**Maklumat tambahan indikasi**

**Tahun 2022**

**Products Approved For Additional Indication (DCA 374 – 7 July 2022)**

<table>
<tr><th>No.</th><th>Product<br>[Active Ingredient]</th><th>Additional Indication</th><th>Product Registration Holder (PRH)</th></tr>
<tr><td>1.</td><td>XARELTO FILM-COATED TABLETS 10MG<br><br>[Rivaroxaban micronized 10mg]</td><td>
INDICATION :<br><br>
Treatment of deep vein thrombosis (DVT) and pulmonary embolism (PE), <u>and prevention of recurrent DVT and PE in adults</u>.<br><br>
POSOLOGY :<br><br>
<u>Treatment of DVT, treatment of PE and prevention of recurrent DVT and PE</u><br>
The recommended dose for the initial treatment of acute DVT or PE is 15 mg twice daily for the first three weeks followed by 20 mg once daily for the continued treatment and prevention of recurrent DVT and PE.<br><br>
Short duration of therapy (at least 3 months) should be considered in patients with DVT or PE provoked by major transient risk factors (i.e. recent major surgery or trauma). Longer duration of therapy should be considered in patients with provoked DVT or PE not related to major transient risk factors, unprovoked DVT or PE, or a history of recurrent DVT or PE.<br><br>
When extended prevention of recurrent DVT and PE is indicated (following completion of at least 6 months therapy for DVT or PE), the recommended dose is 10 mg once daily. In patients in whom the risk of recurrent DVT or PE is considered high, such as those with complicated comorbidities, or who have developed recurrent DVT or PE on extended prevention with Xarelto 10 mg once daily, a dose of Xarelto 20 mg once daily should be considered.<br><br>
The duration of therapy and dose selection should be individualised after careful assessment of the treatment benefit against the risk for bleeding.<br><br>
<table>
<tr><td></td><td>Time Period</td><td>Dosing schedule</td><td>Maximum daily dose</td></tr>
<tr><td>Treatment and</td><td>Day 1-21</td><td>15 mg twice daily</td><td>30 mg</td></tr>
</table>
</td><td>BAYER CO. (MALAYSIA) SDN. BHD.<br>25-03 & 25-04, Level 25, Imazium,<br>No. 8, Jalan SS21/37, Damansara Uptown,<br>47400 Petaling Jaya, Selangor.</td></tr>
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| prevention of recurrent DVT and PE | Day 22 onwards | 20 mg once daily | 20 mg |
| Prevention of recurrent DVT and PE | Following completion of at least 6 months therapy for DVT or PE | 10 mg once daily or 20 mg once daily | 10 mg or 20 mg |

It is essential to adhere to the dosage schedule provided.

If a dose is missed during the 15 mg twice daily treatment phase (day 1 - 21), the patient should take Xarelto immediately to ensure intake of 30 mg Xarelto per day. In this case two 15 mg tablets may be taken at once. The patient should continue with the regular 15 mg twice daily intake as recommended on the following day.

If a dose is missed during the once daily treatment phase, the patient should take Xarelto immediately, and continue on the following day with the once daily intake as recommended. The dose should not be doubled within the same day to make up for a missed dose.

Converting from Vitamin K Antagonists (VKA) to Xarelto

For patients treated for DVT, PE and prevention of recurrence, VKA treatment should be stopped and Xarelto therapy should be initiated once the INR is ≤2.5. When converting patients from VKAs to Xarelto, International Normalized Ratio (INR) values will be falsely elevated after the intake of Xarelto. The INR is not valid to measure the anticoagulant activity of Xarelto, and therefore should not be used.

Converting from Xarelto to Vitamin K antagonists (VKA)

There is a potential for inadequate anticoagulation during the transition from Xarelto to VKA. Continuous adequate anticoagulation should be ensured during any transition to an alternate anticoagulant. It should be noted that Xarelto can contribute to an elevated INR.

