Maklumat tambahan indikasi
Year 2020
Products Approved For Additional Indication (DCA 342 – 9 January 2020)

<table>
<tr><th>NO</th><th>PRODUCT
(ACTIVE INGREDIENT)</th><th>ADDITIONAL INDICATION</th><th>MARKETING AUTHORIZATION HOLDER</th></tr>
<tr><td>1.</td><td>1.1 Zinforo 600mg Powder for Concentrate for Solution for Infusion
[Ceftaroline Fosamil 600 mg]</td><td>
➢ Indication:
Zinforo is indicated for the treatment of the following infection from the age of 2 months:

• Community-acquired pneumonia (CAP)

Consideration should be given to official guidance on the appropriate use of antibacterial agents.

➢ Posology:

Dosage in adults and adolescents aged from 12 to < 18 years with bodyweight ≥ 33 kg

The recommended dosage of Zinforo is 600 mg administered every 12 hours by intravenous infusion over 5 to 60 minutes (standard dose). The duration of treatment (see Table 1) should be guided by the type of infection to be treated, its severity, and the patient's clinical response.

Table 1 Dosage in patients with normal renal function (Creatine Clearance (CrCL) > 50 mL/min)
<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>CAP[c] / 5 – 7</td><td>Adults and adolescents aged from</td><td>600 mg</td><td>5 – 60 / every 12</td></tr>
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</td><td>PFIZER (MALAYSIA) SDN. BHD.
Level 10 & 11, Wisma Averis, Tower 2,
Avenue 5, Bangsar South,
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59200 Kuala Lumpur</td></tr>
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	12 to < 18 years with bodyweight ≥ 33 kg		*hours*
	Adolescents aged from 12 years to < 18 years with bodyweight < 33 kg and children ≥ 2 years to < 12 years	*12 mg/kg to a maximum of 400 mg*	*5 – 60 / every 8 hours*
	≥ 2 months to < 2 years	*8 mg/kg*	*5 – 60 / every 8 hours*

[a] The 5 minute infusion time is based on pharmacokinetic and pharmacodynamics analyses.
[b]Complicated skin and soft tissue (cSSTI) infection
[c] Community-acquired pneumonia (CAP) indication.

<u>Special populations</u>
Patients with renal impairment
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)

Indications / Recommended duration of treatment (days)	*Age group*	*Posology*	*Infusion time (minutes)[a] / Frequency*
CAP[c] / 5 – 7	*Adults and adolescents aged from 12 to < 18 years with bodyweight ≥ 33 kg*	*600 mg*	*5 – 60 / every 12 hours*
	Adolescents aged from 12 years to < 18 years with bodyweight < 33 kg and children ≥ 2 years to < 12 years	*12 mg/kg to a maximum of 400 mg*	*5 – 60 / every 8 hours*
	≥ 2 months to < 2 years	*8 mg/kg*	*5 – 60 / every 8 hours*

[a] Calculated using the the Cockcroft-Gault formula for adults and adolescents aged from 12 to < 18 years with bodyweight ≥ 33 kg and Schwartz formula for children and adolescents with bodyweight less than

		33 kg. 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] Ceftaroline is haemodialyzable; thus Zinforo should be administered after haemodialysis on haemodialysis days.*	
2.	2.1 **Hemlibra 30mg/ml solution for injection** [Emicizumab 30mg/ml] 2.2 **Hemlibra 150mg/ml solution for injection** [Emicizumab 150mg/ml]	➢ Indication: *Hemlibra is indicated for routine prophylaxis of bleeding episodes in patients with* ○ *haemophilia A (congenital factor VIII deficiency) with factor VIII inhibitors* ○ *severe haemophilia A (congenital factor VIII deficiency, FVIII < 1%) without factor VIII inhibitors .* *Hemlibra can be used in all age groups*	**ROCHE (MALAYSIA) SDN. BHD.** Level 21, The Pinnacle Persiaran Lagoon Bandar Sunway 47500 Subang Jaya, Selangor
3.	3.1 **Dysport Powder for Injection** [Clostridium Botulinum Toxin Type A 500U]	➢ Indication: *Botulinum Toxin Type A is indicated for symptomatic treatment of focal spasticity of:* - *Upper limbs in adults* - ***Lower limbs in adults affecting the ankle joint due to stroke or traumatic brain injury (TBI)*** - *Dynamic equinus foot deformity in ambulant paediatric cerebral palsy patients, two years of age or older* *Botulinum Toxin Type A is also indicated in adults for symptomatic treatment of:* - *Spasmodic torticollis* - *Blepharospasm* - *Hemifacial spasm* - *Axillary hyperhidrosis.* - *Moderate to severe glabellar lines* ➢ Posology: ***The units of Botulinum Toxin Type A are specific to the***	**EP PLUS GROUP SDN. BHD.** Block C-3-1, Plaza Mont Kiara No. 2, Jalan Kiara Mont Kiara 50480 Kuala Lumpur

preparation and are not interchangeable with other preparations of botulinum toxin.

