Maklumat tambahan indikasi
Year 2020
Products Approved For Additional Indication (DCA 347 – 6 August 2020)

	PRODUCT (ACTIVE INGREDIENT)	ADDITIONAL INDICATION	MARKETING AUTHORIZATION HOLDER
1.	1.1 **Erleada 60 mg Film-Coated Tablets** [Apalutamide 60 mg]	➢ Indication: *ERLEADA® is indicated in adult men for the treatment of metastatic hormone-sensitive prostate cancer (mHSPC) in combination with androgen deprivation therapy (ADT).*	**JOHNSON & JOHNSON SDN BHD** Lot 3 & 5, Jalan Tandang, 46050 Petaling Jaya, Selangor
2.	2.1 **Stelara 45mg/0.5ml solution for injection in pre-filled syringe** [Ustekinumab 45mg/0.5ml] 2.2 **Stelara 90mg/1ml solution for injection in pre-filled syringe** [Ustekinumab 90mg/1ml] 2.3 **Stelara 130mg/26ml concentrate for solution for infusion** [Ustekinumab 130mg/26ml]	➢ Indication: *Ulcerative Colitis* *(via intravenous administration for induction dosing, and via subcutaneous administration for maintenance dosing)* *Stelara is indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic or have medical contraindications to such therapies.* ➢ Posology: *Stelara solution for subcutaneous injection (pre-filled syringe) is intended for use under the guidance and supervision of a physician experience in the diagnosis and treatment conditions for which Stelara is indicated.* *Stelara concentrate for solution for intravenous infusion (single-use vial) is intended for use under the guidance and supervision of physicians experienced in the diagnosis and treatment of Crohn's disease and **Ulcerative Colitis.** Stelara concentrate for solution for infusion should only be used for the intravenous induction dose.* *Crohn's disease and **Ulcerative Colitis*** *Intravenous induction dosing*	**JOHNSON & JOHNSON SDN BHD** Lot 3 & 5, Jalan Tandang, 46050 Petaling Jaya, Selangor

Stelara treatment is to be initiated with a single intravenous dose based on body weight. The infusion solution is to be composed of the number of vials of Stelara 130 mg as specified in Table 1.

Table 1: Initial intravenous dosing of Stelara

Body Weight of patient at the time of dosing	*Recommended dose*[a]	*Number of 130 mg Stelara Vials*
≤ 55 kg	*260 mg*	*2*
> 55 kg to ≤ 85 kg	*390 mg*	*3*
> 85 kg	*520 mg*	*4*

[a] *Approximately 6mg/kg*

After the initial IV induction dose, Stelara should then be administered subcutaneously.

Subcutaneous maintenance dosing
The first subcutaneous administration of 90 mg Stelara should take place at week 8 after the intravenous dose. After this, dosing every 12 weeks is recommended.

Patients who have not shown adequate response at 8 weeks after the first subcutaneous dose, may receive a second subcutaneous dose at this time.

Patients who lose response on dosing every 12 weeks may benefit from an increase in dosing frequency to every 8 weeks.

Patients may subsequently be dosed every 8 weeks or every 12 weeks according to clinical judgment.

Consideration should be given to discontinuing treatment in patients who show no evidence of therapeutic benefit by week 16 or 16 weeks after switching to the 8-weekly dose.

		Immunomodulators and/or corticosteroids may be continued during treatment with Stelara. In patients who have responded to treatment with Stelara, corticosteroids may be reduced or discontinued in accordance with standard of care. *If therapy in Crohn's disease is interrupted, resumption of treatment with subcutaneous dosing every 8 weeks is safe and effective.* *<u>Elderly (≥ 65 years)</u>* *No dose adjustment is needed for elderly patients.* *<u>Renal and hepatic impairment</u>* *Stelara has not been studied in these patient populations. No dose recommendations can be made.* *<u>Paediatric population</u>* *The safety and efficacy of STELARA in children less than 18 years have not yet been established. No data are available.*	
3.	3.1 **Darzalex™ 20mg/ml concentrate for solution for infusion** [DARATUMUMAB 20 MG/ML]	➢ Indication: *DARZALEX is indicated for the treatment of adult patients with multiple myeloma:* • *in combination with bortezomib, thalidomide, and dexamethasone in newly diagnosed patients who are eligible for autologous stem cell transplant* ➢ Posology: *The DARZALEX dosing schedule in Table 3 is for combination therapy with bortezomib, thalidomide and dexamethasone (4-week cycle regimens) for treatment of newly diagnosed patients eligible for ASCT.* *The recommended dose is DARZALEX 16mg/kg body weight administered as an intravenous infusion according to the*	**JOHNSON & JOHNSON SDN BHD** Lot 3 & 5, Jalan Tandang, 46050 Petaling Jaya, Selangor

