Maklumat tambahan indikasi
Year 2020
Products Approved For Additional Indication (DCA 348 – 3 September 2020)

	PRODUCT (ACTIVE INGREDIENT)	ADDITIONAL INDICATION	MARKETING AUTHORIZATION HOLDER
1.	1.1 **Opdivo 10mg/ml, Concentrate for solution for infusion** [Nivolumab 10mg/ml]	➢ Indication: ***Renal Cell Carcinoma (RCC)*** ***OPDIVO as monotherapy, is indicated for the treatment of adult patients with advanced or metastatic renal cell carcinoma (RCC) who have received prior anti-angiogenic therapy.*** ➢ Posology: *Treatment must be initiated and supervised by physicians experienced in the treatment of cancer.* • *Posology* *The recommended dose of OPDIVO is 3 mg/kg administered intravenously over 60 minutes every 2 weeks. Treatment should be continued as long as clinical benefit is observed or until treatment is no longer tolerated by the patient.* *Dose escalation or reduction is not recommended. 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 1. Detailed guidelines for the management of immune-related adverse reactions are described in section 4.4.*	**DKSH MALAYSIA SDN BHD** B-11-01, The Ascent, Paradigm No. 1, Jalan SS7/26A, Kelana Jaya 47301, Petaling Jaya, Selangor

Table 1: Recommended treatment modifications for OPDIVO

Immune-related adverse reaction	***Severity***	***Treatment modification***
Immune-related pneumonitis	*Grade 2 pneumonitis*	*Withhold dose(s) until symptoms resolve, radiographic abnormalities improve, and management with corticosteroids is complete*
	Grade 3 or 4 pneumonitis	*Permanently discontinue treatment*
Immune- related colitis	*Grade 2 or 3 diarrhoea or colitis*	*Withhold dose(s) until symptoms resolve and management with corticosteroids, if needed, is complete*
	Grade 4 diarrhoea or colitis	*Permanently discontinue treatment*
Immune-related hepatitis	*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*	*Withhold dose(s) until symptoms resolve and management with*

			hypothyroidism, hyperthyroidism, hypophysitis, Grade 2 adrenal insufficiency Grade 3 diabetes *Grade 4 hypothyroidism, hyperthyroidism, hypophysitis* *Grade 3 or 4 adrenal insufficiency* *Grade 4 diabetes*	*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* *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 (see section 4.4)*	
		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)*	
			Grade 4 or recurrent Grade 3; persistent Grade 2 or 3	*Permanently discontinue treatment*	

		despite treatment modification; inability to reduce corticosteroid dose to 10 mg prednisone or equivalent per day	
		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.***	
2.	2.1 **Xigduo XR Tablet 10/1000mg** [Dapagliflozin propanediol 10mg & metformin hydrochloride 1000mg] 2.2 **Xigduo XR Tablet 5/1000mg** [Dapagliflozin propanediol 5mg & metformin hydrochloride 1000mg] 2.3 **Xigduo XR Tablet 10/500mg** [Dapagliflozin propanediol 10mg & metformin hydrochloride 500mg]	➢ *Indication:* *Reduction in risk of hospitalization for heart failure* *Dapagliflozin is indicated to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular disease (CVD) or multiple cardiovascular (CV) risk factors (see Section 5.1 Pharmacodynamic properties – Clinical trials and 4.4 Special warnings and precautions for use for available data on the combination therapy).* *[Note: The approved indication also revised (repositioning of the wording) as follows:* *Xigduo XR is indicated in adults with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control when treatment with both dapagliflozin and metformin is appropriate]* ➢ Posology: *The dosage of antihyperglycaemic therapy with XIGDUO XR should be individualised on the basis of the patient's current regimen, effectiveness, and tolerability while not exceeding the maximum recommended dose of dapagliflozin 10 mg and metformin extended-release 2000 mg.*	**ASTRAZENECA SDN. BHD.** Level 12, Surian Tower, 1, Jalan PJU 7/3, Mutiara Damansara, 47810 Petaling Jaya, Selangor

