Maklumat tambahan indikasi

Tahun 2022

Products Approved For Additional Indication (DCA 377 – 6 Oktober 2022)

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
1.	COMIRNATY Concentrate for Dispersion for Injection COMIRNATY Concentrate for Dispersion for Injection COMIRNATY (Tris/Sucrose) 30 mcg Solution for Injection [BNT162b2 1 dose (0.3ml) contains 30 µg of modRNA [Single-stranded, 5'-capped mRNA formulated as an RNA-lipid nanoparticle (LNP) of nucleoside-modified mRNA (modRNA)]	**POSOLOGY** : **Primary vaccination course** Individuals 12 years of age and older Comirnaty is administered intramuscularly after dilution as a course of 2 doses (0.3 mL each). It is recommended to administer the second dose 3 weeks after the first dose. Severely immunocompromised aged 12 years and older A third primary course dose may be administered intramuscularly at least 28 days after the second dose to individuals who are severely immunocompromised. **Booster dose** A booster dose of Comirnaty should be administered intramuscularly at least 6 months after the primary course with Comirnaty in individuals **12 years** of age and older. **Comirnaty may also be given as a booster in individuals 18 years of age and older who have received a primary course comprised of another mRNA vaccine (mRNA - 1273) or adenoviral vector vaccine (Ad26.CoV2 vaccine and ChAdOx1 nCoV-19 vaccine). The dosing interval for the heterologous booster dose is the same as that authorized for a booster dose of the vaccine used for primary vaccination.** The decision when and for whom to implement a third dose of Comirnaty should be made based on available vaccine effectiveness and safety data.	**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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		Paediatric population There is a paediatric formulation available for children 5 to 11 years of age (i.e. 5 to less than 12 years of age). For details, please refer to the Package Insert for COMIRNATY 10 mcg Concentrate for Dispersion for Injection. The safety and efficacy of Comirnaty in children aged less than 5 years have not yet been established. Elderly population No dosage adjustment is required in elderly individuals ≥65 years of age.	

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<tr><td>2.</td><td>Opdivo 10mg/ml, Concentrate for solution for infusion

[Nivolumab 10mg/ml]</td><td>
INDICATION:

OPDIVO in combination with cabozantinib is indicated for the first-line treatment of adult patients with advanced renal cell carcinoma.

POSOLOGY :

<u>OPDIVO as monotherapy</u>

The recommended dose of OPDIVO is 3 mg/kg administered intravenously over 30 minutes every 2 weeks.

<u>OPDIVO in combination with cabozantinib (tablets)</u>

<u>Renal cell carcinoma</u>

The recommended dose is nivolumab administered intravenously at either 240 mg every 2 weeks or 480 mg every 4 weeks in combination with 40 mg cabozantinib (tablets) administered orally every day.

Table 1: Recommended doses and infusion times for intravenous administration of nivolumab in combination with oral administration of cabozantinib (tablets) for RCC
<table>
<tr><td></td><td>Combination phase</td></tr>
<tr><td>Nivolumab</td><td>240 mg every 2 weeks over 30 minutes or 480 mg every 4 weeks over 30 minutes</td></tr>
<tr><td>Cabozantinib (tablets)</td><td>40 mg once daily</td></tr>
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<u>Duration of treatment</u>

Treatment should be continued as long as clinical benefit is observed or until treatment is
</td><td>DKSH MALAYSIA SDN. BHD.
B-11-01, The Ascent, Paradigm,
No. 1, Jalan SS7/26A, Kelana Jaya,
47301 Petaling Jaya, Selangor.</td></tr>
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no longer tolerated by the patient.

For adjuvant therapy, the maximum treatment duration with OPDIVO is 12 months.

For OPDIVO in combination with cabozantinib, OPDIVO should be continued until disease progression, unacceptable toxicity, or up to 24 months in patients without disease progression. Cabozantinib should be continued until disease progression or unacceptable toxicity. Refer to the package insert for cabozantinib.

