| Hospital price |
|---|
| 150 mg x 56 tabl.: € 3.820,11 |
| 100 mg x 56 tabl.: € 3.820,11 |
| 50 mg x 56 tabl.: € 3.820,11 |

MINIMAL INFORMATIONS OF THE SPC ▼ 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 for how to report adverse reactions. **1. NAME OF THE MEDICINAL PRODUCT** Verzenios 50 mg film-coated tablets Verzenios 100 mg film-coated tablets Verzenios 150 mg film-coated tablets **2. QUALITATIVE AND QUANTITATIVE COMPOSITION** Verzenios 50 mg film-coated tablets Each film-coated tablet contains 50 mg abemaciclib. *Excipients with known effect* Each film-coated tablet contains 14 mg of lactose monohydrate. Verzenios 100 mg film-coated tablets Each film-coated tablet contains 100 mg abemaciclib. Excipients with known effect Each film-coated tablet contains 28 mg of lactose monohydrate. Verzenios 150 mg film-coated tablets Each film-coated tablet contains 150 mg abemaciclib. *Excipients with known effect* Each film-coated tablet contains 42 mg of lactose monohydrate. For the full list of excipients, see section 6.1. **3. PHARMACEUTICAL FORM** Film-coated tablet (tablet). Verzenios 50 mg film-coated tablets Beige, oval tablet of 5.2 x 9.5 mm, debossed with "Lilly" on one side and "50" on the other. Verzenios 100 mg film-coated tablets White, oval tablet of 6.6 x 12.0 mm, debossed with "Lilly" on one side and "100" on the other. Verzenios 150 mg film-coated tablets Yellow, oval tablet of 7.5 x 13.7 mm, debossed with "Lilly" on one side and "150" on the other. **4. CLINICAL PARTICULARS**

**4.1 Therapeutic indications** Verzenios is indicated for the treatment of women with hormone receptor (HR) positive, human epidermal growth factor receptor 2 (HER2) negative locally advanced or metastatic breast cancer in combination with an aromatase inhibitor or fulvestrant as initial endocrine-based therapy, or in women who have received prior endocrine therapy. In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist. **4.2 Posology and method of administration** Verzenios therapy should be initiated and supervised by physicians experienced in the use of anticancer therapies. Posology *Verzenios in combination with endocrine therapy* The recommended dose of abemaciclib is 150 mg twice daily when used in combination with endocrine therapy. Please refer to the Summary of Product Characteristics of the endocrine therapy combination partner for the recommended posology. Verzenios should be taken continuously as long as the patient is deriving clinical benefit from therapy or until unacceptable toxicity occurs. If a patient vomits or misses a dose of Verzenios, the patient should be instructed to take the next dose at its scheduled time; an additional dose should not be taken. *Dose adjustments* Management of some adverse reactions may require dose interruption and/or dose reduction as shown in Tables 1-6. **Table 1. Dose adjustment recommendations for adverse reactions**

| | **Verzenios dose combination therapy** |
|---|---|
| Recommended dose | 150 mg twice daily |
| First dose adjustment | 100 mg twice daily |
| Second dose adjustment | 50 mg twice daily |

**Table 2. Management recommendations for haematologic toxicities** Complete blood counts should be monitored prior to the start of Verzenios therapy, every two weeks for the first two months, monthly for the next two months, and as clinically indicated. Before treatment initiation, absolute neutrophil counts (ANC) ≥1500/mm$^3$, platelets ≥100,000/mm$^3$, and haemoglobin ≥8 g/dL are recommended.

| **Toxicity**[a, b] | **Management recommendations** |
|---|---|
| Grade 1 or 2 | No dose adjustment required. |
| Grade 3 | Suspend dose until toxicity resolves to Grade 2 or less. Dose reduction is not required. |
| Grade 3, recurrent; or Grade 4 | Suspend dose until toxicity resolves to Grade 2 or less.<br>Resume at next lower dose. |
| Patient requires administration of blood cell growth factors | Suspend abemaciclib dose for at least 48 hours after the last dose of blood cell growth factors was administered and until toxicity resolves to Grade 2 or less. Resume at next lower dose unless the dose was already reduced for the toxicity that led to the use of the growth factor. |

[a] **NCI Common Terminology Criteria for Adverse Events (CTCAE) b ANC: Grade 1: ANC < LLN - 1500/mm3; Grade 2: ANC 1000 - <1500/mm3; Grade 3: ANC 500 - <1000/mm3; Grade 4: ANC <500/mm3 LLN = lower limit of normal**

