For PPB use only	
1.17	**Product Information**
1.17.1	**Summary Product Characteristics (SPC)**

1. Name of the medicinal product

Dapagliflozin 5mg (as immediate release), Vildagliptin 100mg & Metformin HCl 1000mg (as extended release) Tablets

2. Qualitative and quantitative composition

Each film coated tablet contains

Dapagliflozin Propanediol Monohydrate

Equivalent to Dapagliflozin 5mg

(As immediate release)

Vildagliptin 100mg

(As extended release)

Metformin Hydrochloride BP 1000mg

(As extended release)

S.No.	Ingredient	Spec.	Overages	Qty. per tablet in mg	Qty. for 100,000 tablets (kg)
Dapagliflozin Part					
1.	Dapagliflozin Propanediol Monohydrate	IHS	Nil	6.15	0.615
2.	Maize Starch	BP	Nil	22.50	2.250
3.	Lactose	BP	Nil	87.95	8.795
4.	Colloidal Anhydrous Silica	BP	Nil	1.40	0.140
5.	Magnesium Stearate	BP	Nil	2.00	0.200
Vildagliptin & Metformin Hydrochloride Part					
1.	Metformin Hydrochloride	BP	Nil	1000.00	100.00
2.	Cetostearyl Alcohol	BP	Nil	50.00	5.000
3.	Ethylcellulose N50	BP	Nil	20.00	2.000
4.	Povidone K30	BP	Nil	20.00	2.000
5.	*Dichloromethane	BP	Nil	---	17.000
	Lubrication				
6.	Hypromellose K4M	BP	Nil	35.50	3.550

7.	Hypromellose K100M	BP	Nil	35.50	3.550
8.	Vildagliptin	IHS	Nil	100.00	10.00
9.	Purified Talc	BP	Nil	5.00	0.500
10.	Colloidal Anhydrous Silica	BP	Nil	4.00	0.400
11.	Magnesium Stearate	BP	Nil	10.00	1.000
	Coating				
12.	Hypromellose E15	BP	Nil	29.90	2.990
13.	Titanium Dioxide	BP	Nil	5.00	0.500
14.	Purified Talc	BP	Nil	5.00	0.500
15.	Tartrazine Yellow	IHS	Nil	0.10	0.010
16.	*Isopropyl Alcohol	BP	Nil	--	25.000
17.	*Dichloromethane	BP	Nil	--	25.000

* Represents solvents, will not be present in the finished Product.

BP – British Pharmacopoeia & IHS – In-House Specification.

3. Pharmaceutical form

Tablet: A yellow color oblong shape biconvexed film coated tablet, scored in the middle on one side and plain on other side of the tablet.

4. Clinical particulars

4.1 Therapeutic indications

Dapamet-V XR is indicated in adults aged 18 years and older with type 2 diabetes mellitus as an adjunct to diet and exercise to improve glycaemic control, in patients inadequately controlled on their maximally tolerated dose of metformin alone, in combination with other glucose-lowering medicinal products, including insulin, in patients inadequately controlled with metformin and these medicinal products and in patients already being treated with the combination of dapagliflozin and metformin as separate tablets. Vildagliptin is indicated in the treatment of type 2 diabetes mellitus. Vildagliptin is indicated in the treatment of adult patients who are unable to achieve sufficient glycaemic control at their maximally tolerated dose of oral metformin alone.

4.2 Posology and method of administration

The recommended dose is one tablet twice daily or as directed by physician. Not recommended for children

below 18 years of age.
Mode of Administration: Oral

4.3 Contraindications

Dapamet-V XR is contraindicated in patients with hypersensitivity to the active substances or to any of the excipients listed, any type of acute metabolic acidosis (such as lactic acidosis, diabetic ketoacidosis), diabetic pre-coma and severe renal failure (GFR < 30 mL/min).

4.4 Special warnings and precautions for use

Lactic acidosis, a very rare but serious metabolic complication, most often occurs at acute worsening of renal function or cardiorespiratory illness or sepsis. Metformin accumulation occurs at acute worsening of renal function and increases the risk of lactic acidosis. In case of dehydration (severe diarrhoea or vomiting, fever or reduced fluid intake), Caution should be exercised in patients for whom a dapagliflozin-induced drop in blood pressure could pose a risk, such as patients with known cardiovascular disease, patients on anti-hypertensive therapy with a history of hypotension or elderly patients. Vildagliptin is not a substitute for insulin in insulin-requiring patients and should not be used in patients with type 1 diabetes.

4.5 Interaction with other medicinal products and other forms of interaction

This medicinal product may add to the diuretic effect of thiazide and loop diuretics and may increase the risk of dehydration and hypotension. Insulin and insulin secretagogues, such as sulphonylureas, cause hypoglycaemia. Therefore, a lower dose of insulin or an insulin secretagogue may be required to reduce the risk of hypoglycaemia when used in combination with Dapagliflozin. Cationic substances that are eliminated by renal tubular secretion (e.g. cimetidine) may interact with metformin by competing for common renal tubular transport systems. Alcohol intoxication is associated with an increased risk of lactic acidosis, particularly in the case of fasting, malnutrition or hepatic impairment due to the metformin active substance of this medicinal product. Consumption of alcohol and medicinal products containing alcohol should be avoided. Vildagliptin has a low potential for interactions with co-administered medicinal products.

4.6 Fertility, Pregnancy and lactation

The use of this medicinal product is not recommended during pregnancy and lactation.

