Ginneken-Noordman, member of the board	CKP (Contactgroep Kahler- en Waldenstrompatienten, the Netherlands) receives no financial support from Pharmion. In 2003 CKP received no financial support from any pharmaceutical industry. Sources of income for CKP include contributions of members, donations, Nederlandse Kankerbestrijding/KWF.'
Contactgroep Myeloom Patiënten VLAANDEREN vzw. (CMP-Vlaanderen vzw.) Losting 14 B-3221 Nieuwrode **Member of:** **Deutsche Leukämie- & Lymphom Hilfe (DLH)** **Arbeitsgemeinschaft Plazmozytom Multiples Myelom (APMM)** **Contactgroep Kahler Patiënten (CKP)**	Johan Creemers Treasurer CMP-Vlaanderen vzw. Zonneweeldelaan 23/32 B-3600 Genk	CMP-Vlaanderen vzw., receives no financial support from Pharmion. In 2003, CMP-Vlaanderen received financial support from the following pharmaceutical industries: • Novartis Pharma 900,00€ • CAF-DCF (Red-Cross) indirect support 750,00€ Balance sheet 2003, see attachment. Other sources, donations by private persons and admission fee Johan Creemers Treasurer CMP-Vlaanderen vzw. Zonneweeldelaan 23/32, B-3600 Genk

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Danish Myeloma Association (Dansk Myelomatose Forening) The Danish Myeloma Association is an independent organisation. The Danish Myeloma Association is member of: The Danish Indtitute of Cancer Epidemiology (Kraeftens Bekaempelse) The Danish Patients Organisation International Myeloma Foundation	Peter Randlov Klosterbakken 40 DK-3500 Vaerlose Denmark Phone: +45 44 48 1427	We receive fiancial support from: The Institute of Cancer Epidemiology, which also hosts our meetings, Novartis (the producers of Aredia).
European Organisation for Rare Diseases (EURORDIS) Plateforme Maladies Rares 102 rue Didot 75014 Paris	Mr Yann Le Cam, chief executive officer	Eurordis met with Laphal representatives prior to Laphal acquisition by Pharmion. The objectives of the meeting were to present risk management program for thalidomide as monitored by Laphal, as defined by AFSSAPS for the temporary use utilisation programme (A.T.U). Eurordis receives no financial support from Pharmion. In 2003, Eurordis received financial support from the following pharmaceutical industries: • OTL Pharma • Actelion Pharmaceuticals Ltd. representing a total of 14% of its annual budget. Other sources include AFM (Association Française des Myopathies), LNCLC (Ligue Nationale Contre le Cancer), Inserm (Institut National pour la Santé et la Recherche Médicale), and the European Commission.
French Network for French patients (Association to be: AFFIRM (Association Française & Francophone pour l'Information et la Recherche sur le Myélome Multiple) 35, Bd Guist'hau 44000 Nantes	Ms Morgane Yvon	
VICTIMS ASSOCIATIONS		
The Thalidomide Society 19 Central Avenue Pimmer, Middlesex HA5 5BT United Kingdom	Ms Margaret Hogg Chairperson	

Name of organization & address	***Person responsible***	***Declaration of interests***
Dutch Thalidomiders A. Romerostraat 10 3573 AA Utrecht, The Netherlands	J.A. Konings	We, the undersigned, declare no interests neither in the capital of the marketing authorisation applicants (MAA) "Pharmion Ltd., Cambrige, UK" and "Laphal Developpement, France" or in the capital of any local or international branch of the company. As individuals we did not work for the applicant, nor did we receive training. Any other financial interests (e.g. unconditional grants) received by our organisations from the pharmaceutical industry and contacts with MAA are listed in annex I of this document.
DYSMELIA A.S.B.L (Association sans but lucratif, Belgian non-profit association)	Nicole Vuylsteke, chairlady ; 24 Monseigneur de Haernelaan, 8500 Kortrijk Charles Dauvin, treasurer ; 124 Rue du Nouveau Monde, 7060 Soignies Dominique Crèvecoeur, delegated member; 12/10 Rue Audrey Hepburn, 1090 BRUSSELS Judith Horvath, delegated member. 19 Chemin du Comte d'Egmont, 7860 LESSINES	Our association was founded in 1963 by Doctor Paul MARCOUX, following the birth of more than 40 children presenting severe malformations at the lower and upper limbs. These malformations were the consequence of the take of thalidomide by the mothers during their pregnancy. We affirm not to have any direct or indirect bond with an unspecified Belgian or foreign pharmaceutical firm. The funds which our association lays out were collected by requests for gifts to private individuals and with the organization by its members of sporting and festive events. The running expenses of daily management of our non-profit group are covered by the annual contributions of its effective members. Moreover, our association is managed and animated only by voluntary people who do not perceive any remuneration.
Bundesverband Contergangeschädigter e.V. - Hilfswerk vorgeburtlich Geschädigter Schwimmbadweg 33 89604 Allmendingen Germany	Margit Hudelmaier President	

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The Scandinavian Society for the Thalidomide cases (FfdN) c/o Ex-Center Info, Röda Korsets sjukhus, Brinellv. 2, 114 28 Stockholm, Sweden	Mr Björn Håkansson Chairman of the board	During 2003 FfdN received financial support from: Pharmion Ltd. Purpose of financial support: to find more thalidomide groups in Europe. Astra Zeneca PLC Purpose of financial support: To co-operate with Astra Zeneca PLC to identify ALL thalidomide victims in Sweden and also to give them a proper compensation (from 1968). Astra Zeneca PLC also gives a financial support for EC-Center, a rehabilitation-centre for thalidomide victims and people with similar disabilities. EX-Center is a joint venture between FfdN and the Red Cross Hospital of Stockholm. FfdN agrees to the position paper.