In patients converting from Xarelto to VKA, VKA should be given concurrently until the INR

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| | | is ≥ 2.0. For the first two days of the conversion period, standard initial dosing of VKA should be used followed by VKA dosing, as guided by INR testing. While patients are on both Xarelto and VKA the INR should not be tested earlier than 24 hours after the previous dose but prior to the next dose of Xarelto. Once Xarelto is discontinued INR testing may be done reliably at least 24 hours after the last dose.<br><br>Converting from parenteral anticoagulants to Xarelto<br><br>For patients currently receiving a parenteral anticoagulant, discontinue the parenteral anticoagulant and start Xarelto 0 to 2 hours before the time that the next scheduled administration of the parenteral medicinal product (e.g. low molecular weight heparins) would be due or at the time of discontinuation of a continuously administered parenteral medicinal product (e.g. intravenous unfractionated heparin).<br><br>Converting from Xarelto to parenteral anticoagulants<br><br>Give the first dose of parenteral anticoagulant at the time the next Xarelto dose would be taken.<br><br><u>Special populations</u><br><br>Renal impairment<br><br>Limited clinical data for patients with severe renal impairment (creatinine clearance 15 - 29 ml/min) indicate that rivaroxaban plasma concentrations are significantly increased. Therefore, Xarelto is to be used with caution in these patients. Use is not recommended in patients with creatinine clearance < 15 ml/min.<br><br>• For the prevention of VTE in adult patients undergoing elective hip or knee replacement surgery, no dose adjustment is necessary in patients with mild renal impairment (creatinine clearance 50 - 80 ml/min) or moderate renal impairment (creatinine clearance 30 - 49 ml/min).<br><br>• For the treatment of DVT, treatment of PE and prevention of recurrent DVT and PE, no dose adjustment from the recommended dose is necessary in patients with mild renal impairment (creatinine clearance 50 - 80 ml/min). | |

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| | | • In patients with moderate (creatinine clearance 30 - 49 ml/min) or severe (creatinine clearance 15 - 29 ml/min) renal impairment: patients should be treated with 15 mg twice daily for the first 3 weeks. Thereafter, when the recommended dose is 20 mg once daily, a reduction of the dose from 20 mg once daily to 15 mg once daily should be considered if the patient's assessed risk for bleeding outweighs the risk for recurrent DVT and PE. The recommendation for the use of 15 mg is based on PK modelling and has not been studied in this clinical setting.<br><br>When the recommended dose is 10 mg once daily, no dose adjustment from the recommended dose is necessary. | |

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| 2. | Keytruda 100mg Solution for Infusion<br><br>[Pembrolizumab 25mg/ml] | **INDICATION:**<br><br>Triple-Negative Breast Cancer<br>KEYTRUDA is indicated for the treatment of adult patients with high-risk early-stage triple-negative breast cancer (TNBC) in combination with chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant treatment after surgery.<br><br>**POSOLOGY :**<br><br>**General**<br><br>**Patient Selection**<br><br>If specified in the indication, select patients for treatment with KEYTRUDA based on the presence of positive PD-L1 expression, MSI-H or dMMR tumor status [see V. Indications].<br><br>PD-L1 expression should be evaluated using the PD-L1 IHC 22C3 pharmDx™ kit or equivalent.<br><br>MSI or MMR tumor status should be evaluated using a validated test.<br><br>**Recommended Dosing**<br><br>KEYTRUDA is administered as an intravenous infusion over 30 minutes.<br><br>The recommended dose of KEYTRUDA with head and neck cancer, cHL, urothelial carcinoma, RCC, adjuvant treatment of melanoma, endometrial carcinoma, previously untreated NSCLC, colorectal cancer, esophageal cancer, or triple-negative breast cancer in adults is either:<br><br>• 200mg every 3 weeks or<br>• 400mg every 6 weeks.<br><br>The recommended dose of KEYTRUDA with unresectable or metastatic melanoma and previously treated NSCLC is 2mg/kg every 3 weeks.<br><br>For use in combination, see the prescribing information for the concomitant therapies. | **MERCK SHARP & DOHME (MALAYSIA) SDN BHD**<br>Lot No. B-22-1 & B-22-2,<br>Level 22,<br>The Ascent, Paradigm No. 1,<br>Jalan SS 7/26A, Kelana Jaya,<br>47301 Petaling Jaya,<br>Selangor. |