**Table 3. Management recommendations for diarrhoea** Treatment with antidiarrhoeal agents, such as loperamide, should be started at the first sign of loose stools.

| **Toxicity**[a] | **Management recommendations** |
|---|---|
| Grade 1 | No dose adjustment required. |
| Grade 2 | If toxicity does not resolve within 24 hours to Grade 1 or less, suspend dose until resolution. Dose reduction is not required. |
| Grade 2 that persists or recurs after resuming the same dose despite maximal supportive measures | Suspend dose until toxicity resolves to Grade 1 or less. Resume at next lower dose. |
| Grade 3 or 4 or requires hospitalisation | |

[a] NCI CTCAE **Table 4. Management recommendations for increased aminotransferases** Alanine aminotransferase (ALT) and aspartate aminostransferase (AST) should be monitored prior to the start of Verzenios therapy, every two weeks for the first two months, monthly for the next two months, and as clinically indicated.

| **Toxicity**[a] | **Management recommendations** |
|---|---|
| Grade 1 (>ULN-3.0 x ULN) Grade 2 (>3.0-5.0 x ULN) | No dose adjustment required. |
| Persistent or Recurrent Grade 2, or Grade 3 (>5.0-20.0 x ULN) | Suspend dose until toxicity resolves to baseline or Grade 1. Resume at next lower dose. |
| Elevation in AST and/or ALT >3 x ULN WITH total bilirubin >2 x ULN, in the absence of cholestasis | Discontinue abemaciclib. |
| Grade 4 (>20.0 x ULN) | Discontinue abemaciclib. |

[a] NCI CTCAE ULN = upper limit of normal **Table 5. Management recommendations for interstitial lung disease (ILD)/pneumonitis**

| **Toxicity**[a] | **Management recommendations** |
|---|---|
| Grade 1 or 2 | No dose adjustment required. |
| Persistent or recurrent Grade 2 toxicity that does not resolve with maximal supportive measures within 7 days to baseline or Grade 1 | Suspend dose until toxicity resolves to baseline or Grade 1. Resume at next lower dose. |
| Grade 3 or 4 | Discontinue abemaciclib. |

[a] NCI CTCAE **Table 6. Management recommendations for non-haematologic toxicities (excluding diarrhoea, increased aminotransferases and interstitial lung disease (ILD)/pneumonitis)**

| **Toxicity**[a] | **Management recommendations** |
|---|---|
| Grade 1 or 2 | No dose adjustment required. |
| Persistent or recurrent Grade 2 toxicity that does not resolve with maximal supportive measures to baseline or Grade 1 within 7 days | Suspend dose until toxicity resolves to Grade 1 or less. Resume at next lower dose. |
| Grade 3 or 4 | |

[a] NCI CTCAE CYP3A4 inhibitors Concomitant use of strong CYP3A4 inhibitors should be avoided. If strong CYP3A4 inhibitors cannot be avoided, the abemaciclib dose should be reduced to 100 mg twice daily. In patients who have had their dose reduced to 100 mg abemaciclib twice daily and in whom coadministration of a strong CYP3A4 inhibitor cannot be avoided, the abemaciclib dose should be further reduced to 50 mg twice daily. In patients who have had their dose reduced to 50 mg abemaciclib twice daily and in whom coadministration of a strong CYP3A4 inhibitor cannot be avoided, the abemaciclib dose may be continued with close monitoring of signs of toxicity. Alternatively, the abemaciclib dose may be reduced to 50 mg once daily or discontinued. If the CYP3A4 inhibitor is discontinued, the abemaciclib dose should be increased to the dose used prior to the initiation of the CYP3A4 inhibitor (after 3 to 5 half-lives of the CYP3A4 inhibitor). Special populations Elderly No dose adjustment is required based on age (see section 5.2). Renal impairment No dose adjustments are necessary in patients with mild or moderate renal impairment. There are no data regarding abemaciclib administration in patients with severe renal impairment, end stage renal disease, or in patients on dialysis (see section 5.2). Abemaciclib should be administered with caution in patients with severe renal impairment, with close monitoring for signs of toxicity. Hepatic impairment No dose adjustments are necessary in patients with mild (Child Pugh A) or moderate (Child Pugh B) hepatic impairment. In patients with severe (Child Pugh C) hepatic impairment, a decrease in dosing frequency to once daily is recommended (see section 5.2). Paediatric population The safety and efficacy of abemaciclib in children and adolescents aged less than 18 years has not been established. No data are available. Method of administration Verzenios is for oral use. The dose can be taken with or without food. It should not be taken with grapefruit or grapefruit juice (see section 4.5). Patients should take the doses at approximately the same times every day. The tablet should be swallowed whole (patients should not chew, crush, or split tablets before swallowing). **4.3 Contraindications** Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

