Tambahan Indikasi yang diluluskan dalam Mesyuarat PBKD 379, 13 Disember 2022

Products approved for additional indication (DCA 379 – 13 Disember 2022)

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
1.	TENOF-EM Tablet [Emtricitabine 200mg and tenofovir disoproxil fumarate 300mg (equivalent to 245 mg of tenofovir disoproxil)]	**INDICATION :** Pre-exposure prophylaxis (PrEP): Emtricitabine/Tenofovir Disoproxil is indicated in combination with safer sex practices for pre-exposure prophylaxis to reduce the risk of sexually acquired HIV-1 infection in adults at high risk. When prescribing TENOF-EM for PrEP, healthcare providers must: - prescribe TENOF-EM as part of a comprehensive prevention strategy because emtricitabine/tenofovir disoproxil is not always effective in preventing the acquisition of HIV-1 infection. - counsel all uninfected individuals to strictly adhere to the recommended TENOF-EM dosing schedule because the effectiveness of emtricitabine/tenofovir disoproxil in reducing the risk of acquiring HIV-1 was strongly correlated with adherence as demonstrated by measurable drug levels in clinical trials. - confirm a negative HIV-1 test immediately prior to initiating TENOF-EM for a PrEP indication. If clinical symptoms consistent with acute viral infection are present and recent (<1 month) exposures are suspected, delay starting PrEP for at least one month and reconfirm HIV-1 status, including acute or primary HIV-1 infection; and - screen for HIV-1 infection at least once every 3 months while taking emtricitabine/tenofovir disoproxil for PrEP. **POSOLOGY :** Pre-exposure prophylaxis (PrEP): This indication is based on clinical trials in men who have sex with men (MSM) at high risk for HIV-1 infection and in heterosexual serodiscordant couples.	**MEDISPEC (M) SDN. BHD.** 55 & 57, Lorong Sempadan 2, (Off Boundary Road), 11400 Ayer Itam, Pulau Pinang.

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<table>
<tr><th>No.</th><th>Product
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<tr><td></td><td></td><td>
<u>Posology</u>

Prevention of HIV in adults: One tablet, once daily.

<u>Adults with renal impairment</u>

Routine monitoring of calculated creatinine clearance and serum phosporus should be performed in patients with mild renal impairment.

TENOF-EM should only be used in individuals with creatinine clearance (CrCl) < 80 mL/min if the potential benefits are considered to outweigh the potential risks. See Table 1.

Table 1: Dosing recommendations in adults with renal impairment
<table>
<tr><td></td><td>Pre-exposure prophylaxis</td></tr>
<tr><td>Mild renal impairment (CrCl 50-80mL/min)</td><td>Limited data from clinical studies support once daily dosing in HIV-1 uninfected individuals with CrCl 60-80 mL/min. Use is not recommended in HIV-1 uninfected individuals with CrCl < 60 mL/min as it has not been studied in this population</td></tr>
<tr><td>Moderate renal impairment (CrCl 30-49 mL/min)</td><td>Not recommended for use in this population.</td></tr>
<tr><td>Severe renal impairment (CrCl < 30 mL/min) and haemodialysis patients.</td><td>Not recommended for use in this population.</td></tr>
</table>
</td><td></td></tr>
</table>

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Products approved for additional indication (DCA 379 – 13 Disember 2022)

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
2.	Jakavi 5mg Tablets Jakavi 10mg Tablets Jakavi 15mg Tablets Jakavi 20mg Tablets [Ruxolitinib phosphate 6.6mg (corresponding to 5mg of ruxolitinib free base) Ruxolitinib phosphate 13.2mg (corresponding to 10mg of ruxolitinib free base) Ruxolitinib phosphate 19.8mg (corresponding to 15mg of ruxolitinib free base) Ruxolitinib phosphate 26.4mg (corresponding to 20mg of ruxolitinib free base)]	**INDICATION** : Graft versus host disease (GvHD) Jakavi is indicated for the treatment of patients aged 12 years and older with acute graft versus host disease or chronic graft versus host disease who have inadequate response to corticosteroids or other systemic therapies (see section 5.1). **POSOLOGY :** Starting dose The recommended starting dose of Jakavi in acute and chronic graft versus host disease (GvHD) is 10 mg given orally twice daily. Jakavi can be added to the continued use of corticosteroids and/or calcineurin inhibitors (CNIs). Dose modifications Graft versus host disease Dose reductions and temporary interruptions of treatment may be needed in GvHD-patients with thrombocytopenia, neutropenia, or elevated total bilirubin after standard supportive therapy including growth-factors, anti-infective therapies and transfusions. One dose level reduction step is recommended (10 mg twice daily to 5 mg twice daily or 5 mg twice daily to 5 mg once daily). In patients who are unable to tolerate Jakavi at a dose of 5 mg once daily, treatment should be interrupted. Detailed dosing recommendations are provided in Table 3.	**NOVARTIS CORPORATION (MALAYSIA) SDN. BHD.** Level 18, Imazium, No.8, Jalan SS21/37, Damansara Uptown, 47400 Petaling Jaya, Selangor.