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| | | When administering KEYTRUDA as part of a combination with intravenous chemotherapy, KEYTRUDA should be administered first.<br><br>For RCC patients treated with KEYTRUDA in combination with axitinib, see the prescribing information regarding dosing of axitinib. When used in combination with KEYTRUDA, dose escalation of axitinib above the initial 5 mg dose may be considered at intervals of six weeks or longer [see Clinical Studies (IIId)].<br><br>For endometrial carcinoma patients treated with KEYTRUDA in combination with lenvatinib, the recommended initial dose of lenvatinib is 20 mg orally once daily until disease progression, unacceptable toxicity, or for KEYTRUDA, up to 24 months in patients without disease progression.<br><br>Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity. Atypical responses (i.e., an initial transient increase in tumor size or small new lesions within the first few months followed by tumor shrinkage) have been observed. Clinically stable patients with initial evidence of disease progression should remain on treatment until disease progression is confirmed.<br><br>For adjuvant treatment of melanoma, KEYTRUDA should be administered for up to one year or until disease recurrence or unacceptable toxicity.<br><br>**For the neoadjuvant and adjuvant treatment of high-risk early-stage TNBC, patients should be treated with neoadjuvant KEYTRUDA in combination with chemotherapy for 8 doses of 200 mg every 3 weeks or 4 doses of 400 mg every 6 weeks or until disease progression that precludes definitive surgery or unacceptable toxicity, followed by adjuvant treatment with KEYTRUDA as monotherapy for 9 doses of 200 mg every 3 weeks or 5 doses of 400 mg every 6 weeks or until disease recurrence or unacceptable toxicity. Patients who experience disease progression that precludes definitive surgery or unacceptable toxicity related to KEYTRUDA as neoadjuvant treatment in combination with chemotherapy should not receive KEYTRUDA monotherapy as adjuvant treatment.** | |

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| 3. | Keytruda 100mg Solution for Infusion<br><br>[Pembrolizumab 25mg/ml] | **INDICATION:**<br><br><u>Renal Cell Carcinoma</u><br><br>KEYTRUDA, as monotherapy, is indicated for the adjuvant treatment of patients with RCC at intermediate high or high risk of recurrence following nephrectomy, or following nephrectomy and resection of metastatic lesions.<br><br>**POSOLOGY :**<br><br>**General**<br><br>**Patient Selection**<br><br>If specified in the indication, select patients for treatment with KEYTRUDA based on the presence of positive PD-L1 expression, MSI-H or dMMR tumor status.<br><br>PD-L1 expression should be evaluated using the PD-L1 IHC 22C3 pharmDx™ kit or equivalent.<br><br>MSI or MMR tumor status should be evaluated using a validated test.<br><br>**Recommended Dosing**<br><br>KEYTRUDA is administered as an intravenous infusion over 30 minutes.<br><br>The recommended dose of KEYTRUDA in adults is either:<br><br>• 200mg every 3 weeks or<br>• 400mg every 6 weeks.<br>For use in combination, see the prescribing information for the concomitant therapies. When administering KEYTRUDA as part of a combination with intravenous chemotherapy, KEYTRUDA should be administered first.<br><br>For RCC patients treated with KEYTRUDA in combination with axitinib, see the prescribing information regarding dosing of axitinib. When used in combination with KEYTRUDA, dose escalation of axitinib above the initial 5 mg dose may be considered at intervals of six weeks or longer. | **MERCK SHARP & DOHME (MALAYSIA) SDN BHD**<br>Lot No. B-22-1 & B-22-2,<br>Level 22,<br>The Ascent, Paradigm No. 1,<br>Jalan SS 7/26A, Kelana Jaya,<br>47301 Petaling Jaya,<br>Selangor. |

