Symposium
IMAGING AND MULTIPLE MYELOMA: Current concepts and controversies

Announcement

Friday 04 March 2016

Hof ter Musschen, Brussel

www.bhs.be

INTRODUCTION

Management of multiple myeloma is a rapidly evolving field. Beside the progress of treatment, with a lot of new drugs and prolonged survival, the definition and imaging techniques of bone disease are changing.

For decades Xrays bone survey has been the gold standard for diagnosis of bone lesions .Now low dose CT-scan, MRI and Pet-CT become more and more reference examinations.

During this symposium, we will have the opportunity to learn from radiologists and nuclearists about these imaging techniques and their role in the diagnosis and follow-up of multiple myeloma, in the context of the new definitions of symptomatic myeloma. We will also listen to the experience of the IFM group regarding the prognostic implication of MRI and Pet-CT. Finally we hope that we will have a constructive and interactive multidisciplinary discussion between hematologists, radiologists and nuclearists, trying to define guidelines for Belgium.
We wish you an inspiring symposium!

Chantal Doyen, committee chair

Karolien Beel
Greet Bries
Jo Caers
Bernard De Prijck
Hade De Samblanx
Hilde Demuynck
Michel Delforge
Anne Deweweire
Karel Fostier
Alain Kentos
Nathalie Meuleman
Philippe Mineur
Fritz Offner
Rik Schots
Melanie Vaes
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Ann Van De Velde
Isabelle Vande Broek
Marie-Christiane Vekemans
Philip Vlummens
KaLung Wu

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PROGRAMME

14.00	Welcome on behalf of the BHS MM subcommittee *C Doyen*
14.10	Updated IMWG definitions generate new questions on imaging *J Caers, CHU Sart Tilman , Liège*
14.20	MRI in MM: use and limitations *F Lecouvet, UCL Saint Luc Brussels*
14.45	CT scan imaging in MM: the new standard *S Pans, UZ Leuven*
15.05	Prospective evaluation of MRI and Pet-Ct in the IFM DFCI 2009 trial *P Moreau, Nantes*
15.40	Diagnostic criteria for Pet- CT in MM *N Whitofs, CHU Sart Tilman, Liège*
16.00	Coffee break
16.30	Clinical cases and roundtable *K Fostier ,UZ Brussel* *M Delforge, UZ Leuven* *C. Doyen, UCL Mont Godinne* *S Pans, UZ Leuven* *M-C Vekemans, UCL Saint Luc* *N Whitofs, CHU Sart Tilman, Liège*
17.15	Conclusion: to Belgian guidelines *N Meuleman, Inst Bordet, Brussels*

GENERAL INFORMATION

Location
Hof ter Musschen
Av. Emmanuel Mounierlaan 2
1200 Brussel
Tel.: +32 (0) 2 774 01 10

Registration
Please register online via the BHS website (www.bhs.be),
or via www.congresscare.com
Registration is free of charge.

Language
The meeting language will be English.

Accreditation
Accreditation is pending nr. 15018893

Website
www.bhs.be

Symposium secretariat

Congress Care
P.O. Box 440
NL-5201 AK 's-Hertogenbosch
The Netherlands
+31-73-690 1415
bhs@congresscare.com
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Postpone the first relapse as long as possible

*ndMM NSCT: newly diagnosed multiple myeloma non stem cell transplant

1, Benboubker et al. NEJM 2014;371:906-917
2, Facon et al. ASCO 2015 Abstract #8524
3, Facon et al. Oral presentation EHA 2015, abstract #S105

BE-REV160008

- 35 months of median duration of response[1]
- 33% patients progression free after 4 years[2]
- + 10,4 months of OS versus a triplet therapy (MPT)[3]