Dose escalation or reduction is not recommended for OPDIVO as monotherapy or in combination with other therapeutic agents. Dosing delay or discontinuation may be required based on individual safety and tolerability. Guidelines for permanent discontinuation or withholding of doses are described in Table 2. Detailed guidelines for the management of immune-related adverse reactions are described in section 4.4.When nivolumab is administered in combination with other therapeutic agents, refer to the package insert of these other combination therapeutic agents regarding dosing.

Table 2: Recommended treatment modifications for OPDIVO or OPDIVO in combination
<table>
<tr><th>Immune-related adverse reaction</th><th>Severity</th><th>Treatment modification</th></tr>
<tr><td rowspan="2">Immune-related pneumonitis</td><td>Grade 2 pneumonitis</td><td>Withhold dose(s) until symptoms resolve, radiographic abnormalities improve, and management with corticosteroids is complete</td></tr>
<tr><td>Grade 3 or 4 pneumonitis</td><td>Permanently discontinue treatment</td></tr>
<tr><td>Immune- related colitis</td><td>Grade 2 or 3 diarrhoea or colitis</td><td>Withhold dose(s) until symptoms resolve and management with corticosteroids, if needed, is</td></tr>
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No.	Product [Active Ingredient]	Additional Indication			Product Registration Holder (PRH)
				complete	
			Grade 4 diarrhoea or colitis	Permanently discontinue treatment	
		Immune-related hepatitis **NOTE: for RCC patients treated with OPDIVO in combination with cabozantinib with liver enzyme elevations, see dosing guidelines following this table.**	Grade 2 elevation in aspartate aminotransferase (AST), alanine aminotransferase (ALT), or total bilirubin	Withhold dose(s) until laboratory values return to baseline and management with corticosteroids, if needed, is complete	
			Grade 3 or 4 elevation in AST, ALT, or total bilirubin	Permanently discontinue treatment	
		Immune-related nephritis and renal dysfunction	Grade 2 or 3 creatinine elevation	Withhold dose(s) until creatinine returns to baseline and management with corticosteroids is complete	
			Grade 4 creatinine elevation	Permanently discontinue treatment	
		Immune-related endocrinopathies	Symptomatic Grade 2 or 3 hypothyroidism, hyperthyroidism, hypophysitis Grade 2 adrenal insufficiency Grade 3 diabetes	Withhold dose(s) until symptoms resolve and management with corticosteroids (if needed for symptoms of acute inflammation) is complete. Treatment should be continued in the presence of hormone replacement therapy[a] as long as no symptoms are present	

No.	Product [Active Ingredient]	Additional Indication			Product Registration Holder (PRH)
			Grade 4 hypothyroidism, hyperthyroidism, hypophysitis Grade 3 or 4 adrenal insufficiency Grade 4 diabetes	Permanently discontinue treatment	
		Immune-related skin adverse reactions	Grade 3 rash	Withhold dose(s) until symptoms resolve and management with corticosteroids is complete	
			Grade 4 rash	Permanently discontinue treatment	
			Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN)	Permanently discontinue treatment	
		Immune-related myocarditis	Grade 2 myocarditis	Withhold dose(s) until symptoms resolve and management with corticosteroids is complete[b]	
			Grade 3 or 4 myocarditis	Permanently discontinue treatment	
		Other immune-related adverse reactions	Grade 3 (first occurrence)	Withhold dose(s)	

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	Grade 4 or recurrent Grade 3; persistent Grade 2 or 3 despite treatment modification; inability to reduce corticosteroid dose to 10 mg prednisone or equivalent per day	Permanently discontinue treatment

Note: Toxicity grades are in accordance with National Cancer Institute Common Terminology Criteria for Adverse Events Version 4.0 (NCI-CTCAE v4).

a Recommendation for the use of hormone replacement therapy is provided in section 4.4.

b The safety of re-initiating nivolumab therapy in patients previously experiencing immune-related myocarditis is not known.