Training: Botulinum Toxin Type A should only be administered by appropriately trained physicians. Ipsen can facilitate training in administration of Botulinum Toxin Type A injections

Focal spasticity in adults

<u>Lower limb spasticity affecting the ankle joint:</u>

Posology

In clinical trials, doses of 1000U and 1500U were divided among selected muscles.

The exact dosage in initial and sequential treatment sessions should be tailored to the individual based on the size and number of muscles involved the severity of the spasticity, also taking into account the presence of local muscle weakness and the patient's response to previous treatment. However, the total dose should not exceed 1500U.

No more than 1 ml should generally be administered at any single injection site.

Muscle	***Recommended Dose Botulinum Toxin Type A (U)***	***Number of injection sites per muscle***
Primary target muscle		
Soleus muscle	*300 - 550U*	*2 - 4*
Gastrocnemius:	*100 - 450U*	*1 - 3*
Medial head	*100 - 450U*	*1 - 3*
Lateral head		
Distal muscles		
Tibialis posterior	*100 - 250U*	*1 - 3*
Flexor digitorum longus	*50 - 200U*	*1 - 2*

Flexor digitorum brevis	*50 - 200U*	*1 - 2*
Flexor hallucis longus	*50 - 200U*	*1 - 2*
Flexor hallucis brevis	*50 - 100U*	*1 - 2*

The degree and pattern of muscle spasticity at the time of re-injection may necessitate alterations in the dose of Botulinum Toxin Type A and muscles to be injected.

Although actual location of the injection sites can be determined by palpation, the use of injection guiding techniques, e.g. electromyography, electrical stimulation or ultrasound are recommended to help accurately target the injection sites.

Repeat Botulinum Toxin Type A treatment should be administered every 12 to 16 weeks, or longer as necessary, based on return of clinical symptoms but no sooner than 12 weeks after the previous injection.

Upper and Lower limbs:
If treatment is required in the upper and lower limbs during the same treatment session, the dose of Botulinum Toxin Type A to be injected in each limb should be tailored to the individual's need according to the relevant posology and without exceeding a total dose of 1500U.

Children: The safety and effectiveness of Botulinum Toxin Type A in the treatment of upper limb spasticity in children have not been demonstrated.

Elderly patients (≥ 65 years): Clinical experience has not identified differences in response between the elderly and younger adult patients. In general, elderly patients should be observed to evaluate their tolerability of Botulinum Toxin Type A, due to the greater frequency of concomitant disease and other drug therapy.

		Method of administration *When treating focal spasticity affecting the upper limbs and lower in adults, Botulinum Toxin Type A is reconstituted with sodium chloride injection B.P. (0.9 % w/v) to yield a solution containing either 100 units per ml, 200 units per ml or 500 units per ml of Botulinum Toxin Type A (see section 6.6). Botulinum Toxin Type A is administered by intramuscular injection into the muscles as described above.*	
4.	4.1 **KEYTRUDA 100MG SOLUTION FOR INFUSION** [Pembrolizumab 100mg]	➢ Indication: *Melanoma* *Keytruda (pembrolizumab) is indicated for the treatment of patients with unresectable or metastatic melanoma.* *Keytruda as monotherapy is indicated for the adjuvant treatment of adults with Stage III melanoma and lymph node involvement who have undergone complete resection.* *Non – Small Cell Lung Carcinoma* • *KEYTRUDA, in combination with pemetrexed and platinum chemotherapy, is indicated for the first-line treatment of patients with metastatic non-squamous non-small cell lung carcinoma (NSCLC), with no EGFR or ALK genomic tumour aberrations.* • *KEYTRUDA, in combination with carboplatin and either paclitaxel or nab-paclitaxel, is indicated for the first-line treatment of patients with metastatic squamous NSCLC.* • *KEYTRUDA, as monotherapy is indicated for the first-line treatment of patients with NSCLC expressing PD-L1 [Tumour Proportion Score (TPS) ≥ 1%] as determined by a validated test, with no EGFR or ALK genomic tumour aberrations, and is:* o *Stage III where patients are not candidates for surgical resection or definitive chemoradiation, or* o *Metastatic*	**MERCK SHARP & DOHME (MALAYSIA) SDN. BHD.** B-22-1 & B-22-2, The Ascent Paradigm No. 1 Jalan SS 7/26A, Kelana Jaya 47301 Petaling Jaya, Selangor

		• *KEYTRUDA, as monotherapy is indicated for the treatment of patients with locally advanced or metastatic NSCLC whose tumours express PD-L1 with a ≥ 1% TPS as determined by a validated test and who have disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumour aberrations should have disease progression on approved therapy for these aberrations prior to receiving KEYTRUDA.* *<u>Head and Neck Cancer</u>* *Keytruda is indicated for the treatment of patients with recurrent or metastatic head and neck squamous cell carcinoma (HNSCC) with disease progression on or after platinum-containing chemotherapy. This indication is approved based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.* *<u>Urothelial Carcinoma</u>* *Keytruda is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who have disease progression during or following platinum-containing chemotherapy or within 12 months of neoadjuvant or adjuvant treatment with platinum-containing chemotherapy.* *Keytruda is indicated for the treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy and whose tumors express PD-L1 [Combined Positive Score (CPS) ≥ 10] as determined by a validated test. This indication is approved based on tumor response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials.* *<u>Classical Hodgkin Lymphoma</u>* *Keytruda as monotherapy is indicated for the treatment of patients with relapsed or refractory classical Hodgkin*	

lymphoma (cHL) who have failed autologous stem cell transplant (ASCT) and brentuximab vedotin (BV), or who are transplant-ineligible and have failed BV. This indication is approved based on tumor response rate and durability of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in the confirmatory trials.