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Products approved for additional indication (DCA 379 – 13 Disember 2022)

<table>
<tr><th>No.</th><th>Product
[Active Ingredient]</th><th>Additional Indication</th><th>Product Registration Holder (PRH)</th></tr>
<tr><td></td><td></td><td>Table 3 Dosing recommendations during ruxolitinib therapy for GvHD patients with thrombocytopenia, neutropenia or elevated total billirubin
<table>
<tr><th>Laboratory parameter</th><th>Dosing recommendation</th></tr>
<tr><td>Platelet count <20,000/mm^3</td><td>Reduce Jakavi by one dose level. If platelet count ≥20,000/mm^3 within seven days, dose may be increased to initial dose level, otherwise maintain reduced dose.</td></tr>
<tr><td>Platelet count <15,000/mm^3</td><td>Hold Jakavi until platelet count ≥20,000/mm^3, then resume at one lower dose level.</td></tr>
<tr><td>Absolute neutrophil count (ANC) ≥500/mm^3 to <750/mm^3</td><td>Reduce Jakavi by one dose level. Resume at initial dose level if ANC >1,000/mm^3.</td></tr>
<tr><td>Absolute neutrophil count <500/mm^3</td><td>Hold Jakavi until ANC >500/mm^3, then resume at one lower dose level. If ANC >1,000/mm^3, dosing may resume at initial dose level.</td></tr>
<tr><td>Total bilirubin elevation not caused by GvHD (no liver</td><td>>3.0 to 5.0 x upper limit of normal (ULN): Continue Jakavi at one lower dose level until ≤3.0 x ULN.</td></tr>
</table></td><td></td></tr>
</table>

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<tr><td></td><td></td><td>
<table>
<tr><td rowspan="2">GvHD)</td><td>>5.0 to 10.0 x ULN: Hold Jakavi up to 14 days until total bilirubin ≤3.0 x ULN. If total bilirubin ≤3.0 x ULN dosing may resume at current dose. If not ≤3.0 x ULN after 14 days, resume at one lower dose level.</td></tr>
<tr><td>>10.0 x ULN: Hold Jakavi until total bilirubin ≤3.0 x ULN, then resume at one lower dose level.</td></tr>
<tr><td>Total bilirubin elevation caused by GvHD (liver GvHD)</td><td>>3.0 x ULN: Continue Jakavi at one lower dose level until total bilirubin ≤3.0 x ULN.</td></tr>
</table>
<u>Special populations</u>

Renal impairment

In patients with severe renal impairment (creatinine clearance less than 30 ml/min) the recommended starting dose based on platelet count for MF patients should be reduced by approximately 50% to be administered twice daily. The recommended starting dose for PV and GvHD patients with severe renal impairment is 5 mg twice daily. Patients should be carefully monitored with regard to safety and efficacy during ruxolitinib treatment.

There are no data for GvHD patients with ESRD.

Hepatic impairment

In patients with mild, moderate or severe hepatic impairment not related to GvHD, the starting dose of ruxolitinib should be reduced by 50%.
</td><td></td></tr>
</table>

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No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
		In patients with GvHD liver involvement and an increase of total bilirubin to >3 x ULN, blood counts should be monitored more frequently for toxicity and a dose reduction by one dose level is recommended. Paediatric population In paediatric patients (12 years of age and older) with GvHD, the safety and efficacy of Jakavi are supported by evidence from the randomised phase 3 studies REACH2 and REACH3. The Jakavi dose in paediatric patients with GvHD aged 12 years and older is the same as in adults. The safety and efficacy of Jakavi have not been established in patients less than 12 years of age. <u>Treatment discontinuation</u> In GvHD, tapering of Jakavi may be considered in patients with a response and after having discontinued corticosteroids. A 50% dose reduction of Jakavi every two months is recommended. If signs or symptoms of GvHD reoccur during or after the taper of Jakavi, re-escalation of treatment should be considered.	