		following dosing schedule (infusion rates presented in Table 5): *Table 3: DARZALEX dosing schedule in combination with bortezomib, thalidomide and dexamethasone ([VTd]; 4-week cycle dosing regimen)* *a First dose of the every-2-week dosing schedule is given at Week 9* *b First dose of the every-2-week dosing schedule is given at Week 1 upon re-initiation of treatment following ASCT* *For dosing instructions of medicinal products administered with DARZALEX, see Clinical Studies and manufacturer's prescribing information.*	
4.	4.1 **KEYTRUDA 100mg SOLUTION FOR INFUSION** [Pembrolizumab 100mg]	➢ *Indication:* *<u>Endometrial Carcinoma</u>* *KEYTRUDA, in combination with lenvatinib, is indicated for the treatment of adult patients with advanced endometrial carcinoma that is not microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR), who have disease progression following prior platinum-based systemic therapy and are not candidates for curative surgery or radiation.*	**MERCK SHARP & DOHME (MALAYSIA) SDN BHD** Lot No. B-22-1 - B-22-2, Level 22, The Ascent, Paradigm No. 1, Jalan SS 7/26A, Kelana Jaya,

Treatment phase	*Weeks*	*Schedule*
Induction	*Weeks 1 to 8*	*weekly (total of 8 doses)*
	Weeks 9 to 16[a]	*every two weeks (total of 4 doses)*
Stop for high dose chemotherapy and ASCT		
Consolidation	*Weeks 1 to 8[b]*	*every two weeks (total of 4 doses)*

		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:* ***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 or RCC or* ***endometrial carcinoma*** *in combination therapy.* • *2 mg/kg for unresectable or metastatic melanoma or previously treated NSCLC as monotherapy.* *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.* ***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 or unacceptable toxicity, or for KEYTRUDA, up to 24 months in patients without disease progression.*** ***Dose modifications*** ***Table 17: Recommended Dose Modifications [see Precautions (VIII)]***	47301 Petaling Jaya, Selangor

Adverse reactions	***Severity***	***Dose modification***

Immune-mediated pneumonitis	*Moderate (Grade 2)*	*Withhold until adverse reactions recover to Grades 0-1**
	Severe or life-threatening (Grades 3 or 4) or recurrent moderate (Grade 2)	*Permanently discontinue*
Immune-mediated colitis	*Moderate or severe (Grades 2 or 3)*	*Withhold until adverse reactions recover to Grades 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 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** *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 *For liver enzyme elevations in RCC patients treated with combination therapy, see dosing guidelines following this table.*	*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**
	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 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	*Based on severity and type of reaction*	*Withhold until adverse reactions*

adverse reactions	*(Grade 2 or Grade 3)*	*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)

* *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 Grades 0-1 within 12 weeks after last dose of KEYTRUDA, then KEYTRUDA should be permanently discontinued.*

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.

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.*
- *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.*
- *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.

5.	5.1 **Levemir Flexpen 100U/ml, 3ml** [Insulin Detemir 100 U/ml] 5.2 **Levemir FlexPen 100U/ml Solution for injection in a prefilled pen** [Insulin Detemir 100 U/ml]	➢ Indication: *Treatment of diabetes mellitus in adults, adolescents and children aged 1 years and above.* ➢ Posology: *<u>Paediatric population</u>* *Levemir® can be used in adolescents and children from the age of 1 year. When changing basal insulin to Levemir®, dose reduction of basal and bolus insulin needs to be considered on an individual basis, in order to minimise the risk of hypoglycaemia. In children and adolescents, glucose monitoring should be intensified and the Levemir® dose adjusted on an individual basis. The safety and efficacy of Levemir® in children below the age of 1 year has not been established. No data are available.*	**NOVO NORDISK PHARMA (MALAYSIA) SDN. BHD.** Menara 1 Sentrum, Level 16 No. 201, Jalan Tun Sambathan 50470 Kuala Lumpur
6.	6.1 **Novorapid® Flexpen® 100 IU/ml** [Insulin Aspart 100 U/ML] 6.2 **NovoRapid FlexPen 100U/ml solution for injection in pre-filled pen** [Insulin Aspart 100 U/ML] 6.3 **Novorapid Penfill 100IU/ml** [Insulin Aspart 100 U/ML]	➢ Indication: *Treatment of diabetes mellitus in adults, adolescents and children aged 1 years and above.* ➢ Posology: *<u>Paediatric population</u>* *NovoRapid® can be used in children **and adolescents aged 1 year and above** in preference to soluble human insulin when a rapid onset of action might be beneficial, for example, in the timing of the injections in relation to meals. **The safety and efficacy of NovoRapid® in children below 1 year of age have not been established. No data are available.***	**NOVO NORDISK PHARMA (MALAYSIA) SDN. BHD.** Menara 1 Sentrum, Level 16 No. 201, Jalan Tun Sambathan 50470 Kuala Lumpur

