1. Name of the drug product:
EDEN ATENOLOL (Atenolol Tablets BP 100 mg)

2. Qualitative and quantitative composition :
Each Film coated Tablet Contains:
Atenolol BP ……100 mg
Approved Colour Used.
Excipients.....QS

Sr. No.	Ingredients	Specifi-cation	Label Claim / Tablet (In mg)	Over-ages added (In %)	Qty. / Tablet (In mg)	Reason For Inclusion
a)	**Dry Mixing**					
1.	Atenolol	BP	100.00	NA	100.00	Medicament
2.	Lactose Monohydrate	BP	NA	NA	177.50	Diluent
3.	Microcrystalline Cellulose	BP	NA	NA	118.44	Diluent
4.	Povidone K-30	BP	NA	NA	1.78	Binder
b)	**Binder Preparation**					
5.	Maize Starch	BP	NA	NA	7.14	Binder
6.	Purified Water	BP	NA	NA	-----	Vehicle
c)	**Lubrication**					
7.	Purified Talc	BP	NA	NA	4.00	Glidant
8.	Croscarmellose Sodium	BP	NA	NA	7.00	Disintegrant
9.	Magnesium Stearate	BP	NA	NA	5.00	Lubricant
10.	Colloidal Anhydrous Silica	BP	NA	NA	1.00	Glidant
11.	Maize Starch	BP	NA	NA	8.14	Disintegrant
	Average Weight of Uncoated Tablet (In mg)				**430.00**	
d)	**Film Coating**					
11.	Hypromellose	BP	NA	NA	6.00	Film Former
12.	Macrogol-6000	BP	NA	NA	0.60	Plasticizer
13.	Titanium Dioxide	BP	NA	NA	1.00	Opacifier
14.	Purified Talc	BP	NA	NA	3.00	Antiadherant
15.	Carmoisine	IH	NA	NA	0.15	Colour
16.	Ponceau 4R	IH	NA	NA	0.45	Colour
17.	Purified Water	BP	NA	NA	----	Vehicle
	Average Weight of Film Coated Tablet (In mg)				**435.00**	

3 Pharmaceutical form: Film coated tablets

Description: Red coloured, round shaped, biconvex film coated tablet plain on both sides.

4 Clinical Particulars

4.1 Therapeutic indications

EDEN ATENOLOL Tablets are indicated in:
Treatment of high blood pressure or chest pain caused by angina. It is also used to lower the risk of death after heart attack.

4.2 Posology and method of administration

Route: Oral

Adults

High blood pressure: 50-100 mg once a day.
Angina: 100 mg once a day or 50 mg twice a day.
Abnormal heart rhythms: The initial dose will be given by infusion. Thereafter, the maintenance dose is usually 50-100 mg taken once a day.
Treatment following a heart attack: The initial dose will be given by infusion. This is followed by a 50 mg oral dose of atenolol 15 minutes later. Another 50 mg oral dose of atenolol is given approximately 12 hours after the infusion. Thereafter; the usual dosage is 100 mg of atenolol taken once a day.

People with severe kidney problems

Patients with kidney problems may be given a reduced dosage to that described for adults above. Haemodialysis patients usually take 50 mg following each dialysis.

Use in Children

Atenolol is not recommended for use in children.

Older people

The adult dosage above may be reduced in the case of elderly patients, particularly in those with kidney problems.

4.3 Contraindications

EDEN ATENOLOL Tablets are contraindicated in sinus bradycardia, heart block greater than first degree, cardiogenic shock and overt cardiac failure. Also it is contraindicated in those patients with a history of hypersensitivity to the atenolol or any of the drug product component.

4.4 Special warnings and precautions for use

Heart Failure: care must be exercised in patients with heart failure because of the negative inotropic effects of atenolol. Such patients should be well controlled on digitalis before therapy commences. Close monitoring for progressive failure is essential. Similarly, care must be taken with patients with poor cardiac reserve.
Ischaemic Heart disease: especially in patients with ischaemic heart disease, treatment should not be discontinued suddenly. The dosage should be gradually reduced, i.e. over 1-2 weeks, if necessary at the same time initiating replacement therapy, to prevent exacerbation of angina pectoris. In addition, hypertension and arrhythmias may develop. Furthermore, there is a risk of myocardial infarction and sudden death.
Untreated Congestive Heart disease: beta-blockers should not be used in such patients. The condition should be stabilised first.
First Degree Heart Block: due to its negative effect on conduction time, beta-blockers should only be given with caution to such patients.
Bradycardia: beta-blockers may induce bradycardia. If the pulse rate decreases to less than 50-55 beats per minute at rest and the patient experiences symptoms related to the bradycardia, the dosage should be reduced.