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▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SPC for how to report adverse reactions. **NAME OF THE MEDICINAL PRODUCT** Revlimid 2.5 mg hard capsules Revlimid 5 mg hard capsules Revlimid 7.5 mg hard capsules Revlimid 10 mg hard capsules Revlimid 15 mg hard capsules Revlimid 20 mg hard capsules Revlimid 25 mg hard capsules **QUALITATIVE AND QUANTITATIVE COMPOSITION** Each capsule contains 2.5 mg of lenalidomide. Each capsule contains 5 mg of lenalidomide. Each capsule contains 7.5 mg of lenalidomide. Each capsule contains 10 mg of lenalidomide. Each capsule contains 15 mg of lenalidomide. Each capsule contains 20 mg of lenalidomide. Each capsule contains 25 mg of lenalidomide. Excipient(s) with known effect: Each capsule contains 73.5 mg of lactose, anhydrous. Each capsule contains 147 mg of lactose, anhydrous. Each capsule contains 144.5 mg of lactose, anhydrous. Each capsule contains 294 mg of lactose, anhydrous. Each capsule contains 289 mg of lactose, anhydrous. Each capsule contains 244.5 mg of lactose, anhydrous. Each capsule contains 200 mg of lactose, anhydrous. For the full list of excipients, see section 6.1 of the SPC. **PHARMACEUTICAL FORM** Hard capsule. Blue-green/white capsules, size 4, 14.3 mm, marked "REV 2.5 mg". White capsules, size 2, 18.0 mm, marked "REV 5 mg". Pale yellow/white capsules, size 2, 18.0 mm, marked "REV 7.5 mg". Blue-green/pale yellow capsules, size 0, 21.7 mm, marked "REV 10 mg". Pale blue/white capsules, size 0, 21.7 mm, marked "REV 15 mg". Blue-green / Pale blue capsules, size 0, 21.7 mm, marked "REV 20 mg". White capsules, size 0, 21.7 mm, marked "REV 25 mg". **CLINICAL PARTICULARS Therapeutic indications Newly diagnosed multiple myeloma** Revlimid is indicated for the treatment of adult patients with previously untreated multiple myeloma who are not eligible for transplant (see section 4.2 of the SPC). **Multiple myeloma** Revlimid in combination with dexamethasone is indicated for the treatment of multiple myeloma in adult patients who have received at least one prior therapy. **Myelodysplastic syndromes** Revlimid is indicated for the treatment of patients with transfusion-dependent anaemia due to low- or intermediate-1-risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate. **Posology and method of administration** Revlimid treatment should be supervised by a physician experienced in the use of anti-cancer therapies (see section 4.4 of the SPC, karyotype). Posology **Newly diagnosed multiple myeloma** *Lenalidomide in combination with dexamethasone until disease progression in patients who are not eligible for transplant* Lenalidomide treatment must not be started if the Absolute Neutrophil Counts (ANC) is < 1.0 x 10^9/L, and/or platelet counts are < 50 x 10^9/L. *Recommended dose* The recommended starting dose of lenalidomide is 25 mg orally once daily on days 1-21 of repeated 28-day cycles. The recommended dose of dexamethasone is 40 mg orally once daily on days 1, 8, 15 and 22 of repeated 28-day cycles. Patients may continue lenalidomide and dexamethasone therapy until disease progression or intolerance. Dosing is continued or modified based upon clinical and laboratory findings (see section 4.4 of the SPC). For patients ≥75 years of age, the starting dose of dexamethasone is 20 mg/day on Days 1, 8, 15 and 22 of each 28-day treatment cycle. The recommended dose of lenalidomide for patients suffering from moderate renal impairment is 10 mg once daily. Recommended dose adjustments during treatment and restart of treatment: Dose adjustments, as summarised below, are recommended to manage grade 3 or 4 thrombocytopenia, neutropenia, or other grade 3 or 4 toxicity judged to be related to lenalidomide. *Dose reduction steps* Starting dose Lenalidomide 25 mg Dexamethasone 40 mg,Dose level -1 Lenalidomide 20 mg Dexamethasone 20 mg,Dose level -2 Lenalidomide 15 mg Dexamethasone 12 mg,Dose level -3 Lenalidomide 10 mg Dexamethasone 8 mg,Dose level- 4 Lenalidomide 5 mg Dexamethasone 4 mg,Dose level -5 Lenalidomide 2.5 mg Dexamethasone NA *Thrombocytopenia* When platelets: Fall to < 25 x 10^9/L Recommended course: Stop lenalidomide dosing for remainder of cycle[a],When platelets: Return to ≥ 50 x 10^9/L Recommended course: Decrease by one dose level when dosing resumed at next cycle a If Dose Limiting Toxicity (DLT) occurs on > Day15 of a cycle, lenalidomide dosing will be interrupted for at least the remainder of the current 28-day cycle. *Neutropenia* When neutrophils: First fall to < 0.5 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When neutrophils: Return to ≥ 1 x 10^9/L when neutropenia is the only observed toxicity Recommended course: Resume lenalidomide at Starting dose once daily,When neutrophils: Return to ≥ 0.5 x 10^9/L when dose-dependent haematological toxicities other than neutropenia are observed Recommended course: Resume lenalidomide at Dose level -1 once daily,When neutrophils: For each subsequent drop below < 0.5 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When neutrophils: Return to ≥ 0.5 x 10^9/L Recommended course: Resume lenalidomide at next lower dose level once daily. In case of neutropenia, the use of growth factors in patient management should be considered. If the dose of lenalidomide was reduced for a hematologic DLT, the dose of lenalidomide may be re-introduced to the next higher dose level (up to the starting dose) at the discretion of the treating physician if continued lenalidomide / dexamethasone therapy resulted in improved bone marrow function (no DLT for at least 2 consecutive cycles and an ANC ≥1,500/ µL with a platelet count ≥ 100,000/µL at the beginning of a new cycle at the current dose level). *Lenalidomide in combination with melphalan and prednisone followed by maintenance monotherapy in patients who are not eligible for transplant* Lenalidomide treatment must not be started if the ANC is < 1.5 x 10^9/L, and/or platelet counts are < 75 x 10^9/L. *Recommended dose* The recommended starting dose is lenalidomide 10 mg/day orally on days 1-21 of repeated 28-day cycles for up to 9 cycles, melphalan 0.18 mg/kg orally on days 1-4 of repeated 28 day cycles, prednisone 2 mg/kg orally on days 1-4 of repeated 28-day cycles. Patients who complete 9 cycles or who are unable to complete the combination therapy due to intolerance are treated with lenalidomide alone,10 mg/day orally on days 1-21 of repeated 28-day cycles given until disease progression. Dosing is continued or modified based upon clinical and laboratory findings (see section 4.4 of the SPC). Recommended dose adjustments during treatment and restart of treatment: Dose adjustments, as summarised below, are recommended to manage grade 3 or 4 thrombocytopenia, neutropenia, or other grade 3 or 4 toxicity judged to be related to lenalidomide. *Dose reduction steps* Starting dose Lenalidomide: 10 mg[a] Melphalan: 0.18 mg/kg Prednisone: 2 mg/kg,Dose level -1 Lenalidomide: 7.5 mg Melphalan: 0.14 mg/kg Prednisone: 1 mg/kg,Dose level -2 Lenalidomide: 5 mg Melphalan: 0.10 mg/kg Prednisone: 0.5 mg/kg,Dose level -3 Lenalidomide: 2.5 mg Melphalan: NA Prednisone: 0.25 mg/kg [a] *If neutropenia is the only toxicity at any dose level, add granulocyte colony stimulating factor (G-CSF) and maintain the dose level of lenalidomide.