- Posology:

General

Patient Selection for single agent treatment Non-Small Cell Lung Carcinoma or Urothelial Carcinoma

Select patients for treatment with Keytruda based on the presence of positive PD-L1 expression in:

- *Locally advanced or metastatic advanced NSCLC.*
- *locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.*

Recommended Dosing

Keytruda is administered as an intravenous infusion over 30 minutes every 3 weeks.

The recommended dose of Keytruda is:

- *200 mg for NSCLC that has been previously untreated, head and neck cancer, urothelial carcinoma, classical Hodgkin Lymphoma or for the* ***adjuvant treatment of melanoma as monotherapy.***
- *200 mg for NSCLC in combination therapy.*
- *2 mg/kg for unresectable or metastatic melanoma or previously treated NSCLC as monotherapy.*

When administering Keytruda as part of a combination with pemetrexed and platinum chemotherapy, Keytruda should

be administered first. See also the prescribing information for pemetrexed and the selected platinum chemotherapy.

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. ***For adjuvant treatment of melanoma, Keytruda should be administered for up to one year or until disease recurrence or unacceptable toxicity***

Dose modifications

Adverse reactions	***Severity***	***Dose modification***
Immune-mediated pneumonitis	*Moderate (Grade 2)*	*Withhold until adverse reactions recover to Grade 0-1**
	Severe or life-threatening (Grade 3 or 4) or recurrent moderate (Grade 2)	*Permanently discontinue*
Immune-mediated colitis	*Moderate or severe (Grade 2 or 3)*	*Withhold until adverse reactions recover to Grade 0-1**
	Life-threatening (Grade 4) or recurrent severe (Grade 3)	*Permanently discontinue*
Immune-mediated nephritis	*Moderate (Grade 2)*	*Withhold until adverse reactions recover to Grade 0-1**
	Severe or life-threatening (Grade 3 or 4)	*Permanently discontinue*
Immune-	*Severe or life-*	*Withhold until*

mediated endocrinopathies	*threatening (Grade 3 or 4)*	*adverse reactions recover to Grade 0-1* 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	*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 Grade 0-1**
	AST or ALT >5 times ULN or total bilirubin >3 times ULN	*Permanently discontinue*
	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	*Severe skin reactions (Grade 3) or suspected SJS or TEN*	*Withhold until adverse reactions recover to Grade 0-1**

Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	*Severe skin reactions (Grade 4) or confirmed SJS or TEN*	*Permanently discontinue*
Other immune-mediated adverse	*Based on severity and type of reaction (Grade 2 or Grade 3*	*Withhold until adverse reactions recover to Grade 0-1**

Note: toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 (NCI CTCAE v.4)
** If corticosteroid dosing cannot be reduced to ≤10 mg prednisone or equivalent per day within 12 weeks or a treatment-related toxicity does not resolve to Grade 0-1 within 12 weeks after last dose of Keytruda, then Keytruda should be permanently discontinued.*
In patients with cHL with Grade 4 hematological toxicity, Keytruda should be withheld until adverse reactions recover to Grade 0-1.

	Severe or life-threatening (Grade 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 Grade 3 or Grade 4*	*Permanently discontinue*

Preparation and administration

- *Protect from light. Do not freeze. Do not shake.*
- *Equilibrate the vial of Keytruda to room temperature.*
- *Prior to dilution, the vial of liquid can be out of refrigeration (temperatures at or below 25°C) for up to 24 hours.*
- *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.*
- *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) to prepare a diluted solution with a final concentration ranging from 1 to 10 mg/mL. Mix diluted solution by gentle inversion.*
- *Do not freeze the infusion solution.*
- *The product does not contain preservative. The diluted product should be used immediately. If not used immediately, diluted solutions of Keytruda solutions 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 24 hours. If refrigerated, allow the vials and/or IV bags to come to room temperature prior to use.*
- *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.*
- *Do not co-administer other drugs through the same infusion line.*
- *Discard any unused portion left in the vial.*

Renal Impairment

No dose adjustment is needed for patients with mild or moderate renal impairment. Keytruda has not been studied in patients with severe renal impairment.

		Hepatic Impairment *No dose adjustment is needed for patients with mild hepatic impairment. Keytruda has not been studied in patients with moderate or severe hepatic impairment.*	