**4.8 Undesirable effects** Summary of the safety profile The most commonly occurring adverse reactions are diarrhoea, infections, neutropenia, anaemia, fatigue, nausea, vomiting and decreased appetite. Tabulated list of adverse reactions In the following table, adverse reactions are listed in order of MedDRA body system organ class and frequency. Frequency gradings are: 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), and not known (cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness. **Table 7. Adverse reactions reported in phase 3 studies of abemaciclib in combination with endocrine therapy (N=768)**

| **System organ class** *Frequency* *Preferred term* | **Abemaciclib plus endocrine therapy**[a] | | |
|---|---|---|---|
| | **All Grades Toxicity (%)** | **Grade 3 Toxicity (%)** | **Grade 4 Toxicity (%)** |
| **Infections and infestations** | | | |
| *Very common* | | | |
| Infections[b] | 43.6 | 5.2 | 1.0 |
| **Blood and lymphatic system disorders** | | | |
| *Very common* | | | |
| Neutropenia | 45.1 | 22.9 | 2.5 |
| Leukopenia | 25.7 | 8.5 | 0.3 |
| Anaemia | 30.1 | 7.0 | 0.1 |
| Thrombocytopenia | 14.3 | 2.2 | 1.0 |
| Common | | | |
| Lymphopenia | 7.3 | 3.0 | 0.1 |
| Uncommon | | | |
| Febrile neutropenia | 0.9 | 0.7 | 0.1 |
| **Metabolism and nutrition disorders** | | | |
| *Very common* | | | |
| Decreased appetite | 26.4 | 1.3 | 0 |
| **Nervous system disorders** | | | |
| *Very common* | | | |
| Dysgeusia | 14.3 | 0 | 0 |
| Dizziness | 12.9 | 0.5 | 0 |
| **Eye disorders** | | | |
| *Common* | | | |
| Lacrimation increased | 6.8 | 0.1 | 0 |
| **Vascular disorders** | | | |
| *Common* | | | |
| Venous thromboembolism[c] | 5.3 | 1.7 | 0.3 |
| **Respiratory, thoracic and mediastinal disorders** *Common* Interstitial lung disease (ILD)/pneumonitis | 3.4 | 0.4 | 0.1 |
| **Gastrointestinal disorders** | | | |
| *Very common* | | | |
| Diarrhoea Vomiting Nausea | 84.6<br>27.7<br>43.5 | 11.7<br>1.2<br>2.1 | 0<br>0<br>0 |
| **Skin and subcutaneous tissue disorders** | | | |
| *Very common* | | | |
| Alopecia | 20.7 | 0 | 0 |
| Pruritus | 13.5 | 0 | 0 |
| Rash | 12.9 | 1.0 | 0 |
| Common | | | |
| Dry skin | 9.0 | 0 | 0 |
| **Musculoskeletal and connective tissue disorders** | | | |
| *Common* | | | |
| Muscular weakness | 8.3 | 0.5 | 0 |
| **General disorders and administration site conditions** | | | |
| *Very common* | | | |
| Fatigue | 40.5 | 2.3 | 0 |
| Pyrexia | 10.7 | 0.1 | 0 |
| **Investigations** | | | |
| *Very common* | | | |
| Alanine aminotransferase increased | 15.1 | 4.8 | 0.3 |
| Aspartate aminotransferase increased | 14.2 | 2.9 | 0 |