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For endometrial carcinoma patients treated with KEYTRUDA in combination with lenvatinib, the recommended initial dose of lenvatinib is 20 mg orally once daily until disease progression, unacceptable toxicity, or for KEYTRUDA, up to 24 months in patients without disease progression.<br><br>
Patients should be treated with KEYTRUDA until disease progression or unacceptable toxicity. Atypical responses (i.e., an initial transient increase in tumor size or small new lesions within the first few months followed by tumor shrinkage) have been observed. Clinically stable patients with initial evidence of disease progression should remain on treatment until disease progression is confirmed.<br><br>
For adjuvant treatment of melanoma or RCC, KEYTRUDA should be administered for up to one year or until disease recurrence or unacceptable toxicity.<br><br>
Dose modifications<br><br>
No dose reductions of KEYTRUDA are recommended. Withhold or discontinue KEYTRUDA to manage adverse reactions as described in Table.<br><br>
Table: Recommended Dose Modifications
<table>
<tr><th>Adverse reactions</th><th>Severity</th><th>Dose modification</th></tr>
<tr><td rowspan="2">Immune-mediated pneumonitis</td><td>Moderate (Grade 2)</td><td>Withhold until adverse reactions recover to Grades 0-1*</td></tr>
<tr><td>Severe or life-threatening (Grades 3 or 4) or recurrent moderate (Grade 2)</td><td>Permanently discontinue</td></tr>
<tr><td>Immune-mediated colitis</td><td>Moderate or severe (Grades 2 or 3)</td><td>Withhold until adverse reactions recover to Grades 0-1*</td></tr>
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| | | | Life-threatening (Grade 4) or recurrent severe (Grade 3) | Permanently discontinue | |
| | | Immune-mediated nephritis | Moderate (Grade 2) | Withhold until adverse reactions recover to Grades 0-1* | |
| | | | Severe or life-threatening (Grade 3 or 4) | Permanently discontinue | |
| | | Immune-mediated endocrinopathies | Severe or life-threatening (Grades 3 or 4) | Withhold until adverse reactions recover to Grades 0-1*<br><br>For patients with severe (Grade 3) or life-threatening (Grade 4) endocrinopathy that improves to Grade 2 or lower and is controlled with hormone replacement, continuation of KEYTRUDA may be considered. | |
| | | Immune-mediated hepatitis<br><br>For liver enzyme elevations in | Aspartate aminotransferase (AST) or alanine aminotransferase (ALT) >3 to 5 times upper limit of normal (ULN) or total bilirubin >1.5 to 3 times ULN | Withhold until adverse reactions recover to Grades 0-1* | |
| | | RCC patients treated with | AST or ALT >5 times ULN or total bilirubin >3 times ULN | Permanently discontinue | |

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| | | combination therapy, see dosing guidelines following this table. | For patients with liver metastases who begin treatment with moderate (Grade 2) elevation of AST or ALT, if AST or ALT increases ≥50% relative to baseline and lasts ≥1 week | Permanently discontinue | |
| | | Immune-mediated skin reactions or Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) | Severe skin reactions (Grade 3) or suspected SJS or TEN | Withhold until adverse reactions recover to Grades 0-1* | |
| | | | Severe skin reactions (Grade 4) or confirmed SJS or TEN | Permanently discontinue | |
| | | Other immune-mediated adverse reactions | Based on severity and type of reaction (Grade 2 or Grade 3) | Withhold until adverse reactions recover to Grades 0-1* | |
| | | | Severe or life-threatening (Grades 3 or 4) myocarditis, encephalitis, or Guillain-Barré syndrome | Permanently discontinue | |
| | | | Life-threatening (Grade 4) or recurrent severe (Grade 3) | Permanently discontinue | |
| | | Infusion-related reactions | Severe or life-threatening (Grades 3 or 4) | Permanently discontinue | |
| | | Note: toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 (NCI CTCAE v.4)<br>* If corticosteroid dosing cannot be reduced to ≤10 mg prednisone or equivalent per day | | | |