Prinzmetal's anginal: Atenolol may increase the number and duration of anginal attacks in patients with Prinzmetal's angina due to unopposed alpha-receptor mediated coronary artery vasoconstriction. For these patients atenolol should only be used with the utmost care.
Peripheral Circulatory Disease: In patients with peripheral circulatory disorders (Raynaud's disease or syndrome, intermittent claudication), beta-blockers should be used with great caution as aggravation of these disorders may occur. Severe peripheral circulatory disorders are a contra-indication.
Respiratory disorders: In patients with chronic obstructive pulmonary disorders, airway obstructions may be aggravated. Therefore, atenolol should only be used for these patients with the utmost care.
Diabetics: the symptoms of hypoglycaemia may be masked by atenolol, in particular tachycardia. Diabetic patients should be warned that this 'warning sign' may not occur.
Insulin sensitivity may be reduced in patients treated with atenolol.
Thyrotoxicosis: Beta-blockade may mask cardiovascular signs of thyrotoxicosis.
Allergies: Atenolol may increase both the sensitivity towards allergens and the seriousness of anaphylactic reactions. Atenolol may reduce the efficacy of the usual dose of adrenaline (epinephrine) used to treat allergic reactions.
Hypersensitivity: atenolol may cause a hypersensitivity reaction including angio-oedema and urticaria.
Psoriasis: patients with anamnestically known psoriasis should take beta-blockers only after careful consideration.
Elderly: these patients should be treated with caution, starting with a lower dosage but tolerance is usually good in the elderly (see section 4.2).
Surgery: When a patient is scheduled for surgery, and it has been decided to interrupt beta-blockade, therapy should be discontinued for at least 24 hours. Continuation of beta-blockade reduces the risk of arrhythmias during induction and intubation, however the risk of hypotension may be increased as well.
If treatment is continued, caution should be observed with the use of certain anaesthetic drugs. The patient may be protected against vagal reactions by intravenous administration of atropine.

4.5 Interaction with other medicinal products and other forms of interaction
Adrenergic neurone-blocking agents Adrenergic-neurone blocking agents such as guanethidine, reserpine, diuretics and anti-hypertensive agents, including the vasodilator group, will have an additive effect on the hypotensive action of the drug.
Anaesthetic agents -Caution must be exercised when using anaesthetic agents with atenolol. The anaesthetist should be informed and the choice of anaesthetic should be an agent with as little negative inotropic activity as possible. Use of beta-blockers with anaesthetic drugs may result in attenuation of the reflex tachycardia and increase the risk of hypotension. Anaesthetic agents causing myocardial depression are best avoided.
Antiarrhythmic agents (Class 1)- Class I anti-arrhythmic drugs (e.g. disopyramide) and amiodarone may have a potentiating effect on atrial-conduction time and induce negative inotropic effect.
Calcium channel blockers -Combined use of beta-blockers and calcium channel blockers with negative inotropic effects e.g. verapamil, diltiazem can lead to an exaggeration of these effects particularly in patients with impaired ventricular function and/or sino-atrial or atrio-ventricular conduction abnormalities. This may result in severe hypotension, bradycardia and cardiac failure. Neither the beta-blocker nor the calcium channel blocker should be administered intravenously within 48 hours of discontinuing the other.
Clonidine-Beta-blockers may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. If the two drugs are co-administered, the beta-blocker should be

withdrawn several days before discontinuing clonidine. If replacing clonidine by beta-blocker therapy, the introduction of beta-blockers should be delayed for several days after clonidine administration has stopped.

4.6 Pregnancy and Lactation

Pregnancy: Atenolol crosses the placental barrier and appears in the cord blood. No studies have been performed on the use of atenolol in the first trimester and the possibility of foetal injury cannot be excluded. Atenolol has been used under close supervision for the treatment of hypertension in the third trimester. Administration of atenolol to pregnant women in the management of mild to moderate hypertension has been associated with intra-uterine growth retardation. The use of atenolol in women who are, or may become, pregnant requires that the anticipated benefit be weighed against the possible risks, particularly in the first and second trimesters.

Breastfeeding: There is significant accumulation of atenolol in breast milk. Neonates born to mothers who are receiving atenolol at parturition or breat-feeding may be at risk for hypoglycaemia and bradcardia. Caution should be exercised when Atenolol is administered during pregnancy or to a woman who is breast feeding.

4.7 Effects on ability to drive and use machines

Atenolol may affect your ability to drive or use machines. If the tablets make you feel sick, dizzy or tired, or give you a headache, do not drive or use machines and contact your doctor immediately.

4.8 Undesirable effects

More common:

Blurred vision, cold hands or feet, confusion, difficult or labored breathing dizziness, faintness, or lightheadedness when getting up from a lying or sitting position suddenly, shortness of breath, sweating, tightness in chest, unusual tiredness or weakness.

Less common:

Anxiety, chest pain or discomfort, chills, cold sweats, cough, dizziness or lightheadedness, fainting, fast heartbeat, leg pain, noisy breathing, slow or irregular heartbeat, sudden shortness of breath or troubled breathing.

Rare:

Bloody urine, decreased frequency or amount of urine, increased blood pressure, increased thirst, loss of appetite, lower back or side pain, nausea, swelling of face, fingers, or lower legs, vomiting, weight gain.

4.9 Overdose

Overdosage with Atenolol has been reported with patients surviving acute doses as high as 5 gm. One death was reported in a man who may have taken as much as 10 gm acutely.