		XIGDUO XR should generally be administered once daily with the evening meal. The following tablet strengths are available: • *XIGDUO XR 10/500 (dapagliflozin 10 mg/metformin HCl extended-release 500 mg)* • *XIGDUO XR 10/1000 (dapagliflozin 10 mg/metformin HCl extended-release 1000 mg)* • *XIGDUO XR 5/1000 (dapagliflozin 5 mg/metformin HCl extended-release 1000 mg)* *Initial therapy* *If therapy with a combination tablet containing dapagliflozin and metformin is considered appropriate, the recommended dose of dapagliflozin is 10 mg once daily. The recommended starting dose of metformin extended-release is 500 mg once daily, which can be titrated to 2000 mg once daily. The maximum dose of XIGDUO XR is dapagliflozin 10 mg/metformin extended-release 2000 mg taken as two 5 mg/1000 mg tablets once daily.* *Add on combination therapy* *In patients treated with metformin, the dose of XIGDUO XR should provide metformin at the dose already being taken, or the nearest therapeutically appropriate dose. Following a switch from metformin immediate-release to metformin extended-release, glycaemic control should be monitored closely and dosage adjustments made accordingly.* *When dapagliflozin is used as an add-on therapy with insulin or an insulin secretagogue, a lower dose of insulin or an insulin secretagogue may be considered to reduce the risk of hypoglycaemia.* *No studies have been performed specifically examining the safety and efficacy of XIGDUO XR in patients previously treated with other antihyperglycaemic agents and switched to XIGDUO XR. Any change in therapy of type 2 diabetes should be undertaken with care and appropriate monitoring as changes in glycaemic control can occur.* *If no adequate strength of Xigduo XR is available, individual mono-*	

components should be used instead of the fixed dose combination.

Patients should be informed that XIGDUO XR tablets must be swallowed whole and never crushed, cut, or chewed. Occasionally, the inactive ingredients of XIGDUO XR will be eliminated in the faeces as a soft, hydrated mass that may resemble the original tablet.

Renal Impairment
An eGFR should be assessed before initiation of treatment with metformin containing products and at least annually thereafter. In patients at an increased risk of further progression of renal impairment and in the elderly, renal function should be assessed more frequently, e.g.

*eGFR mL/min/1.73 m^2 **	*Metformin*	*Dapagliflozin*
60-89	*Maximum daily dose of metformin extended-release is 2000 mg. Dose reduction may be considered in relation to declining renal function.*	*Maximum total daily dose is 10 mg.*
45-59	*Maximum daily dose is 2000 mg. The starting dose is at most half of the maximum dose.*	*Maximum total daily dose is 10 mg.*
30-44	*Maximum daily dose is 1000 mg. The starting dose is at most half of the maximum dose.*	*Dapagliflozin is not recommended.*
<30	*Metformin is contraindicated.*	*Dapagliflozin is not recommended.*

every 3-6 months.

The maximum daily dose of metformin should preferably be divided into 2-3 daily doses. Factors that may increase the risk of lactic