* *Thrombocytopenia* When platelets: First fall to < 25 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When platelets: Return to ≥ 25 x 10^9/L Recommended course: Resume lenalidomide and melphalan at Dose level -1 ,When platelets: For each subsequent drop below 30 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When platelets: Return to ≥ 30 x 10^9/L Recommended course: Resume lenalidomide at next lower dose level (Dose level -2 or -3) once daily. *Neutropenia* When neutrophils: First fall to < 0.5 x 10^9/L[a] Recommended course: Interrupt lenalidomide treatment,When neutrophils: Return to ≥ 0.5 x 10^9/L when neutropenia is the only observed toxicity Recommended course: Resume lenalidomide at Starting dose once daily,When neutrophils: Return to ≥ 0.5 x 10^9/L when dose-dependent haematological toxicities other than neutropenia are observed Recommended course: Resume lenalidomide at Dose level -1 once daily,When neutrophils: For each subsequent drop below < 0.5 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When neutrophils: Return to ≥ 0.5 x 10^9/L Recommended course: Resume lenalidomide at next lower dose level once daily. *[a] If the subject has not been receiving G-CSF therapy, initiate G-CSF therapy. On Day 1 of next cycle, continue G-CSF as needed and maintain dose of melphalan if neutropenia was the only DLT. Otherwise, decrease by one dose level at start of next cycle.* In case of neutropenia, the use of growth factors in patient management should be considered. **Multiple myeloma with at least one prior therapy** *Recommended dose* The recommended starting dose of lenalidomide is 25 mg orally once daily on days 1-21 of repeated 28-day cycles. The recommended dose of dexamethasone is 40 mg orally once daily on days 1-4, 9-12, and 17-20 of each 28-day cycle for the first 4 cycles of therapy and then 40 mg once daily on days 1-4 every 28 days. Dosing is continued or modified based upon clinical and laboratory findings (see section 4.4 of the SPC). Prescribing physicians should carefully evaluate which dose of dexamethasone to use, taking into account the condition and disease status of the patient. Lenalidomide treatment must not be started if the ANC < 1.0 x 10^9/L, and/or platelet counts < 75 x 10^9/L or, dependent on bone marrow infiltration by plasma cells, platelet counts < 30 x 10^9/L. Recommended dose adjustments during treatment and restart of treatment: Dose adjustments, as summarised below, are recommended to manage grade 3 or 4 neutropenia or thrombocytopenia, or other grade 3 or 4 toxicity judged to be related to lenalidomide. *Dose reduction steps* Starting dose 25 mg,Dose level -1 15 mg,Dose level -2 10 mg,Dose level -3 5 mg *Thrombocytopenia* When platelets: First fall to < 30 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When platelets: Return to ≥ 30 x 10^9/L Recommended course: Resume lenalidomide at Dose level -1 ,When platelets: For each subsequent drop below 30 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When platelets: Return to ≥ 30 x 10^9/L Recommended course: Resume lenalidomide at next lower dose level (Dose level -2 or -3) once daily. Do not dose below 5 mg once daily. *Neutropenia* When neutrophils: First fall to < 0.5 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When neutrophils: Return to ≥ 0.5 x 10^9/L when neutropenia is the only observed toxicity Recommended course: Resume lenalidomide at Starting dose once daily,When neutrophils: Return to ≥ 0.5 x 10^9/L when dose-dependent haematological toxicities other than neutropenia are observed Recommended course: Resume lenalidomide at Dose level -1 once daily,When neutrophils: For each subsequent drop below < 0.5 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When neutrophils: Return to ≥ 0.5 x 10^9/L Recommended course: Resume lenalidomide at next lower dose level (Dose level -1, -2 or -3) once daily. Do not dose below 5 mg once daily. In case of neutropenia, the use of growth factors in patient management should be considered. **Myelodysplastic syndromes** Lenalidomide treatment must not be started if the ANC < 0.5 x 10^9/L and/or platelet counts < 25 x 10^9/L. *Recommended dose* The recommended starting dose of lenalidomide is 10 mg orally once daily on days 1-21 of repeated 28-day cycles. Dosing is continued or modified based upon clinical and laboratory findings (see section 4.4 of the SPC). Recommended dose adjustments during treatment and restart of treatment: Dose adjustments, as summarized below, are recommended to manage grade 3 or 4 neutropenia or thrombocytopenia, or other grade 3 or 4 toxicity judged to be related to lenalidomide. *Dose reduction steps* Starting dose 10 mg once daily on days 1-21 every 28 days,Dose level -1 5.0 mg once daily on days 1-28 every 28 days,Dose level -2 2.5 mg once daily on days 1-28 every 28 days,Dose level -3 2.5 mg every other day 1-28 every 28 days For patients who are dosed initially at 10 mg and who experience thrombocytopenia or neutropenia: *Thrombocytopenia* When platelets: Fall to < 25 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When platelets: Return to ≥ 25 x 10^9/L - < 50 x 10^9/L on at least 2 occasions for ≥ 7 days or when the platelet count recovers to ≥ 50 x 10^9/L at any time Recommended course: Resume lenalidomide at next lower dose level (Dose level -1, -2 or -3) *Neutropenia* When neutrophils: Fall to < 0.5 x 10^9/L Recommended course: Interrupt lenalidomide treatment,When neutrophils: Return to ≥ 0.5 x 10^9/L Recommended course: Resume lenalidomide at next lower dose level (Dose level -1, -2 or -3) *Discontinuation of lenalidomide* Patients without at least a minor erythroid response within 4 months of therapy initiation, demonstrated by at least a 50% reduction in transfusion requirements or, if not transfused, a 1g/dl rise in haemoglobin, should discontinue lenalidomide treatment. *All patients* For other grade 3 or 4 toxicities judged to be related to lenalidomide, treatment should be stopped and only restarted at next lower dose level when toxicity has resolved to ≤ grade 2 depending on the physician's discretion. Lenalidomide interruption or discontinuation should be considered for grade 2 or 3 skin rash. Lenalidomide must be discontinued for angioedema, grade 4 rash, exfoliative or bullous rash, or if Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) is suspected, and should not be resumed following discontinuation from these reactions. Special populations *Paediatric population* Revlimid should not be used in children and adolescents from birth to less than 18 years because of safety concerns (see section 4.4 of the SPC). *Older people* Currently available pharmacokinetic data are described in section 5.2 of the SPC. Lenalidomide has been used in clinical trials in multiple myeloma patients up to 91 years of age and in myelodysplastic syndromes patients up to 95 years of age (see section 5.1 of the SPC). In patients with newly diagnosed multiple myeloma aged 75 years and older who received lenalidomide, there was a higher incidence of serious adverse reactions and adverse reactions that led to treatment discontinuation (see section 4.4 of the SPC). Patients with newly diagnosed multiple myeloma aged 75 years and older should be carefully assessed before treatment is considered (see section 4.4 of the SPC). Newly diagnosed multiple myeloma For patients older than 75 years of age treated with lenalidomide in combination with dexamethasone, the starting dose of dexamethasone is 20 mg/day on Days 1, 8, 15 and 22 of each 28-day treatment cycle. No dose adjustment is proposed for patients older than 75 years who are treated with lenalidomide in combination with melphalan and prednisone. In clinical trials of newly diagnosed multiple myeloma in transplant non eligible patients, lenalidomide combined therapy was less tolerated in patients older than 75 years of age compared to the younger population. These patients discontinued at a higher rate due to intolerance (Grade 3 or 4 adverse events and serious adverse events), when compared to patients < 75 years (see section 4.4 of the SPC). Multiple myeloma with at least one prior therapy The percentage of multiple myeloma patients aged 65 or over was not significantly different between the lenalidomide/dexamethasone and placebo/dexamethasone groups. No overall difference in safety or efficacy was observed between these patients and younger patients, but greater pre-disposition of older individuals cannot be ruled out. For myelodysplastic syndromes patients treated with lenalidomide, no