The predominant symptoms reported following Atenolol overdose are lethargy, disorder of respiratory drive, wheezing, sinus pause and bradycardia. Additionally, common effects associated with overdosage of any beta-adrenergic blocking agent and which might also be expected in Atenolol overdose are congestive heart failure, hypotension, bronchospasm and/or hypoglycemia.

Treatment of overdose should be directed to the removal of any unabsorbed drug by induced emesis, gastric lavage, or administration of activated charcoal. Atenolol can be removed from the general circulation by hemodialysis. Other treatment modalities should be employed at the physician's discretion and may include:

BRADYCARDIA: Atropine intravenously. If there is no response to vagal blockade, give

isoproterenol cautiously. In refractory cases, a transvenous cardiac pacemaker may be indicated.
HEART BLOCK (SECOND OR THIRD DEGREE): Isoproterenol or transvenous cardiac pacemaker.
CARDIAC FAILURE: Digitalize the patient and administer a diuretic. Glucagon has been reported to be useful.
HYPOTENSION: Vasopressors such as dopamine or norepinephrine (levarterenol). Monitor blood pressure continuously.
BRONCHOSPASM: A beta2 stimulant such as isoproterenol or terbutaline and/or aminophylline.
HYPOGLYCEMIA: Intravenous glucose.
Based on the severity of symptoms, management may require intensive support care and facilities for applying cardiac and respiratory support.

5 Pharmacological properties

5.1 Pharmacodynamic properties

Beta-adrenergic blocking agents (hereafter called Beta-blockers) compete with Beta-adrenergic agonists for available Beta receptor sites. Unselective Beta- blockers inhibit the $Beta_1$ receptors (located chiefly in cardiac muscle) and $Beta_2$ receptors (located chiefly in the bronchial and vascular musculature), inhibiting the chronotropic, inotropic and vasodilator responses to Beta-adrenergic stimulation. Atenolol is cardioselective and preferentially inhibits $Beta_1$ adrenoceptors. $Beta_1$ selectivity has been confirmed by the inability of Atenolol to reverse the $Beta_2$ mediated vasodilating effects of Epinephrine or Isoproterenol. This contrasts with the effect of nonselective Beta-blockers which completely reverse the vasodilating effects of Epinephrine.

5.2 Pharmacokinetic properties

Absorption

Atenolol is consistently absorbed when administered orally, with approximately 50 – 60% of the dose administered being absorbed. After an oral dose of 100mg a mean peak serum level of 880ng/ml was reached in approximately 3 hours, declining to approximately 63ng/ml in 24 hours.

Distribution

Atenolol is widely distributed throughout the body, but only a small amount of the drug reaches the brain, Atenolol is not significantly bound to serum proteins. In pregnancy, atenolol readily crosses the placenta, the umbilical and maternal serum being approximately equal at birth.

Metabolism

Metabolism of atenolol in man is minimal. In animal studies a hydroxylated compound with minor Beta- blocking activity, has been identified as a minor metabolite of Atenolol, but Atenolol does not appear to be metabolized to a significant extent in man.

Elimination

Atenolol is excreted unchanged, mainly through the kidneys. About 40 – 50% of a single oral dose is excreted in the urine of healthy subjects. The elimination half-life of Atenolol is approximately 6 - 7 hours.

In renal dysfunction, the elimination of Atenolol is closely related to the glomerular filtration rate, although important accumulation probably only occurs if the glomerular filtration is less than 30mL/minute.

5.3 Preclinical safety data

There are no pre-clinical data available of Atenolol Tablets.

6 Pharmaceutical particulars

6.1 List of excipients
Lactose Monohydrate, Microcrystalline Cellulose, Maize Starch, Povidone K-30, Purified Water, Purified Talc, Croscarmellose Sodium, Magnesium Stearate, Colloidal Anhydrous Silica, Hypromellose, Macrogol-6000, Titanium Dioxide, Carmoisine, Ponceau 4R.

1.3.1.6.2 Incompatibilities
Not applicable

6.3 Shelf life
36 months

6.4 Special precautions for storage
Store at temperature not exceeding 30°C in dry place.
Protect from light

6.5 Nature and contents of container
Packing:
Primary packing: 14 Tablets in an ALU-PVC blister.
Secondary packing: 2 Blisters are packed in a carton along with leaflet.
Tertiary packing: Shrink such 10 cartons. Such 60 Shrinks are packed in a 5 Ply corrugated box sealed with BOPP tape & strap with strapping roll.

7 Applicant / Manufacturer
Applicant

Applicant name and address	**M/s. EDEN U.K. PHARMACEUTICALS LTD.** J-116, Daminja Avenue Housing Estate, Fegge Onitsha, Anambra State, Nigeria
Contact person's phone number	
Contact person's email	

Manufacturer

Manufacturer name and address	**M/s. IMPULSE PHARMA PVT. LTD.** J-201, J-202/1 , MIDC Tarapur, Boisar, Dist. Palghar - 401506, Maharashtra State, India.
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