		acidosis should be reviewed before considering initiation of metformin in patients with eGFR <60 ml/min. *If no adequate strength of XIGDUO XR is available, individual monocomponents should be used instead of the fixed dose combination.* ** GFR was originally used to establish these dosing categories based on renal function, all values were normalized to an average surface area (size) of 1.73 m^2. As eGFR is considered a reasonable estimate of GFR and is more widely used in clinical practice, treatment recommendations in this prescribing information are based on eGFR.* *Hepatic Impairment* *Since impaired hepatic function has been associated with some cases of lactic acidosis in patients taking metformin, XIGDUO XR should not be used in patients with clinical or laboratory evidence of hepatic impairment (see section 4.4 Special Warnings and Precautions for Use – Use in hepatic impairment).* *Paediatric and Adolescent* *Safety and effectiveness of XIGDUO XR in paediatric and adolescent patients have not been established.* *Use in the Elderly* *Because metformin is eliminated by the kidney, and because elderly patients are more likely to have decreased renal function, XIGDUO XR should be used with caution as age increases.*	
3.	3.1 **OFEV Soft Capsules 100 mg** [Nintedanib esilate 120.40 mg (equivalent to 100 mg of nintedanib free base)] 3.2 **OFEV Soft Capsules 150 mg** [Nintedanib esilate 180.60 mg (equivalent to 150 mg of nintedanib free base)]	➢ Indication*:* *OFEV is indicated to slow the rate of decline in pulmonary function in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD).*	**Boehringer Ingelheim (Malaysia) Sdn. Bhd.** Suite 15-5 Level 15, Wisma UOA Damansara II, No. 6, Jalan Changkat Semantan, Damansara Heights, 50490 Kuala Lumpur

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<td>4.</td>
<td>4.1 Maviret (Glecaprevir 100mg/ Pibrentasvir 40mg) Film Coated Tablets
[Glecaprevir 100mg and Pibrentasvir 40mg]</td>
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➢ Indication:

Maviret is indicated for the treatment of chronic hepatitis C virus (HCV) infection in adolescents aged 12 to <18 years.

➢ Posology:

• Recommended dosage

Maviret is glecaprevir and pibrentasvir fixed-dose combination tablets.

The recommended oral dosage of Maviret is 300 mg/120 mg (three 100 mg glecaprevir/40 mg pibrentasvir tablets) once daily at the same time with food.

Patients should be instructed to swallow tablets whole with food and not to chew, crush or break the tablets as it may alter the bioavailability of the agents.

Tables 1 and 2 provide the recommended Maviret treatment duration based on the patient population in HCV mono-infected and HCV/HIV-1 co-infected patients with compensated liver disease (with or without cirrhosis) and with or without renal impairment including patients receiving dialysis.

Table 1. Recommended Maviret treatment duration for patients without prior HCV therapy
<table>
<tr><td rowspan="2">Patient Population</td><td colspan="2">Recommended Treatment Duration</td></tr>
<tr><td>No Cirrhosis</td><td>Compensated Cirrhosis (Child Pugh A)</td></tr>
<tr><td>GT 1-6</td><td>8 weeks</td><td><u>8 weeks</u></td></tr>
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</td>
<td>Abbvie Sdn. Bhd.,
9th Floor Menara Lien Hoe, No.8, Persiaran Tropicana,
Tropicana Golf & Country Resort,
47410 Petaling Jaya,
Selangor</td>
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Table 2. Recommended Maviret treatment duration for patients who failed prior therapy with peg-IFN + ribavirin +/- sofosbuvir, or sofosbuvir + ribavirin

Patient Population	*Recommended Treatment Duration*	
	No Cirrhosis	*Compensated Cirrhosis (Child Pugh A)*
GT 1, 2, 4-6	***8 weeks***	***12 weeks***
GT 3	***16 weeks***	***16 weeks***

- ***For patients who failed prior therapy with an NS3/4A- and/or an NS5A-inhibitor, see WARNINGS AND PRECAUTIONS.***

[Warnings and Precautions:
<u>Patients who failed a prior regimen containing an NS5A- and/or an NS3/4A-inhibitor</u>
Genotype 1-infected (and a very limited number of genotype 4-infected) patients with prior failure on regimens that may confer resistance to glecaprevir/pibrentasvir were studied in the MAGELLAN-1 study. The risk of failure was, as expected, highest for those exposed to both classes. A resistance algorithm predictive of the risk for failure by baseline resistance has not been established. Accumulating double class resistance was a general finding for patients who failed re-treatment with glecaprevir/pibrentasvir in MAGELLAN-1. No re-treatment data is available for patients infected with genotypes 2, 3, 5 or 6. Maviret is not recommended for the re-treatment of patients with prior exposure to NS3/4Aand/or NS5A-inhibitors.]