overall difference in safety and efficacy was observed between patients aged over 65 and younger patients. Because elderly patients are more likely to have decreased renal function, care should be taken in dose selection and it would be prudent to monitor renal function. *Patients with renal impairment* Lenalidomide is substantially excreted by the kidney; patients with greater degrees of renal impairment can have impaired treatment tolerance (see section 4.4 of the SPC). Care should be taken in dose selection and monitoring of renal function is advised. No dose adjustments are required for patients with mild renal impairment and multiple myeloma or myelodysplastic syndromes. The following dose adjustments are recommended at the start of therapy and throughout treatment for patients with moderate or severe impaired renal function or end stage renal disease. There are no Phase III trial experiences with End Stage Renal Disease (ESRD) (Clcr < 30 mL/min, requiring dialysis). *Multiple myeloma* **Renal function (CLcr):** Moderate renal impairment (30 ≤ Clcr < 50 mL/min) **Dose adjustment** (Days 1 to 21 of repeated 28- day cycles): 10 mg once daily[1] **Renal function (CLcr):** Severe renal impairment (Clcr < 30 mL/min, not requiring dialysis) **Dose adjustment** (Days 1 to 21 of repeated 28- day cycles): 7.5 mg once daily[2] 15 mg every other day,**Renal function (CLcr):** End Stage Renal Disease (ESRD) (Clcr < 30 mL/min, requiring dialysis) **Dose adjustment** (Days 1 to 21 of repeated 28- day cycles): 5 mg once daily. On dialysis days, the dose should be administered following dialysis. [1] The dose may be escalated to 15 mg once daily after 2 cycles if patient is not responding to treatment and is tolerating the treatment. [2] In countries where the 7.5 mg capsule is available. After initiation of lenalidomide therapy, subsequent lenalidomide dose modification in renally impaired patients should be based on individual patient treatment tolerance, as described above. *Myelodysplastic syndromes* **Renal function (CLcr):** Moderate renal impairment (30 ≤ Clcr < 50 mL/min) **Dose adjustment:** Starting dose 5 mg once daily (days 1-21 of repeated 28-day cycles), **Dose adjustment:** Dose level -1* 2.5 mg once daily (days 1-28 of repeated 28-day cycles), **Dose adjustment:** Dose level -2* 2.5 mg once every other day (days 1-28 of repeated 28-day cycles),**Renal function (CLcr):** Severe renal impairment (Clcr < 30 mL/min, not requiring dialysis) **Dose adjustment:** Starting dose 2.5 mg once daily (days 1-21 of repeated 28-day cycles), **Dose adjustment:** Dose level -1* 2.5 mg every other day (days 1-28 of repeated 28-day cycles), **Dose adjustment:** Dose level -2* 2.5 mg twice a week (days 1-28 of repeated 28-day cycles),**Renal function (CLcr):** End Stage Renal Disease (ESRD) (Clcr < 30 mL/min, requiring dialysis) On dialysis days, the dose should be administered following dialysis. **Dose adjustment:** Starting dose 2.5 mg once daily (days 1-21 of repeated 28-day cycles), **Dose adjustment:** Dose level -1* 2.5 mg every other day (days 1-28 of repeated 28-day cycles), **Dose adjustment:** Dose level -2* 2.5 mg twice a week (days 1-28 of repeated 28-day cycles) * Recommended dose reduction steps during treatment and restart of treatment to manage grade 3 or 4 neutropenia or thrombocytopenia, or other grade 3 or 4 toxicity judged to be related to lenalidomide, as described above. *Patients with hepatic impairment* Lenalidomide has not formally been studied in patients with impaired hepatic function and there are no specific dose recommendations. Method of administration Oral use. Revlimid capsules should be taken at about the same time on the scheduled days. The capsules should not be opened, broken or chewed. The capsules should be swallowed whole, preferably with water, either with or without food. If less than 12 hours has elapsed since missing a dose, the patient can take the dose. If more than 12 hours has elapsed since missing a dose at the normal time, the patient should not take the dose, but take the next dose at the normal time on the following day. **Contraindications** Hypersensitivity to the active substance or to any of the excipients, listed in section 6.1 of the SPC. Women who are pregnant. Women of childbearing potential unless all of the conditions of the Pregnancy Prevention Programme are met (see sections 4.4 and 4.6 of the SPC). **Undesirable effects** Summary of the safety profile *Newly diagnosed multiple myeloma in patients treated with lenalidomide in combination with low dose dexamethasone* The serious adverse reactions observed more frequently (≥5%) with lenalidomide in combination with low dose dexamethasone (Rd and Rd18) than with melphalan, prednisone and thalidomide (MPT) were: Pneumonia (9.8%) Renal failure (including acute) (6.3%) The adverse reactions observed more frequently with Rd or Rd18 than MPT were: diarrhoea (45.5%), fatigue (32.8%), back pain (32.0%), asthenia (28.2%), insomnia (27.6%), rash (24.3%), decreased appetite (23.1%), cough (22.7%), pyrexia (21.4%), and muscle spasms (20.5%). *Newly diagnosed multiple myeloma patients treated with lenalidomide in combination with melphalan and prednisone* The serious adverse reactions observed more frequently (≥5%) with melphalan, prednisone and lenalidomide followed by lenalidomide maintenance (MPR+R) or melphalan, prednisone and lenalidomide followed by placebo (MPR+p) than melphalan, prednisone and placebo followed by placebo (MPp+p) were: Febrile neutropenia (6.0%) Anaemia (5.3%) The adverse reactions observed more frequently with MPR+R or MPR+ p than MPp+p were: neutropenia (83.3%), anaemia (70.7%), thrombocytopenia (70.0%), leukopenia (38.8%), constipation (34.0%), diarrhoea (33.3%), rash (28.9%), pyrexia (27.0%), peripheral oedema (25.0%), cough (24.0%), decreased appetite (23.7%), and asthenia (22.0%). *Multiple myeloma with at least one prior therapy* In two Phase III placebo-controlled studies, 353 patients with multiple myeloma were exposed to the lenalidomide/dexamethasone combination and 351 to the placebo/dexamethasone combination. The most serious adverse reactions observed more frequently in lenalidomide/dexamethasone than placebo/dexamethasone combination were: Venous thromboembolism (deep vein thrombosis, pulmonary embolism) (see section 4.4 of the SPC) Grade 4 neutropenia (see section 4.4 of the SPC). The observed adverse reactions which occurred more frequently with lenalidomide and dexamethasone than placebo and dexamethasone in pooled multiple myeloma clinical trials (MM-009 and MM-010) were fatigue (43.9%), neutropenia (42.2%), constipation (40.5%), diarrhoea (38.5%), muscle cramp (33.4%), anaemia (31.4%), thrombocytopenia (21.5%), and rash (21.2%). *Myelodysplastic syndromes* The overall safety profile of Revlimid in patients with myelodysplastic syndromes is based on data from a total of 286 patients from one Phase II study and one Phase III study (see section 5.1 of the SPC). In the Phase II, all 148 patients were on lenalidomide treatment. In the Phase III study, 69 patients were on lenalidomide 5 mg, 69 patients on lenalidomide 10 mg and 67 patients were on placebo during the double-blind phase of the study. Most adverse reactions tended to occur during the first 16 weeks of therapy with lenalidomide. Serious adverse reactions include: Venous thromboembolism (deep vein thrombosis, pulmonary embolism) (see section 4.4 of the SPC) Grade 3 or 4 neutropenia, febrile neutropenia and grade 3 or 4 thrombocytopenia (see section 4.4 of the SPC). The most commonly observed adverse reactions which occurred more frequently in the lenalidomide groups compared to the control arm in the Phase III study were neutropenia (76.8%), thrombocytopenia (46.4%), diarrhoea (34.8%), constipation (19.6%), nausea (19.6%), pruritus (25.4%), rash (18.1%), fatigue (18.1%) and muscle spasms (16.7%). Tabulated list of adverse reactions

