	ATOZ Pharmaceuticals Pvt. Ltd. **Chennai – India.**
Product Name	**Dapamet XR 5mg/1000mg** (Dapagliflozin 5mg & Metformin Hydrochloride 1000mg Extended Release Tablets)
Composition	Each film coated tablets contains Dapagliflozin Propanediol Monohydrate Equivalent to Dapagliflozin 5mg Metformin Hydrochloride BP 1000mg (As extended release)
SUMMARY OF PRODUCT CHARACTERISTICS	

1. Name of the medicinal product

Dapagliflozin 5mg & Metformin Hydrochloride 1000mg Extended Release Tablets

2. Qualitative and quantitative composition

Each film coated tablets contains
Dapagliflozin Propanediol Monohydrate Equivalent to Dapagliflozin 5mg
Metformin Hydrochloride BP 1000mg
(As extended release)

S.N	Ingredient	Spec.	Overages	Qty. per tablet in mg	Std. Qty. for 100,000 tablets in kg
1.	Metformin Hydrochloride	BP	Nil	1000.00	100.00
2.	Cetostearyl Alcohol	BP	Nil	50.00	5.000
3.	Calcium Hydrogen Phosphate	BP	Nil	120.00	12.000
4.	Ethylcellulose N50	BP	Nil	20.00	2.000
5.	Povidone K30	BP	Nil	20.00	2.000
6.	*Dichloromethane	BP	Nil	----	15.000
	Lubrication				
7.	Hypromellose K4	BP	Nil	17.50	1.750
8.	Hypromellose K100	BP	Nil	17.50	1.750
9.	Carbomer 934	USP	Nil	36.00	3.600
10.	Purified Talc	BP	Nil	5.00	0.500
11.	Colloidal Anhydrous Silica	BP	Nil	4.00	0.400
12.	Magnesium Stearate	BP	Nil	10.00	1.000
Coating					
13.	Hypromellose E15	BP	Nil	17.00	1.700
14.	Titanium Dioxide	BP	Nil	3.65	0.365
15.	Purified Talc	BP	Nil	3.00	0.300
16.	Dapagliflozin Propanediol Monohydrate	IHS	Nil	6.15	0.615

17.	Tartrazine Yellow	IHS	Nil	0.20	0.020
18.	*Isopropyl Alcohol	BP	Nil	--	20.000
19.	*Dichloromethane	BP	Nil	--	20.000

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 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

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 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.

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.

4.6 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 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: In the event of an overdose, appropriate supportive treatment should be initiated as dictated by the patient's clinical status.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Dapamet 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.

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%.

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 63-2761.

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.

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.

5.3 Preclinical safety data

Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential and fertility.

6. Pharmaceutical Particulars

6.1 List of excipients

Cetostearyl Alcohol

Calcium Hydrogen Phosphate

Ethylcellulose N50

Povidone K30

Hypromellose K4

Hypromellose K100

Carbomer 934

Purified Talc

Colloidal Anhydrous Silica

Magnesium Stearate

Hypromellose E15

Titanium Dioxide

Tartrazine Yellow

Isopropyl Alcohol

Dichloromethane
6.2 Incompatibilities
None known.
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 x10's (10 tablets are packed in one ALU-ALU blister and 3ALU-ALU blisters kept in one carton along with package insert).
6.6 Special precautions for disposal and other handling
Not applicable.
7. Marketing authorisation holder
Company name: INNOCIA LIFESCIENCES PVT. LTD., Address: Block A, No.12, Balaji Nagar, Ambattur, Chennai-600 053 Country: INDIA.
8. Marketing authorisation number(s)
Telephone: 044 26585811, 26585855 Telefax: -

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E-Mail: ah@innocialife.com