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<table>
<tr><th>No.</th><th>Product
[Active Ingredient]</th><th>Additional Indication</th><th>Product Registration Holder (PRH)</th></tr>
<tr><td>3.</td><td>Lusefi 2.5mg film-coated tablet

Lusefi 5mg film-coated tablet

[Luseogliflozin hydrate 2.575mg (equivalent to luseogliflozin 2.5mg)

Luseogliflozin hydrate 5.150mg (equivalent to luseogliflozin 5mg)]</td><td>INDICATION:

There are no changes to the approved indication.

[Note: Updated information will be reflected under section “CLINICAL STUDIES” of the package insert with the new clinical study for luseogliflozin in combination with GLP-1 receptor agonists.
“Long-term study of luseogliflozin in add-on combination with GLP-1 receptor agonists

To patients with type 2 diabetes mellitus whose plasma control was insufficiently controlled by diet and exercise therapies and GLP-1 receptor agonists alone (76 subjects), 2.5 mg or 5 mg (when the dose was increased) of luseogliflozin was orally administered once daily before breakfast for 52 weeks. The results were as the following table. The incidence of the adverse drug reaction of hypoglycemia was 6.6% (5/76 subjects).

<table>
<tr><td rowspan="2">Concomitant drugs</td><td colspan="2">HbA1c (NGSP value) (%)</td></tr>
<tr><td>At the start of administration</td><td>Change from the value before the administration at 52 weeks</td></tr>
<tr><td>GLP-1 receptor agonists (n = 76)</td><td>8.52 ± 1.08</td><td>- 0.68
[- 0.9, - 0.5]</td></tr>
</table>
At the start of administration: mean ± standard deviation
Change from the value before the administration: mean, 2-sided 95% confidence interval shown in [ ]”].</td><td>HOE PHARMACEUTICALS SDN. BHD.
Lot 10, Jalan Sultan Mohamed 6,
Bandar Sultan Suleiman,
42000 Port Klang,
Selangor.</td></tr>
</table>

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Products approved for additional indication (DCA 379 – 13 Disember 2022)

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
4.	Pamorelin Powder for Suspension for Injection 3.75 mg [Triptorelin embonate]	**INDICATION:** Pamorelin 3.75 mg is indicated as adjuvant treatment, in combination with tamoxifen or an aromatase inhibitor in women with early stage hormone receptor-positive breast cancer (oestrogen and/or progesterone) at high risk of recurrence and who are confirmed as premenopausal after completion of chemotherapy. **POSOLOGY:** Breast cancer: An intramuscular injection administered every 4 weeks in combination with tamoxifen or an aromatase inhibitor (AI). Pamorelin 3.75 mg should be commenced after completion of chemotherapy, once pre-menopausal status has been confirmed. The treatment with Pamorelin 3.75 mg should be initiated at least 6-8 weeks before starting aromatase inhibitor treatment. A minimum of two injections of Pamorelin 3.75 mg (with an interval of 4 weeks between injections) should be administered before commencement of aromatase inhibitor treatment. During treatment with an aromatase inhibitor, Pamorelin 3.75 mg should not be interrupted to avoid rebound increases in circulating estrogens in pre-menopausal women. The recommended treatment duration for adjuvant treatment in combination with other hormonotherapy is up to 5 years.	**ORIENT EUROPHARMA (M) SDN. BHD.** E-08, Garden Shoppe, One City, Jalan USJ 25/1C, 47650 Subang Jaya, Selangor.