Tabulated summary for combination therapy The adverse reactions observed in patients treated treated for multiple myeloma are listed below by system organ class and frequency. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000), not known (cannot be estimated from the available data). The following table is derived from data gathered during the multiple myeloma studies with combination therapy. The data were not adjusted according to the longer duration of treatment in the lenalidomide-containing arms continued until disease progression versus the comparator arms in the pivotal multiple myeloma studies (see section 5.1 of the SPC). Adverse reactions have been included under the appropriate category in the table below according to the highest frequency observed in any of the main clinical trials. **Table 1: ADRs reported in clinical studies in patients with multiple myeloma treated with lenalidomide in combination with dexamethasone, or with melphalan and prednisone** System Organ Class / Preferred Term: Infections and Infestations All ADRs/Frequency: Very Common Pneumonia, Upper respiratory tract infection, Bacterial, viral and fungal infections (including opportunistic infections), Nasopharyngitis, Pharyngitis, Bronchitis Common Sepsis, Sinusitis Grade 3—4 ADRs/Frequency: Common Pneumonia, Bacterial, viral and fungal infections (including opportunistic infections), Sepsis, Bronchitis,System Organ Class / Preferred Term: Neoplasms Benign, Malignant and Unspecified (incl cysts and polyps) All ADRs/Frequency: Uncommon Basal cell carcinoma Squamous skin cancer^,* Grade 3—4 ADRs/Frequency: Common Acute myeloid leukaemia, Myelodysplastic syndrome, Squamous cell carcinoma of skin** Uncommon T-cell type acute leukaemia, Basal cell carcinoma, Tumour lysis syndrome,System Organ Class / Preferred Term: Blood and Lymphatic System Disorders All ADRs/Frequency: Very Common Neutropenia^, Thrombocytopenia ^, Anaemia, Haemorrhagic disorder ^, Leucopenias Common Febrile neutropenia, Pancytopenia Uncommon Haemolysis, Autoimmune haemolytic anaemia, Haemolytic anaemia Grade 3—4 ADRs/Frequency: Very Common Neutropenia^, Thrombocytopenia^, Anaemia, Leucopenias Common Febrile neutropenia^, Pancytopenia, Haemolytic anaemia Uncommon Hypercoagulation, Coagulopathy,System Organ Class / Preferred Term: Immune System Disorders All ADRs/Frequency: Uncommon Hypersensitivity^ ,System Organ Class / Preferred Term: Endocrine Disorders All ADRs/Frequency: Common Hypothyroidism ,System Organ Class / Preferred Term: Metabolism and Nutrition Disorders All ADRs/Frequency: Very Common Hypokalaemia, Hyperglycaemia, Hypocalcaemia, Decreased appetite, Weight decreased Common Hypomagnesaemia, Hyperuricaemia, Dehydration Grade 3—4 ADRs/Frequency: Common Hypokalaemia, Hyperglycaemia, Hypocalcaemia, Diabetes mellitus, Hypophosphataemia, Hyponatraemia, Hyperuricaemia, Gout, Decreased appetite, Weight decreased,System Organ Class / Preferred Term: Psychiatric Disorders All ADRs/Frequency: Very Common Depression, Insomnia Uncommon Loss of libido Grade 3—4 ADRs/Frequency: Common Depression, Insomnia,System Organ Class / Preferred Term: Nervous System Disorders All ADRs/Frequency: Very Common Peripheral neuropathies (excluding motor neuropathy), Dizziness, Tremor, Dysgeusia, Headache Common Ataxia, Balance impaired Grade 3—4 ADRs/Frequency: Common Cerebrovascular accident, Dizziness, Syncope Uncommon Intracranial haemorrhage ^, Transient ischaemic attack, Cerebral ischaemia,System Organ Class / Preferred Term: Eye Disorders All ADRs/Frequency: Very Common Cataracts, Blurred vision Common Reduced visual acuity Grade 3—4 ADRs/Frequency: Common Cataract Uncommon Blindness,System Organ Class / Preferred Term: Ear and Labyrinth Disorders All ADRs/Frequency: Common Deafness (Including Hypoacusis), Tinnitus ,System Organ Class / Preferred Term: Cardiac Disorders All ADRs/Frequency: Common Atrial fibrillation, Bradycardia Uncommon Arrhythmia, QT prolongation, Atrial flutter, Ventricular extrasystoles Grade 3—4 ADRs/Frequency: Common Myocardial infarction (including acute) ^, Atrial fibrillation, Congestive cardiac failure, Tachycardia, Cardiac failure, Myocardial ischaemia ,System Organ Class / Preferred Term: Vascular Disorders All ADRs/Frequency: Very Common Venous thromboembolic events, predominantly deep vein thrombosis and pulmonary embolism^ Common Hypotension, Hypertension, Ecchymosis^ Grade 3—4 ADRs/Frequency: Very Common Venous thromboembolic events, predominantly deep vein thrombosis and pulmonary embolism^ Common Vasculitis Uncommon Ischemia, Peripheral ischemia, Intracranial venous sinus thrombosis,System Organ Class / Preferred Term: Respiratory, Thoracic and Mediastinal Disorders All ADRs/Frequency: Very Common Dyspnoea, Epistaxis^ Grade 3—4 ADRs/Frequency: Common Respiratory distress, Dyspnoea,System Organ Class / Preferred Term: Gastrointestinal Disorders All ADRs/Frequency: Very Common Diarrhoea, Constipation, Abdominal pain, Nausea, Vomiting, Dyspepsia Common Gastrointestinal haemorrhage (including rectal haemorrhage, haemorrhoidal haemorrhage, peptic ulcer haemorrhage and gingival bleeding)^, Dry mouth, Stomatitis, Dysphagia Uncommon Colitis, Caecitis Grade 3—4 ADRs/Frequency: Common Diarrhoea, Constipation, Abdominal pain, Nausea, Vomiting,System Organ Class / Preferred Term: Hepatobiliary Disorders All ADRs/Frequency: Common Abnormal liver function tests Uncommon Hepatic failure^ Grade 3—4 ADRs/Frequency: Common Cholestasis, Abnormal liver function tests Uncommon Hepatic failure^,System Organ Class / Preferred Term: Skin and Subcutaneous Tissue Disorders All ADRs/Frequency: Very Common Rashes, Pruritus Common Urticaria, Hyperhidrosis, Dry skin, Skin hypergimentation, Eczema, Erythema Uncommon Skin discolouration, Photosensitivity reaction Grade 3—4 ADRs/Frequency: Common Rashes ,System Organ Class / Preferred Term: Musculoskeletal and Connective Tissue Disorders All ADRs/Frequency: Very Common Muscle spasms, Bone pain, Musculoskeletal and connective tissue pain and discomfort, Arthralgia Common Muscular weakness, Joint swelling, Myalgia Grade 3—4 ADRs/Frequency: Common Muscular weakness, Bone pain Uncommon Joint swelling,System Organ Class / Preferred Term: Renal and Urinary Disorders All ADRs/Frequency: Very Common Renal failure (including acute) Common Haematuria^, Urinary retention, Urinary incontinence Uncommon Acquired Fanconi syndrome Grade 3—4 ADRs/Frequency: Uncommon Renal tubular necrosis,System Organ Class / Preferred Term: Reproductive System and Breast Disorders All ADRs/Frequency: Common Erectile dysfunction ,System Organ Class / Preferred Term: General Disorders and Administration Site Conditions All ADRs/Frequency: Very Common Fatigue, Oedema (including peripheral oedema), Pyrexia, Asthenia, Influenza like illness syndrome (including pyrexia, cough, myalgia, musculoskeletal pain, headache and rigors) Common Chest pain, Lethargy Grade 3—4 ADRs/Frequency: Common Fatigue, Pyrexia, Asthenia,System Organ Class / Preferred Term: Investigations All ADRs/Frequency: Common C-reactive protein increased ,System Organ Class / Preferred Term: Injury, Poisoning and Procedural Complications All ADRs/Frequency: Common Fall, Contusion^ ^See 4.8 of the SPC description of selected adverse reactions * Squamous skin cancer was reported in clinical trials in previously treated myeloma patients with lenalidomide/dexamethasone compared to controls ** Squamous cell carcinoma of skin was reported in a clinical trial in newly diagnosed myeloma patients with lenalidomide/dexamethasone compared to controls Tabulated summary from monotherapy The adverse reactions observed in patients treated for myelodysplastic syndromes are listed below by system organ class and frequency. Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); not known (cannot be estimated from the available data). The following table is derived from data gathered during the main studies in monotherapy for myelodysplastic syndromes. Adverse reactions have been included under the appropriate category in the table below according to the highest frequency observed in any of the main clinical trials. Table 2: ADRs reported in clinical trials in patients with myelodysplastic syndromes treated with lenalidomide# System Organ Class / Preferred Term: Infections and Infestations All ADRs/Frequency: Very Common Bacterial, viral and fungal infections (including opportunistic infections) Grade 3—4 ADRs/Frequency: Very Common Pneumonia[a] Common Bacterial, viral and fungal infections (including opportunistic infections) [b]System Organ Class / Preferred Term: Blood and Lymphatic System Disorders All ADRs/Frequency: Very Common Thrombocytopenia^, Neutropenia^, Leucopenias Grade 3—4 ADRs/Frequency: Very Common Thrombocytopenia^,[c], Neutropenia^,[c], Leucopenias Common Febrile Neutropenia^,[c] ,System Organ Class / Preferred Term: Endocrine Disorders All ADRs/Frequency: Very Common Hypothyroidism ,System Organ Class / Preferred Term: Metabolism and Nutrition Disorders All ADRs/Frequency: Very Common Decreased appetite Common Iron overload, Weight decreased Grade 3—4 ADRs/Frequency: Common Hyperglycaemia[a], Decreased appetite,System Organ Class / Preferred Term: Psychiatric Disorders Grade 3—4 ADRs/Frequency: Common Altered mood[d]—System Organ Class / Preferred Term: Nervous System Disorders All ADRs/Frequency: Very Common Dizziness, Headache Common Paraesthesia ,System Organ Class / Preferred Term: Cardiac Disorders Grade 3—4 ADRs/Frequency: Common Acute myocardial infarction^,[c], Atrial fibrillation[c], Cardiac failure[c] ,System Organ Class / Preferred Term: Vascular Disorders All ADRs/Frequency: Common Hypertension, Haematoma Grade 3—4 ADRs/Frequency: Common Venous thromboembolic events, predominantly deep vein thrombosis and pulmonary embolism^,[c]System Organ Class / Preferred Term: Respiratory, Thoracic and Mediastinal Disorders All ADRs/Frequency: Very Common Epistaxis^ Grade 3—4 ADRs/Frequency: Common Bronchitis ,System Organ Class / Preferred Term: Gastrointestinal Disorders All ADRs/Frequency: Very Common Diarrhoea, Abdominal pain (including upper), Nausea, Vomiting, Constipation Common Dry mouth, Dyspepsia Grade 3—4 ADRs/Frequency: Common Diarrhoea[a], Nausea, Toothache ,System Organ Class / Preferred Term: Hepatobiliary Disorders All ADRs/Frequency: Common Abnormal liver function tests Grade 3—4 ADRs/Frequency: Common Abnormal liver function tests ,System Organ Class / Preferred Term: Skin and Subcutaneous Tissue Disorders All ADRs/Frequency: Very Common Rashes, Dry Skin, Pruritus Grade 3—4 ADRs/Frequency: Common Rashes, Pruritus ,System Organ Class / Preferred Term: Musculoskeletal and Connective Tissue Disorders All ADRs/Frequency: Very Common Muscle spasms, Musculoskeletal pain (including back pain and pain in extremity), Arthralgia, Myalgia Grade 3—4 ADRs/Frequency: Common Back pain[e] ,System Organ Class / Preferred Term: Renal and Urinary Disorders Grade 3—4 ADRs/Frequency: Common Renal failure[c] ,System Organ Class / Preferred Term: General Disorders and Administration Site Conditions All ADRs/Frequency: Very Common Fatigue, Peripheral oedema, Influenza like illness syndrome (including pyrexia, cough, pharyngitis, myalgia, musculoskeletal pain, headache) Grade 3—4 ADRs/Frequency: Common Pyrexia,System Organ Class / Preferred Term: Injury, Poisoning and Procedural Complications Grade 3—4 ADRs/Frequency: Common Fall ^see section 4.8 of the SPC description of selected adverse reactions [a]Adverse events reported as serious in myelodysplastic syndromes clinical trials ~Altered mood was reported as a common serious adverse event in the myelodysplastic syndromes Phase III study; it was not reported as a grade 3 or 4 adverse event # Algorithm applied for myelodysplastic syndromes: Myelodysplastic syndromes Phase III study (double-blind safety population, difference between lenalidomide 5/10mg and placebo by initial dosing regimen occurring in at least 2 subjects) All treatment-emergent adverse events with ≥ 5% of subjects in lenalidomide and at least 2% difference in proportion between lenalidomide and placebo All treatment-emergent grade 3 or 4 adverse events in 1% of subjects in lenalidomide and at least 1% difference in proportion between lenalidomide and placebo All treatment-emergent serious adverse events in 1% of subjects in lenalidomide and at least 1% difference in proportion between lenalidomide and placebo Myelodysplastic syndromes Phase II study All treatment-emergent adverse events with ≥ 5% of lenalidomide treated subjects All treatment-emergent grade 3 or 4 adverse\events in 1% of lenalidomide treated subjects All treatment-emergent serious adverse events in 1% of lenalidomide treated subjects Algorithm applied for inclusion in the SmPC: All ADRs captured by the Phase III study algorithm are included in the EU SmPC. For these ADRs, an additional check of the frequency of the ADRs captured by the Phase II study algorithm was undertaken and, if the frequency of the ADRs in the Phase II study was higher than in the Phase III study, the event was included in the EU SmPC at the frequency it occurred in the Phase II study. Tabulated summary of post-marketing adverse reactions In addition to the above adverse reactions identified from the pivotal clinical trials, the following table is derived from data gathered from post-marketing data. Table 3: ADRs reported in in post-marketing use in patients with multiple myeloma treated with lenalidomide System Organ Class / Preferred Term: Neoplasms Benign, Malignant and Unspecified (incl cysts and polyps) Grade 3—4 ADRs/Frequency: Rare Tumour lysis syndrome ,System Organ Class / Preferred Term: Endocrine Disorders All ADRs/Frequency: Common Hyperthyroidism ,System Organ Class / Preferred Term: Respiratory, Thoracic and Mediastinal Disorders Grade 3—4 ADRs/Frequency: Not Known Interstitial pneumonitis,System Organ Class / Preferred Term: Gastrointestinal Disorders Grade 3—4 ADRs/Frequency: Not Known Pancreatitis, Gastrointestinal perforation (including diverticular, intestinal and large intestine perforations) ^ ,System Organ Class / Preferred Term: Hepatobiliary Disorders All ADRs/Frequency: Not Known Acute hepatic failure^, Hepatitis toxic^, Cytolytic hepatitis^, Cholestatic hepatitis^, Mixed cytolytic/cholestatic hepatitis^ Grade 3—4 ADRs/Frequency: Not Known Acute hepatic failure^, Hepatitis toxic^,System Organ Class / Preferred Term: Skin and Subcutaneous Tissue Disorders Grade 3—4 ADRs/Frequency: Uncommon Angioedema Rare Stevens-Johnson Syndrome^, Toxic epidermal necrolysis^ Not Known Leukocytoclastic vasculitis ^see section 4.8 of the SPC description of selected adverse reactions Description of selected adverse reactions *Teratogenicity* Lenalidomide is structurally related to thalidomide. Thalidomide is a known human teratogenic active substance that causes severe life-threatening birth defects. Lenalidomide induced in monkeys malformations similar to those described with thalidomide (see sections 4.6 and 5.3 of the SPC). If lenalidomide is taken during