4.7 Effects on ability to drive and use machines

Dapamet-V XR has no or negligible influence on the ability to drive and use machines. Patients should be alerted to the risk of hypoglycaemia when this medicinal product is used in combination with other glucose-lowering medicinal products known to cause hypoglycaemia.

4.8 Undesirable effects

Urinary tract infection, Dizziness, Constipation, Dry mouth, Rash & Back pain.

4.9 Overdose

High overdose or concomitant risks of Metformin may lead to lactic acidosis.
Treatment: The most effective method of removing metformin is haemodialysis. However, vildagliptin cannot be removed by haemodialysis, although the major hydrolysis metabolite (LAY 151) can. Supportive management is recommended.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Dapamet-V XR combines two anti-hyperglycaemic medicinal products with different and complementary mechanisms of action to improve glycaemic control in patients with type 2 diabetes: dapagliflozin, a SGLT2 inhibitor, and metformin hydrochloride, a member of the biguanide class. Dapagliflozin is a highly potent (Ki: 0.55 nM), selective and reversible inhibitor of SGLT2. Metformin is a biguanide with anti-hyperglycaemic effects, lowering both basal and postprandial plasma glucose. It does not stimulate insulin secretion and therefore does not produce hypoglycaemia. Vildagliptin acts primarily by inhibiting DPP-4, the enzyme responsible for the degradation of the incretin hormones GLP-1 (glucagon-like peptide-1) and GIP (glucose-dependent insulinotropic polypeptide).

5.2 Pharmacokinetic properties

Absorption: Dapagliflozin was rapidly and well absorbed after oral administration. Maximum dapagliflozin plasma concentrations (Cmax) were usually attained within 2 hours after administration in the fasted state. After an oral dose of metformin, tmax is reached in 2.5 h. Absolute bioavailability of a 500 mg or 850 mg metformin tablet is approximately 50-60% in healthy subjects. After an oral dose, the non-absorbed fraction recovered in faeces was 20-30%. Oral administration in the fasting state, vildagliptin is rapidly absorbed with peak plasma concentrations observed at 1.7 hours

Distribution: Dapagliflozin is approximately 91% protein bound. Protein binding was not altered in various disease states (e.g. renal or hepatic impairment). The mean steady-state volume of distribution of dapagliflozin was 118 litres. Plasma protein binding is negligible. Metformin partitions into erythrocytes. The blood peak is lower than the plasma peak and appears at approximately the same time. The red blood cells most likely represent a secondary compartment of distribution. The mean Vd ranged between 63-276. The plasma protein binding of vildagliptin is low (9.3%) and vildagliptin distributes equally between plasma and red blood cells. The mean volume of distribution of vildagliptin at steady-state after intravenous administration (Vss) is 71 litres, suggesting extravascular distribution.

Biotransformation: Dapagliflozin is extensively metabolised, primarily to yield dapagliflozin 3-O-glucuronide, which is an inactive metabolite. Metformin is excreted unchanged in the urine. No metabolites have been identified in humans. Metabolism is the major elimination pathway for vildagliptin in humans, accounting for 69% of the dose. The major metabolite (LAY 151) is pharmacologically inactive and is the hydrolysis product of the cyano moiety, accounting for 57% of the dose, followed by the amide hydrolysis product (4% of dose).

Elimination: The mean plasma terminal half-life (t1/2) for dapagliflozin was 12.9 hours following a single oral dose of dapagliflozin 10 mg to healthy subjects. The mean total systemic clearance of dapagliflozin administered intravenously was 207 mL/min. Renal clearance of metformin is > 400 mL/min, indicating that metformin is eliminated by glomerular filtration and tubular secretion. Oral administration of [14C] vildagliptin, approximately 85% of the dose was excreted into the urine and 15% of the dose was recovered in the faeces.

5.3 Preclinical safety data

There are no pre-clinical data of relevance to the prescriber.

6. Pharmaceutical particulars

6.1 List of excipients

Maize Starch
Lactose
Colloidal Anhydrous Silica
Magnesium Stearate
Cetostearyl Alcohol
Ethylcellulose N50

Povidone K30

Hypromellose K4M

Hypromellose K100M

Purified Talc

Hypromellose E15

Titanium Dioxide

Tartrazine Yellow

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

24 Months

6.4 Special precautions for storage

Store below 30°C. Protect from light & moisture.

6.5 Nature and contents of container

Commercial Presentation: 4's, 7's, 10's, 14's, 20's, 30's & 100's

3 x 10's (10 tablets are packed in one PVC blister and 3 such PVC blisters are kept in one carton along with package insert).

6.6 Special precautions for disposal and other handling

Not applicable.

7. Marketing authorisation holder and Manufacturing Site Address

Marketing authorisation holder:

Company name: INNOCIA LIFESCIENCES PVT. LTD.,

Address: Block A, No.12, Balaji Nagar, Ambattur, Chennai-600 053

Country: INDIA.

Manufacturing Site:

ATOZ Pharmaceutials Pvt.Ltd.,

No.12, Balaji Nagar, Ambattur, Chennai-600053,

India.

8. Marketing authorisation number(s)

Telephone: 044 26585811, 26585855

Telefax: -

E-Mail: ah@innocialife.com

9. Date of first registration / Renewal of the registration

Date of first Authorization: 18.01.2021

Date of Latest Renewal: Not Applicable

10. Date of revision of the text: Not Applicable

11. Dosimetry (If Applicable): Not Applicable

12. Instructions for preparation of radiopharmaceuticals (If Applicable): Not Applicable