



Celgene Limited  
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12th June, 2008

Dear XXXX

**Thalidomide Pharmion ▼ (thalidomide 50mg hard capsule) – Pregnancy Prevention Programme and the supply of unlicensed medicine to meet the special needs of individual patients**

On 16th April 2008 the European Commission granted to Pharmion Limited a centralised marketing authorisation, entitling the company to market Thalidomide Pharmion throughout the EU. Pharmion was acquired by Celgene in March 2008.

Thalidomide Pharmion is authorised in combination with melphalan and prednisone as first-line treatment of patients with untreated multiple myeloma, aged  $\geq 65$  years, or those ineligible for high-dose chemotherapy.

The teratogenic effects of thalidomide are well known, but the Commission, on the advice of the Committee for Medicinal Products for Human Use (CHMP) concluded that, provided appropriate procedures were in place to avoid foetal exposure, Thalidomide Pharmion's benefits for the above indication outweigh its potential risks. Thalidomide Pharmion must be prescribed and dispensed in accordance with the Thalidomide Pharmion Pregnancy Prevention Programme (PPP).

The purpose of this letter is to introduce the Thalidomide Pharmion PPP, and to explain how the granting of marketing authorisation affects the supply of thalidomide that has hitherto been available as an unlicensed medicine to meet the special needs of individual patients.

**Thalidomide Pharmion Pregnancy Prevention Programme**

Celgene has developed the Thalidomide Pharmion PPP, which provides healthcare professionals with educational and other materials to prevent unborn children from being exposed to thalidomide.

The Thalidomide Pharmion PPP is a condition of the European marketing authorisation of Thalidomide Pharmion. Procedures for implementing the Thalidomide Pharmion PPP in the UK have been developed in collaboration with patient groups and healthcare professionals and the implementation of the PPP in the UK has been endorsed by the Medicines and Healthcare Products Regulatory Agency (MHRA).

**Supply of unlicensed thalidomide to meet the special needs of individual patients**

Until now, healthcare professionals requiring thalidomide to meet the special needs of individual patients in the UK could obtain unlicensed formulations of thalidomide because there was no licensed product available capable of meeting those needs. Pending the commercial launch of Thalidomide Pharmion (currently expected for late June 2008) Celgene will continue to meet requests for Thalidomide Pharmion from healthcare professionals registered through the existing Risk Management Programme. After the launch of licensed Thalidomide Pharmion, supply of unlicensed thalidomide should cease

## Prescribing information

### THALIDOMIDE PHARMION ▼

*Refer to the Summary of Product Characteristics before prescribing*

**Name and composition:** Thalidomide Pharmion 50mg hard capsule **Indications:** Thalidomide Pharmion in combination with melphalan and prednisone as first line treatment of patients with untreated multiple myeloma, aged  $\geq 65$  years or ineligible for high dose chemotherapy. Thalidomide Pharmion is prescribed and dispensed according to the Thalidomide Pharmion Pregnancy Prevention Programme. Thalidomide Pharmion is not to be used for patients under 18 years of age. **Dosage and Route:** The recommended oral dose is 200 mg per day for a maximum of twelve 6-week cycles. Thalidomide Pharmion should be taken as a single dose at bedtime, to reduce the impact of somnolence. Dose delay, reduction or discontinuation may be necessary - see Summary of Product Characteristics for detail. Treatment must be initiated and monitored under the supervision of physicians with expertise in managing immunomodulatory or chemotherapeutic agents and a full understanding of the risks of thalidomide therapy and monitoring requirements **Side effects:** See *Summary of Product Characteristics for detail*. Neutropenia, leukopenia, constipation, somnolence, paraesthesia, peripheral neuropathy, anaemia, lymphopenia, thrombocytopenia, dizziness, dysaesthesia, tremor and peripheral oedema, cardiac failure, bradycardia, abnormal coordination, pulmonary embolism, interstitial lung disease, bronchopneumopathy, dyspnea, vomiting, dry mouth, toxic skin eruption, rash, dry skin, pneumonia, deep vein thrombosis, pyrexia, asthenia, malaise, confusional state, depression.

#### Special Warnings & Precautions:

**Teratogenic effects:** Thalidomide is a powerful human teratogen, inducing a high frequency of severe and life-threatening birth defects. Thalidomide must never be used by women who are pregnant or could become pregnant. The conditions of the Thalidomide Pharmion Pregnancy Prevention Programme must be fulfilled for all male and female patients.