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| | | within 12 weeks or a treatment-related toxicity does not resolve to Grades 0-1 within 12 weeks after last dose of KEYTRUDA, then KEYTRUDA should be permanently discontinued.<br><br>In patients with cHL with Grade 4 hematological toxicity, KEYTRUDA should be withheld until adverse reactions recover to Grades 0-1.<br><br>In patients with RCC being treated with KEYTRUDA in combination with axitinib:<br><br>• If ALT or AST ≥3 times ULN but <10 times ULN without concurrent total bilirubin ≥2 times ULN, withhold both KEYTRUDA and axitinib until these adverse reactions recover to Grades 0–1. Consider corticosteroid therapy. Consider rechallenge with a single drug or sequential rechallenge with both drugs after recovery. If rechallenging with axitinib, consider dose reduction as per the axitinib prescribing information.<br>• If ALT or AST ≥10 times ULN or >3 times ULN with concurrent total bilirubin ≥2 times ULN, permanently discontinue both KEYTRUDA and axitinib and consider corticosteroid therapy.<br><br>When administering KEYTRUDA in combination with lenvatinib for the treatment of endometrial carcinoma, interrupt one or both as appropriate. No dose reductions are recommended for KEYTRUDA. Withhold, dose reduce, or discontinue lenvatinib in accordance with the instructions in the lenvatinib prescribing information.<br><br>**Preparation and administration**<br><br>• Protect from light. Do not freeze. Do not shake.<br>• Equilibrate the vial of KEYTRUDA to room temperature.<br>• Prior to dilution, the vial of liquid can be out of refrigeration (temperatures at or below 25°C) for up to 24 hours.<br>• Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration. KEYTRUDA is a clear to slightly opalescent, colorless to slightly yellow solution. Discard the vial if visible particles are observed.<br>• Withdraw the required volume up to 4 mL (100 mg) of KEYTRUDA and transfer into an intravenous bag containing 0.9% sodium chloride or 5% glucose (dextrose) | |

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| | | to prepare a diluted solution with a final concentration ranging from 1 to 10 mg/mL. Mix diluted solution by gentle inversion.<br>• Do not freeze the infusion solution.<br>• The product does not contain preservative. The diluted product should be used immediately. If not used immediately, diluted solutions of KEYTRUDA may be stored at room temperature for a cumulative time of up to 6 hours. Diluted solutions of KEYTRUDA may also be stored under refrigeration at 2°C to 8°C; however, the total time from dilution of KEYTRUDA to completion of infusion should not exceed 96 hours. If refrigerated, allow the vials and/or IV bags to come to room temperature prior to use.<br>• Translucent to white proteinaceous particles may be seen in the diluted solution. Administer infusion solution intravenously over 30 minutes using a sterile, non-pyrogenic, low-protein binding 0.2 to 5 µm in-line or add-on filter.<br>• Do not co-administer other drugs through the same infusion line.<br>• Discard any unused portion left in the vial.<br><br>**Pediatric Patients**<br><br>In cHL, the recommended dose of KEYTRUDA in pediatric patients is 2 mg/kg (up to a maximum of 200 mg), administered as an intravenous infusion over 30 minutes every 3 weeks.<br><br>**Renal Impairment**<br><br>No dose adjustment is needed for patients with mild or moderate renal impairment. KEYTRUDA has not been studied in patients with severe renal impairment.<br><br>**Hepatic Impairment**<br><br>No dose adjustment is needed for patients with mild hepatic impairment. KEYTRUDA has not been studied in patients with moderate or severe hepatic impairment. | |