pregnancy, a teratogenic effect of lenalidomide in humans is expected. *Neutropenia and thrombocytopenia Newly diagnosed multiple myeloma patients treated with lenalidomide in combination with low dose dexamethasone* The combination of lenalidomide with low dose dexamethasone in newly diagnosed multiple myeloma patients is associated with a decreased incidence of grade 4 neutropenia (8.5% in Rd and Rd18, compared with 15% in MPT). Grade 4 febrile neutropenia was observed infrequently (0.6% compared with 0.7% in MPT). The combination of lenalidomide with low dose dexamethasone in newly diagnosed multiple myeloma patients is associated with a decreased incidence of grade 3 and 4 thrombocytopenia (8.1 in Rd and Rd18 compared to 11% in MPT). *Newly diagnosed multiple myeloma patients treated with lenalidomide in combination with melphalan and prednisone* The combination of lenalidomide with melphalan and prednisone in newly diagnosed multiple myeloma patients is associated with a higher incidence of grade 4 neutropenia (34.1% in MPR+R/MPR+p compared with 7.8% in MPp+p). There was a higher incidence of grade 4 febrile neutropenia observed (1.7% in MPR+R/MPR+p compared to 0.0% in MPp+p). The combination of lenalidomide with melphalan and prednisone in newly diagnosed multiple myeloma patients is associated with a higher incidence of grade 3 and grade 4 thrombocytopenia (40.4% in MPR+R/MPR+p treated patients, compared with 13.7% in MPp+p-treated patients). *Multiple myeloma with at least one prior therapy* The combination of lenalidomide with dexamethasone in multiple myeloma patients is associated with a higher incidence of grade 4 neutropenia (5.1% in lenalidomide/dexamethasone-treated patients compared with 0.6% in placebo/dexamethasone-treated patients). Grade 4 febrile neutropenia episodes were observed infrequently (0.6% in lenalidomide/dexamethasone-treated patients compared to 0.0% in placebo/dexamethasone treated patients).The combination of lenalidomide with dexamethasone in multiple myeloma patients is associated with a higher incidence of grade 3 and grade 4 thrombocytopenia (9.9% and 1.4%, respectively, in lenalidomide/dexamethasone-treated patients compared to 2.3% and 0.0% in placebo/dexamethasone-treated patients). *Myelodysplastic syndromes* In myelodysplastic syndromes patients, lenalidomide is associated with a higher incidence of grade 3 or 4 neutropenia (74.6% in lenalidomide-treated patients compared with 14.9% in patients on placebo in the Phase III study). Grade 3 or 4 febrile neutropenia episodes were observed in 2.2% of lenalidomide-treated patients compared with 0.0% in patients on placebo). Lenalidomide is associated with a higher incidence of grade 3 or 4 thrombocytopenia (37% in lenalidomide-treated patients compared with 1.5% in patients on placebo in the Phase III study). *Venous thromboembolism* An increased risk of DVT and PE is associated with the use of lenalidomide with dexamethasone in patients with multiple myeloma, and to a lesser extent in patients treated with melphalan and prednisone or as monotherapy in patients with myelodysplastic syndromes treated with lenalidomide monotherapy (see section 4.5 of the SPC). Concomitant administration of erythropoietic agents or previous history of DVT may also increase thrombotic risk in these patients. *Myocardial infarction* Myocardial infarction has been reported in patients receiving lenalidomide, particularly in those with known risk factors. *Haemorrhagic disorders* Haemorrhagic disorders are listed under several system organ classes: Blood and lymphatic system disorders; nervous system disorders (intracranial haemorrhage); respiratory, thoracic and mediastinal disorders (epistaxis); gastrointestinal disorders (gingival bleeding, haemorrhoidal haemorrhage, rectal haemorrhage); renal and urinary disorders (haematuria); injury, poisoning and procedural complications (contusion) and vascular disorders (ecchymosis). *Allergic reactions* Cases of allergic reaction/hypersensitivity reactions have been reported. A possible cross-reaction between lenalidomide and thalidomide has been reported in the literature. *Severe skin reactions* SJS and TEN have been reported. Patients with a history of severe rash associated with thalidomide treatment should not receive lenalidomide. *Second primary malignancies* *In clinical trials in previously treated myeloma patients with lenalidomide/dexamethasone compared to controls, mainly comprising of basal cell or squamous cell skin cancers. *Acute myeloid leukaemia Multiple myeloma* Cases of AML have been observed in clinical trials of newly diagnosed multiple myeloma in patients taking lenalidomide treatment in combination with melphalan or immediately following high dose melphalan and ASCT (see section 4.4 of the SPC). This increase was not observed in clinical trials of newly diagnosed multiple myeloma in patients taking lenalidomide in combination with low dose dexamethasone compared to thalidomide in combination with melphalan and prednisone. *Myelodysplastic syndromes* Baseline variables including complex cytogenetics and TP53 mutation are associated with progression to AML in subjects who are transfusion dependent and have a Del (5q) abnormality (see section 4.4 of the SPC). The estimated 2-year cumulative risk of progression to AML were 13.8% in patients with an isolated Del (5q) abnormality compared to 17.3% for patients with Del (5q) and one additional cytogenetic abnormality and 38.6% in patients with a complex karyotype. In a post-hoc analysis of a clinical trial of Revlimid in myelodysplastic syndromes, the estimated 2-year rate of progression to AML was 27.5 % in patients with IHC-p53 positivity and 3.6% in patients with IHC-p53 negativity (p=0.0038). In the patients with IHC-p53 positivity, a lower rate of progression to AML was observed amongst patients who achieved a transfusion independence (TI) response (11.1%) compared to a non-responder (34.8%). *Hepatic disorders* The following post-marketing adverse reactions have been reported (frequency unknown): acute hepatic failure and cholestasis (both potentially fatal), toxic hepatitis, cytolytic hepatitis, mixed cytolytic/cholestatic hepatitis. *Rhabdomyolysis* Rare cases of rhabdomyolysis have been observed, some of them when lenalidomide is administered with a statin. *Thyroid disorders* Cases of hypothyroidism and cases of hyperthyroidism have been reported (see section 4.4 of the SPC Thyroid disorders). *Gastrointestinal disorders* Gastrointestinal perforations have been reported during treatment with lenalidomide. Gastrointestinal perforations may lead to septic complications and may be associated with fatal outcome. Reporting of suspected adverse reactions Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to the Federal Agency for medicines and Health Products (FAMHP) via www.fagg-afmps.be/en/. **MARKETING AUTHORISATION HOLDER** Celgene Europe Limited 1 Longwalk Road Stockley Park Uxbridge UB11 1DB United Kingdom **MARKETING AUTHORISATION NUMBER(S)** *Revlimid 2.5 mg* : EU/1/07/391/005 *Revlimid 5 mg* : EU/1/07/391/001 *Revlimid 7.5 mg* : EU/1/07/391/006 *Revlimid 10 mg* : EU/1/07/391/002 *Revlimid 15 mg* : EU/1/07/391/003 *Revlimid 20 mg* : EU/1/07/391/009 *Revlimid 25 mg* : EU/1/07/391/004 **MODE OF DELIVERY** Medicinal product subject to medical prescription. **DATE OF REVISION OF THE TEXT** 11/06/2015 Detailed information on this medicinal product is available on the website of the European Medicines Agency: http://www.ema.europa.eu/.