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Products approved for additional indication (DCA 379 – 13 Disember 2022)

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
5.	Yulareb 150mg film-coated tablets Yulareb 100mg film-coated tablets Yulareb 50mg film-coated tablets [Abemaciclib 150mg Abemaciclib 100mg Abemaciclib 50mg]	**INDICATION:** <u>Early Breast Cancer</u> YULAREB in combination with endocrine therapy is indicated for the adjuvant treatment of adult patients with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative, node-positive early breast cancer at high risk of recurrence. In pre- or perimenopausal women, aromatase inhibitor endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist. **POSOLOGY:** Early Breast Cancer: YULAREB should be taken continuously for two years, or until disease recurrence or unacceptable toxicity occurs	**ZUELLIG PHARMA SDN. BHD.** No. 15, Persiaran Pasak Bumi, Sek. U8, Perindustrian Bukit Jelutong, 40150 Shah Alam, Selangor.

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Products approved for additional indication (DCA 379 – 13 Disember 2022)

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
6.	Zinforo 600mg Powder for Concentrate for Solution for Infusion [Ceftaroline Fosamil 600mg]	**INDICATION:** Ceftaroline fosamil is indicated for the treatment of the following infections in neonates , infants, children, adolescents and adults (see sections 4.4 and 5.1): • Complicated skin and soft tissue infections (cSSTI) • Community-acquired pneumonia (CAP) Consideration should be given to official guidance on the appropriate use of antibacterial agents. **POSOLOGY :** Dosage in paediatric patients The recommended dosage of ceftaroline fosamil is 600 mg administered every 12 hours by intravenous infusion over 5 to 60 minutes (standard dose), with appropriate reductions for paediatric patients (see Table 1). The duration of treatment should be guided by the type of infection to be treated, its severity, and the patient's clinical response. For the treatment of cSSTI confirmed or suspected to be caused by Staphylococcus aureus (S. aureus) with a Minimum Inhibitory Concentration (MIC) <2 mg/L to ceftaroline, the dose of ceftaroline fosamil is 600 mg administered every 12 hours by intravenous infusion over 5 to 60 minutes (standard dose), with appropriate reductions for paediatric patients (see Table 1). For the treatment of patients with cSSTI confirmed or suspected to be caused by S. aureus with an MIC = 2 mg/L or 4 mg/L to ceftaroline, the dose of ceftaroline fosamil is 600 mg administered every 8 hours by intravenous infusion over 120 minutes (high dose), with appropriate reductions for paediatric patients (see Table 1). Table 1 Dosage in patients with Creatinine Clearance (CrCL) >50 mL/min*	**PFIZER (MALAYSIA) SDN. BHD.** Level 10 & 11, Wisma Averis, Tower 2, Avenue 5, Bangsar South, No.8, Jalan Kerinchi, 59200 Kuala Lumpur, Wilayah Persekutuan Kuala Lumpur.

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<tr><td></td><td></td><td>
<table>
<tr><th>Indications / Recommended duration of treatment (days)</th><th>Age group</th><th>Posology</th><th>Infusion time (minutes)[a] / Frequency</th></tr>
<tr><td rowspan="4"><u>Standard dose</u>
cSSTI[b] / 5 – 14
CAP[c] / 5 – 7</td><td>Adults and adolescents aged from 12 to <18 years with bodyweight ≥33 kg</td><td>600 mg</td><td>5 – 60/every 12 hours</td></tr>
<tr><td>Adolescents aged from 12 years to <18 years with bodyweight <33 kg and children ≥2 years to <12 years</td><td>12 mg/kg to a maximum of 400 mg</td><td>5 – 60/every 8 hours</td></tr>
<tr><td>≥2 months to <2 years</td><td>8 mg/kg</td><td>5 – 60/every 8 hours</td></tr>
<tr><td>Birth to < 2 months[d]</td><td>6 mg/kg</td><td>60 / every 8 hours</td></tr>
<tr><td rowspan="3"><u>High dose</u>
cSSTI[b] confirmed or suspected to be caused by S. aureus with an MIC = 2 mg/L or 4 mg/L to ceftaroline[d] / 5 – 14</td><td>Adults</td><td>600 mg</td><td>120 / every 8 hours</td></tr>
<tr><td>Adolescents and children aged from ≥2 years to < 18 years</td><td>12 mg/kg to a maximum of 600 mg</td><td>120 / every 8 hours</td></tr>
<tr><td>≥2 months to <2 years</td><td>10 mg/kg</td><td>120 / every 8 hours</td></tr>
</table>
a The 5 minute infusion time is based on pharmacokinetic and pharmacodynamic analyses.
b Complicated skin and soft tissue infections (cSSTI) indication.
c Community-acquired pneumonia (CAP) indication.
d Neonatal and high dose recommendations is based on pharmacokinetic and pharmacodynamic analyses. See sections 4.4 and 5.1.
* Calculated using the Cockcroft-Gault formula for adults and Schwartz formula (in mL/min/1.73 m^2) for paediatric patients