Patients should be monitored for the following serious adverse events: deep venous thrombosis and pulmonary embolism symptoms, peripheral neuropathy symptoms, syncope and bradycardia, toxic skin reactions, somnolence. Dose delay, reduction or discontinuation may be necessary. Due to the increased risk of thromboembolic events, thromboprophylaxis is recommended for at least the first five months of treatment. **Caution:** In patients with severe renal or hepatic impairment, preexisting peripheral neuropathy or a history of thromboembolic events. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption. **Effect on ability to drive and use machines:** Caution is recommended when driving or operating machines as fatigue, dizziness, and somnolence have been reported. **Contraindications:** Hypersensitivity to thalidomide or to any of the excipients, pregnant women, women of childbearing potential unless all the conditions of the Thalidomide Pharmion Pregnancy Prevention Programme are met, patients unable to follow or comply with the required contraceptive measures. **Interactions:** May enhance the sedation induced by anxiolytics, hypnotics, antipsychotics, H1 anti-histamines, opiate derivatives, barbiturates and alcohol. Caution with beta blockers, anticholinesterase agents or medicinal products known to induce torsade de pointes. Caution with medicinal products known to induce neuropathy. Closely monitor INR if using concomitant warfarin. Concomitant use of erythropoietic agents, hormone replacement therapy and combined oral contraceptive pills may increase the thrombotic risk. **Overdose:** Cases of overdose have been reported in the literature. No fatalities have been reported and all overdose patients recovered without sequelae. There is no antidote and appropriate supportive care should be used. **Legal category:** Prescription Only Medicine **Basic NHS price:** £10.66 per 50mg capsule **Marketing Authorisation Number and Holder:** EU/1/08/443/001. Pharmion Ltd, Riverside House, Riverside Walk, Windsor, SL4 1NA

**Date of preparation:** 21 May 2008

Adverse events should be reported to Celgene Ltd Medical Information (Tel: 08448 010 045 in the UK or 1800 333 111 in Ireland). In addition, information about adverse event reporting can be found at [www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)

unless a special need can be demonstrated to continue to exist for certain individual patients. MHRA Guidance Note 14 (January 2008; available at: [www.mhra.gov.uk/Publications/Regulatoryguidance/Medicines/index.htm](http://www.mhra.gov.uk/Publications/Regulatoryguidance/Medicines/index.htm)) on the supply of unlicensed medicinal products advises that, as a rule, an unlicensed medicinal product, which is a pharmaceutical equivalent of an available licensed product, should not be placed on the market once a licensed product is obtainable from normal distribution channels in a reasonable time.

After the introduction of Thalidomide Pharmion▼ (thalidomide 50mg hard capsule) to the market, the product will only be made available to pharmacies that have enrolled in the Thalidomide Pharmion PPP, and have registered by completing a pharmacy registration form contained within the **Healthcare Professionals Educational Kit**, which must be returned to Celgene. Those pharmacies currently supplying patients with unlicensed Thalidomide Pharmion should register with the Thalidomide Pharmion PPP to avoid interruption in the supply of thalidomide for their patients – The Healthcare Professionals Educational Kit will be sent out to currently registered users in June 2008. Celgene will be working closely with current dispensers of unlicensed thalidomide to ensure continuity of supply with Thalidomide Pharmion (The Healthcare Professionals Educational Kit can be obtained from Celgene by calling 0808 156 3059).

#### **Further information**


If you have further questions regarding the switch over to the Thalidomide Pharmion PPP, please contact Celgene on 0808 156 3059.

#### **Call for Reporting**

Healthcare professionals should report any adverse event suspected to be associated with the use of Thalidomide Pharmion to the Medicines and Healthcare products Regulatory Agency using a Yellow Card available directly from the MHRA, CHM Freepost, London SW8 5BR, or electronically via the MHRA website ([www.yellowcard.gov.uk](http://www.yellowcard.gov.uk)).

Suspected adverse reactions may also be reported to Celgene by phone on 08448 010 045 (Medical Information), by fax on 08448 010 046 or e-mail at [drugsafetyUK@celgene.com](mailto:drugsafetyUK@celgene.com).

Yours sincerely



Tom Oakley  
Regulatory & Drug Safety Manager  
Celgene Ltd

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