7.	7.1 **Ryzodeg® FlexTouch® 100 U/ml Solution for Injection** [Insulin aspart 30 U/ml Insulin degludec 70 U/ml]	➢ Indication: *Treatment of diabetes mellitus in adolescents and children from the age of 2 years.* ➢ Posology: <u>*Paediatric population:*</u> *Ryzodeg® can be used in adolescents and children from the age of 2 years. When changing from another insulin regimen to Ryzodeg®, dose reduction of total insulin needs to be considered on an individual basis in order to minimise the risk of hypoglycaemia. Ryzodeg® should be used with special caution in children 2 to 5 years old because data from the clinical trial indicate that there may be a higher risk for severe hypoglycaemia in children in this age group.*	**NOVO NORDISK PHARMA (MALAYSIA) SDN. BHD.** Menara 1 Sentrum, Level 16 No. 201, Jalan Tun Sambathan 50470 Kuala Lumpur
8.	8.1 **Adcetris 50mg, powder for concentrate for solution for infusion** [Brentuximab Vedotin 50mg]	➢ Indication: *ADCETRIS is indicated for the treatment of adult patients with previously untreated CD30+ Stage IV Hodgkin lymphoma (HL), in combination with doxorubicin, vinblastine and dacarbazine.* ➢ Posology: ***Previously Untreated HL*** ***The recommended dose in combination with chemotherapy (doxorubicin [A], vinblastine [V] and dacarbazine [D] [AVD]) is 1.2 mg/kg administered as an intravenous infusion over 30 minutes on days 1 and 15 of each 28-day cycle for 6 cycles (see section Pharmacodynamics).*** ***Primary prophylaxis with growth factor support (G-CSF) is recommended for all patients with previously untreated HL receiving combination therapy beginning with the first dose (see section Warnings and Precautions).*** ***Refer to the package insert (PI) of chemotherapy agents***	**TAKEDA MALAYSIA SDN BHD** Unit TB-L-13-1, Level 13 Tower B Plaza 33 No.1 Jalan Kemajuan, Seksyen 13 46200 Petaling Jaya, Selangor

			given in combination with Adcetris for patients with previously untreated HL. *HL at increased risk of relapse or progression* *The recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks.* *Adcetris treatment should start following recovery from ASCT based on clinical judgment. These patients should receive up to 16 cycles (see section Pharmacodynamics).* *Relapsed or refractory HL* *The recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks.* *The recommended starting dose for the retreatment of patients who have previously responded to treatment with Adcetris is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Alternatively, treatment may be started at the last tolerated dose (see section Pharmacodynamics).* *Treatment should be continued until disease progression or unacceptable toxicity (see section Warnings and Precautions).* *Patients who achieve stable disease or better should receive a minimum of 8 cycles and up to a maximum of 16 cycles (approximately 1 year) (see section Pharmacodynamics).* *Relapsed or refractory sALCL* *The recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks.* *The recommended starting dose for the retreatment of patients who have previously responded to treatment with ADCETRIS is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks. Alternatively, treatment may be started at the last tolerated dose (see section Pharmacodynamics).* *Treatment should be continued until disease progression or unacceptable toxicity (see section Wanings and Precautions).* *Patients who achieve stable disease or better should receive a minimum of 8 cycles and up to a maximum of 16 cycles (approximately 1 year) (see section Pharmacodynamics).*	

		CTCL *The recommended dose is 1.8 mg/kg administered as an intravenous infusion over 30 minutes every 3 weeks.* *Patients with CTCL should receive up to 16 cycles (see section Pharmacodynamics).* **For full details on dose adjustment and special patient population, please refer to the package insert.*	