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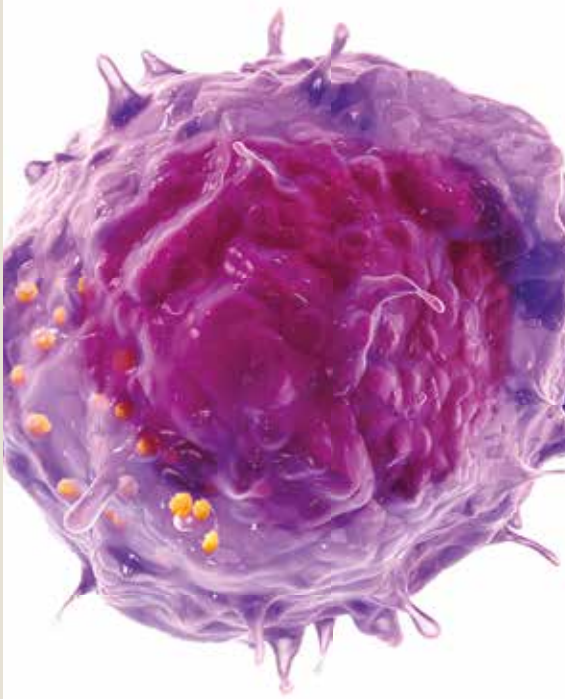
THERE'S A NATURAL KILLER INSIDE ME

WITH THE POTENTIAL TO TAKE ON MULTIPLE MYELOMA



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