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Dosing in special populations
<u>Pediatric Use</u>
No dose adjustment of Maviret is required in adolescents aged 12 to <18 years. The safety and efficacy of Maviret in children aged less than 12 years have not yet been established. No data are available.
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<td>5.</td>
<td>5.1 Dexilant Delayed Release Capsules 60mg
[dexlansoprazole 60mg]

5.2 Dexilant Delayed Release Capsules 30mg
[dexlansoprazole 30mg]</td>
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➢ Indication:

• Healing of Erosive Esophagitis
DEXILANT is indicated in patients 12 years of age and older for healing of all grades of erosive esophagitis (EE) for up to 8 weeks

• Maintenance of Healed Erosive Esophagitis
DEXILANT is indicated for maintaining healing of erosive esophagitis and relief of heartburn for up to 4 months in adolescents 12 to 17 years of age and up to 6 months in adults.

➢ Posology:

DEXILANT® is available as capsules in 30 mg and 60 mg strengths for adult use and patients 12 years of age and older. Directions for use in each indication are summarized in Table 9.

<table>
<tr><th>Indication</th><th>Recommended dose</th><th>Frequency</th></tr>
<tr><td>Healing erosive esophagitis</td><td>60mg</td><td>Once daily for up to 8 weeks</td></tr>
<tr><td>Maintenance of Healed erosive esophagitis and relief of heartburn</td><td>30mg*</td><td>Once daily**</td></tr>
<tr><td>Symptomatic Non-Erosive GERD</td><td>30mg</td><td>Once daily for 4 weeks</td></tr>
</table>
</td>
<td>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</td>
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		** In patients who had moderate or severe erosive esophagitis, a maintenance dose of 60mg may be used.* *** Controlled studies did not extend beyond 6 months in adults, and beyond 4 months in adolescents 12 to 17 years of age.* *No dose adjustment for DEXILANT® is necessary for patients with mild hepatic impairment (Child-Pugh Class A). DEXILANT® 30mg should be considered for patients with moderate hepatic impairment (Child-Pugh Class B). No studies have been conducted in patients with severe hepatic impairment (Child-Pugh Class C).* *No dosage adjustment is necessary for elderly patients or for patients with renal impairment.* *Patients should use the lowest dose and shortest duration PPI therapy appropriate to the condition being treated.* *Missed dose* *If a capsule is missed at its usual time, it should be taken as soon as possible. But if it is too close to the time of the next dose, only the prescribed dose should be taken at the appointed time. A double dose should not be taken.*	
6.	6.1 **Revolade Film-Coated Tablet 50mg** [Eltrombopag Olamine 50mg] 6.2 **Revolade Film-Coated Tablet 25mg** [Eltrombopag Olamine 25mg]	➢ Indication: *Revolade is indicated in combination with standard immunosuppressive therapy for the first-line treatment of adult and adolescent patients 12 years and older with severe aplastic anaemia (first-line SAA).* ➢ *Posology:* *<u>First-line severe aplastic anaemia</u>* *Initiate Revolade concurrently with standard immunosuppressive therapy.* *<u>Initial dose regimen:</u>* *The recommended initial dose regimen is listed in Table 3. Do not exceed the initial dose of Revolade.*	**NOVARTIS CORPORATION (MALAYSIA) SDN. BHD.** Level 22, Tower B, Plaza 33 No. 1, Jalan Kemajuan, Seksyen 13 46200 Petaling Jaya, Selangor

Table 3. Recommended Initial Revolade Dose Regimen in the First-Line Treatment Severe Aplastic Anemia pivotal study

Age	*Dose regimen*
Patients 12 years and older	*150mg once daily for 6 months*

For patients with severe aplastic anaemia of Asian ancestry (such as Chinese, Japanese, Taiwanese, Korean, or Thai) or those with mild, moderate or severe hepatic impairment (Child-Pugh Class A, B, C), decrease the initial Revolade dose by 50 % as listed in Table 4.