OPDIVO **as monotherapy or in combination with other therapeutic agents** should be permanently discontinued for:

• Grade 4 or recurrent Grade 3 adverse reactions;

• Persistent Grade 2 or 3 adverse reactions despite management

OPDIVO in combination with cabozantinib in RCC

When OPDIVO is used in combination with cabozantinib, the above treatment modifications in Table 2 also apply to the OPDIVO component. In addition, for liver enzyme elevations, in patients with RCC being treated with OPDIVO in combination with cabozantinib:

- **If ALT or AST > 3 times ULN but ≤ 10 times ULN without concurrent total bilirubin ≥ 2 times ULN, both OPDIVO and cabozantinib should be withheld until these adverse reactions recover to Grades 0-1. Corticosteroid therapy may be considered. Rechallenge with a single medicine or rechallenge with both medicines after recovery may be considered. If rechallenging with cabozantinib, refer to cabozantinib package insert.**
- **If ALT or AST > 10 times ULN or > 3 times ULN with concurrent total bilirubin ≥ 2**

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
		times ULN, both OPDIVO and cabozantinib should be permanently discontinued and corticosteroid therapy may be considered. <u>Special populations</u> Paediatric population The safety and efficacy of OPDIVO in children below 18 years of age have not been established. No data are available. Elderly No dose adjustment is required for elderly patients (≥ 65 years). Renal impairment Based on the population pharmacokinetic (PK) results, no dose adjustment is required in patients with mild or moderate renal impairment. Data from patients with severe renal impairment are too limited to draw conclusions on this population. Hepatic impairment Based on the population PK results, no dose adjustment is required in patients with mild hepatic impairment. Data from patients with moderate or severe hepatic impairment are too limited to draw conclusions on these populations. OPDIVO must be administered with caution in patients with moderate (total bilirubin > 1.5x to 3x the upper limit of normal [ULN] and any AST) or severe (total bilirubin > 3x ULN and any AST) hepatic impairment. <u>Method of administration</u> OPDIVO is for intravenous use only. It is to be administered as an intravenous infusion over a period of 30 minutes. The infusion must be administered through a sterile, non-pyrogenic, low protein binding in-line filter with a pore size of 0.2-1.2 µm. OPDIVO must not be administered as an intravenous push or bolus injection. The total dose of OPDIVO required can be infused directly as a 10 mg/mL solution or can be diluted to as low as 1 mg/mL with sodium chloride 9 mg/mL (0.9%) solution for injection or glucose 50 mg/mL (5%) solution for injection.	

No.	Product [Active Ingredient]	Additional Indication	Product Registration Holder (PRH)
3.	Praluent 150 mg solution for injection in pre-filled syringe Praluent 75 mg solution for injection in pre-filled syringe Praluent 150 mg solution for injection in pre-filled pen Praluent 75 mg solution for injection in pre-filled pen [Alirocumab 150mg/ml] [Alirocumab 75mg/ml] [Alirocumab 150mg/ml] [Alirocumab 75mg/ml]	**INDICATION:** <u>Established atherosclerotic cardiovascular disease</u> Praluent is indicated in adults with established atherosclerotic cardiovascular disease to reduce cardiovascular risk by lowering LDL-C levels, as an adjunct to correction of other risk factors: - in combination with the maximum tolerated dose of a statin with or without other lipid-lowering therapies or, - alone or in combination with other lipid-lowering therapies in patients who are statin-intolerant, or for whom a statin is contraindicated. For study results with respect to effects on LDL-C, cardiovascular events and populations studied see section 5.1.	**SANOFI-AVENTIS (MALAYSIA) SDN. BHD.** Unit TB-18-1, Level 18, Tower B, Plaza 33, No.1, Jalan Kemajuan, Seksyen 13, 46200 Petaling Jaya, Selangor.

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4.	Imbruvica 140mg Capsules [Ibrutinib 140mg]	**INDICATION :** IMBRUVICA as a single agent is indicated for the treatment of adult patients with Waldenström's macroglobulinaemia (WM) who have received at least one prior therapy, or in first line treatment for patients unsuitable for chemo-immunotherapy. **POSOLOGY :** The recommended dose for the treatment of WM, either as a single agent or in combination is 420 mg (three capsules) once daily.	**JOHNSON & JOHNSON SDN. BHD.** Level 8, The Pinnacle, Persiaran Lagoon, Bandar Sunway, 46150 Petaling Jaya, Selangor.