<u>Special populations</u>
Patients with renal impairment
</td><td></td></tr>
</table>

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The dose should be adjusted when creatinine clearance (CrCL) is ≤50 mL/min, as shown in Table 2. Dose recommendations for children and adolescents are based on PK modelling. End Stage Renal Disease (ESRD) patients can only be dosed as in Table 2.

For ESRD, there is insufficient information to recommend dosage adjustments in adolescents aged from 12 to <18 years with bodyweight <33 kg and in children aged from 2 to 12 years. There is insufficient information to recommend dosage adjustments in paediatric patients <2 years with moderate or severe renal impairment or ESRD.

Table 2 Dosage in patients with renal impairment (CrCL ≤50 mL/min)
<table>
<tr><th>Indications / Recommended duration of treatment (days)</th><th>Age group</th><th>Creatinine clearance (mL/min)[a]</th><th>Posology</th><th>Infusion time (minutes)[b] / Frequency</th></tr>
<tr><td rowspan="4">Standard dose cSSTI[c] / 5 – 14
CAP[d] / 5 – 7</td><td rowspan="3">Adults and adolescents aged from 12 to <18 years with bodyweight ≥33 kg</td><td>>30 to ≤50</td><td>400 mg</td><td rowspan="3">5 – 60 / every 12 hours</td></tr>
<tr><td>≥15 to ≤30</td><td>300 mg</td></tr>
<tr><td>ESRD, including haemodialysis[f]</td><td>200 mg</td></tr>
<tr><td rowspan="2">Adolescents aged from 12 years to <18 years with bodyweight <33 kg and children ≥2 years to < 12 years</td><td>>30 to ≤50</td><td>8 mg/kg to a maximum of 300 mg</td><td rowspan="2">5 – 60 / every 8 hours</td></tr>
<tr><td>≥15 to ≤30</td><td>6 mg/kg to a maximum of 200 mg</td></tr>
<tr><td>High dose cSSTI[c] confirmed or suspected to be caused by S. aureus with an</td><td>Adults</td><td>>30 to ≤50</td><td>400 mg</td><td>120/ every 8 hours</td></tr>
</table>
</td><td></td></tr>
</table>

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<table>
<tr><td rowspan="3">MIC = 2 mg/L or 4 mg/L to ceftaroline[e] / 5 – 14</td><td rowspan="2"></td><td>≥15 to ≤30</td><td>300 mg</td><td rowspan="2"></td></tr>
<tr><td>ESRD, including haemodialysis[f]</td><td>200 mg</td></tr>
<tr><td rowspan="2">Adolescents and children aged from ≥ 2 years to < 18 years</td><td>> 30 to ≤ 50</td><td>10 mg/kg to a maximum of 400 mg</td><td rowspan="2">120 / every 8 hours</td></tr>
<tr><td>≥ 15 to ≤ 30</td><td>8 mg/kg to a maximum of 300 mg</td></tr>
</table>
a Calculated using the Cockcroft-Gault formula for adults and Schwartz formula for paediatric patients (in mL/min/1.73 m^2). Dose is based on CrCL. CrCL should be closely monitored and the dose adjusted according to changing renal function.
b The 5 minute infusion time is based on pharmacokinetic and pharmacodynamic analyses.
c Complicated skin and soft tissue infections (cSSTI) indication.
d Community-acquired pneumonia (CAP) indication.
e Based on pharmacokinetic and pharmacodynamic analyses.
f Ceftaroline is haemodialyzable; thus ceftaroline fosamil should be administered after haemodialysis on haemodialysis days.

Patients with hepatic impairment
No dosage adjustment is considered necessary in patients with hepatic impairment.
Elderly patients
No dosage adjustment is required for the elderly with creatinine clearance (CrCL) values >50 mL/min.
</td><td></td></tr>
</table>