If baseline ALT or AST levels are > 6 x ULN, do not initiate Revolade until transaminase levels are < 5 x ULN. Determine the initial dose for these patients based on Table 3 or Table 4.

Table 4. Recommended Initial Revolade Dose Regimen for Patients if Asian Ancestry or Those with Mild, Moderate, or Severe Hepatic Impairment (Child-Pugh Class A, B, C) in the First–Line Treatment of Severe Aplastic Anemia

Age	*Dose regimen*
Patients 12 years and older	*75mg once daily for 6 months*

Table 5. Dose of standard immunosuppressive therapy administered with Revolade in the first-line SAA pivotal study

Agent	*Dose administered in the pivotal study*
Horse antithymocyte globulin (h-ATG)	*40 mg/kg/day, based on actual body weight, administered intravenously on Days 1 to 4 of the 6-month treatment period.*
Cyclosporine (therapeutic dose for 6*	*<u>Patients aged 12 years and older</u>:*

months, from Day 1 to Month 6, adjusted to obtain a target therapeutic trough level between 200 and 400 micrograms/L)	*3 mg/kg, based on actual body weight, orally every 12 hours (total daily dose of 6 mg/kg/day) for 6 months, starting on Day 1.* *Patients >20 years of age with a body mass index >35 or patients aged 12 to 20 years with a body mass index >95th percentile:* *3 mg/kg, based on adjusted body weight#, orally every 12 hours (total daily dose of 6 mg/kg/day) for 6 months, starting on Day 1.*
Cyclosporine (maintenance dose, from Month 6 to Month 24)	*<u>For patients who achieve a hematologic response at 6 months</u>:* *2 mg/kg/day administered orally at a fixed dose for an additional 18 months.*
** Dose of cyclosporine may need to be adjusted to achieve the above recommended target trough levels when cyclosporine is used concomitantly with other therapies; refer to the appropriate cyclosporine prescribing information.* *# Calculated as the midpoint between the ideal body weight and actual body weight.*	

*<u>Monitoring and dose adjustment for Revolade</u>**:***
Perform clinical hematology and liver tests regularly throughout therapy with Revolade.

Table 6. Dose adjustments of Revolade for Elevated Platelet Counts in the First-line Treatment of Severe Aplastic Anemia

Platelet count result	*Dose adjustment or response*
>200 x 10^9/L to ≤ 400 x 10^9/L	*Decrease the daily dose by 25 mg every 2 weeks to lowest dose that maintains platelet count ≥ 50 x 10^9/L.*
>400 x 10^9/L	*Discontinue Revolade for one week.* *Once the platelet count is <200 x 10^9/L, reinitiate Revolade at a daily dose reduced by 25 mg.*

Table 7 summarizes the recommendations for dose interruption, reduction, or discontinuation of Revolade in the management of elevated liver transaminase levels and thromboembolic events.

Table 7. Recommended dose modification for Revolade for ALT and AST Elevations and Thromboembolic Events.

Event	*Recommendation*
ALT or AST elevations	*<u>Increase in ALT or AST > 6 x ULN</u>* *Discontinue Revolade. Once ALT or AST is < 5 x ULN, reinitiate Revolade at the same dose.* *<u>Increase in ALT or AST > 6 x ULN after reinitiating Revolade</u>* *Discontinue Revolade and monitor ALT or AST at*

			least every 3 to 4 days. Once ALT or AST is < 5 x ULN, reinitiate Revolade at a daily dose reduced by 25mg compared to previous dose. *<u>If ALT or AST returns to > 6 x ULN on the reduced dose</u>* *Reduce the daily dose of Revolade by 25 mg until ALT or AST is <5 x ULN.*	
			Thromboembolic events (e.g, deep vein thrombosis, pulmonary embolus, stroke, myocardial infarction)	*Discontinue Revolade but remain on horse antithymocyte globulin (h-ATG) and cyclosporine.*	
			The total duration of Revolade treatment is 6 months.		