[a] Abemaciclib in combination with letrozole, anastrozole, or fulvestrant. [b] Infections includes all PTs that are part of the System Organ Class Infections and infestations. [c] Venous thromboembolic events include DVT, pulmonary embolism, cerebral venous sinus thrombosis, subclavian, axillary vein thrombosis,DVT inferior vena cava and pelvic venous thrombosis Description of selected adverse reactions *Neutropenia* Neutropenia was reported frequently (45.1%). and a Grade 3 or 4 decrease in neutrophil counts (based on laboratory findings) was reported in 28.2% of patients receiving abemaciclib in combination with aromatase inhibitors or fulvestrant. The median time to onset of Grade 3 or 4 neutropenia was 29 to 33 days, and median time to resolution was 11 to 15 days. Febrile neutropenia was reported in 0.9% patients. Dose modification is recommended for patients who develop Grade 3 or 4 neutropenia (see section 4.2). *Diarrhoea* Diarrhoea was the most commonly reported adverse reaction (see Table 7). Incidence was greatest during the first month of abemaciclib treatment and was lower subsequently. The median time to onset of the first diarrhoea event was approximately 6 to 8 days across studies, and the median duration of diarrhoea was 9 to 12 days (Grade 2) and 6 to 8 days (Grade 3) across studies. Diarrhoea returned to baseline or lesser grade with supportive treatment such as loperamide and/or dose adjustment (see section 4.2). *Increased aminotransferases* In patients receiving abemaciclib in combination with aromatase inhibitors or fulvestrant, ALT and AST elevations were reported frequently (15.1% and 14.2%, respectively). Grade 3 or 4 ALT or AST elevations (based on laboratory findings) were reported in 6.1% and 4.2% patients. The median time to onset of Grade 3 or 4 ALT elevation was 57 to 61 days, and median time to resolution was 14 days. The median time to onset of Grade 3 or 4 AST elevation was 71 to 185 days, and median time to resolution was 13 to 15 days. Dose modification is recommended for patients who develop Grade 3 or 4 ALT or AST increase (see section 4.2). *Creatinine* Although not an adverse reaction, abemaciclib has been shown to increase serum creatinine in 98.3% of patients (based on laboratory findings), 1.9% Grade 3 or 4 (based on laboratory findings). In patients receiving an aromatase inhibitor or fulvestrant alone, 78.4% reported an increase in serum creatinine (all laboratory grades). Abemaciclib has been shown to increase serum creatinine due to inhibition of renal tubular secretion transporters without affecting glomerular function (as measured by iohexol clearance) (see section 4.5). In clinical studies, increases in serum creatinine occurred within the first month of abemaciclib dosing, remained elevated but stable through the treatment period, were reversible upon treatment discontinuation, and were not accompanied by changes in markers of renal function, such as blood urea nitrogen (BUN), cystatin C, or calculated glomerular filtration rate based on cystatin C. 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 via: Belgium: l'Agence fédérale des médicaments et des produits de santé, Division Vigilance, Boîte Postale 97, B- 1000 Bruxelles, Madou (www.afmps.be or adversedrugreactions@fagg-afmps.be) Luxembourg: **Centre Régional de Pharmacovigilance de Nancy**, Bâtiment de Biologie Moléculaire et de Biopathologie (BBB), CHR de Nancy – Hôpitaux de Brabois, Rue du Morvan, 54511 VANDOEUVRE LES NANCY CEDEX, tel. : (+33) 3 83 65 60 85/87, fax : (+33) 3 83 65 61 33, e-mail crpv@chru-nancy.fr or **Direction de la Santé, Division de la Pharmacie et des Médicaments**, Allée Marconi – Villa Louvigny, L- 2120 Luxembourg, tel. : (+352) 247-85592, fax : (+352) 247-95615, e-mail pharmacovigilance@ms.etat.lu. Link for the form: http://www.sante.public.lu/fr/politique-sante/ministere-sante/direction-sante/div-pharmacie-medicaments/index.html **7. MARKETING AUTHORISATION HOLDER** Eli Lilly Nederland B.V., Papendorpseweg 83, 3528BJ Utrecht, The Netherlands. **8. MARKETING AUTHORISATION NUMBER(S)**

EU/1/18/1307/001 EU/1/18/1307/002 EU/1/18/1307/003 EU/1/18/1307/004 EU/1/18/1307/005
EU/1/18/1307/006 EU/1/18/1307/007 EU/1/18/1307/008 EU/1/18/1307/009 EU/1/18/1307/010
EU/1/18/1307/011 EU/1/18/1307/012 EU/1/18/1307/013 EU/1/18/1307/014 EU/1/18/1307/015
EU/1/18/1307/016 EU/1/18/1307/017 EU/1/18/1307/018 EU/1/18/1307/019 EU/1/18/1307/020
EU/1/18/1307/021 **9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION** Date of first authorisation: 27 September 2018 **10. DATE OF REVISION OF THE TEXT** 16 January 2020 METHOD OF DELIVERY Medicinal product subject to restricted medical prescription. Detailed information on this medicinal product is available on the website of the European Medicines Agency: http://www.ema.europa.eu