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| 4. | Benlysta Powder for Solution for Infusion 120mg<br><br>[Belimumab 80mg/ml] | **INDICATION :**<br><br>BENLYSTA is indicated for:<br>- treatment of active lupus nephritis in adult patients in combination with background immunosuppressive therapies.<br><br>**POSOLOGY :**<br><br>BENLYSTA is administered intravenously by infusion, and must be reconstituted and diluted prior to administration (see Use and Handling).<br><br>BENLYSTA treatment should be initiated and supervised by a qualified physician experienced in the diagnosis and treatment of SLE. BENLYSTA should be administered by a healthcare professional prepared to treat hypersensitivity reactions including anaphylaxis.<br><br>BENLYSTA should be infused over a 1-hour period.<br><br>BENLYSTA must not be administered as an intravenous push or bolus.<br><br>The infusion rate may be slowed or interrupted if the patient develops an infusion reaction.<br><br>The infusion must be discontinued immediately if the patient experiences a potentially life threatening adverse reaction (see Contraindications, Warnings and Precautions).<br><br>Patients should be monitored during and for an appropriate period of time after administration of BENLYSTA (see Warnings and Precautions, Adverse Reactions).<br><br>**Premedication for patients with allergies**<br><br>Premedication with an oral antihistamine, with or without an antipyretic, may be administered before the infusion of BENLYSTA (see Warnings and Precautions, Clinical Studies).<br><br>**Adults**<br><br>SLE | **GLAXOSMITHKLINE PHARMACEUTICAL SDN. BHD.**<br>HZ.01, Horizon Penthouse,<br>1 Powerhouse,<br>1, Persiaran Bandar Utama, Bandar Utama,<br>47800 Petaling Jaya,<br>Selangor. |

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| | | The recommended dosage regimen is 10 mg/kg on Days 0, 14 and 28, and at 4-week intervals thereafter. Discontinuation of treatment with BENLYSTA should be considered if there is no improvement in disease control after 6 months of treatment.<br><br>Lupus nephritis<br><br>The recommended dosage regimen is 10 mg/kg on Days 0, 14 and 28, and at 4-week intervals thereafter.<br><br>In patients with active lupus nephritis, BENLYSTA should be used in combination with corticosteroids and mycophenolate or cyclophosphamide for induction, or mycophenolate or azathioprine for maintenance.<br><br>**Children**<br><br>SLE<br><br>BENLYSTA has not been studied in patients less than 18 years of age. There are no data on the safety and efficacy of BENLYSTA in this age group.<br><br>Lupus nephritis<br><br>The safety and efficacy of BENLYSTA in children and adolescents aged below 18 years have not been studied, therefore, BENLYSTA is not recommended for use in children and adolescents with active lupus nephritis.<br><br>**Elderly**<br><br>The efficacy and safety of Benlysta in the elderly has not been established. Data on patients >65 years are limited to < 1.6% of the studied population. Therefore, the use of Benlysta in elderly patients is not recommended unless the benefits are expected to outweigh the risks. In case administration of BENLYSTA to elderly patient is deemed necessary, dose adjustment is not required (see Pharmacokinetics - Special Patient Groups).<br><br>**Renal impairment**<br><br>No formal studies of BENLYSTA have been performed in patients with renal impairment. | |

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| | | BENLYSTA has been studied in a limited number of SLE patients with renal impairment. Dosage adjustment is not required in patients with renal impairment (see Pharmacokinetics - Special Patient Groups).<br><br>**Hepatic impairment**<br><br>No formal studies of BENLYSTA have been performed in patients with hepatic impairment. However, patients with hepatic impairment are unlikely to require dose modification (see Pharmacokinetics - Special Patient Groups). | |