SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE FINISHED PHARMACEUTICAL PRODUCT

ANTIPRESS-50
Atenolol Tablets BP

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

Atenolol BP	:	50 mg
Excipients	:	Q.S.
Colour	:	Sunset Yellow FCF

For excipients, see 6.1.

3. PHARMACEUTICAL FORM

Tablet
For oral administration.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

- The management of Hypertension.
- The management of Angina pectoris.
- The management of Cardiac Dysrhythmias
- Myocardial infarction: Early intervention in the acute phase and long-term prophylaxis after recovery from myocardial infarction.

4.2 Posology and method of administration

Adults

Hypertension:

Most patients respond to 100mg daily given as a single dose. Some patients, however, will respond to 50mg given as a single daily dose. The effect will be fully established after one to two weeks. A further reduction in blood pressure may be achieved by combining Atenolol with other antihypertensive agents. For example, co-administration of Atenolol with a diuretic provides a highly effective and convenient antihypertensive therapy.

Angina:

Most patients with angina pectoris will respond to 100mg given orally once daily or 50mg given twice daily. It is unlikely that additional benefit will be gained by increasing the dose.

Dysrhythmias:
Having controlled the dysrhythmias with intravenous Atenolol a suitable maintenance dosage is 50mg - 100mg daily, given as a single dose.

Myocardial infarction:
15 minutes after the administration of the intravenous dose an oral dose of 50mg may be given provided that no untoward effects occur from the intravenous dose. This should be followed by a further 50mg 12 hours after the intravenous dose and then 12 hours later by 100mg to be given once daily for up to ten days. If bradycardia and/or hypotension requiring treatment, or any other untoward effects occur, Atenolol should be discontinued.

Renal failure:
Atenolol is excreted via the kidneys, dosage adjustment should therefore be considered in patients with severe impairment of renal function. As a guide, for patients with a serum creatinine of 300- 600µMol/Litre, the Atenolol oral dose should be 50mg daily or 100mg once every two days, for patients with a serum creatinine of >600µMol/Litre, the oral dose of Atenolol should be 50mg on alternate days or 100mg once every four days.
Patients on haemodialysis should be given 50mg Atenolol orally following each dialysis. Because of the possibility of marked falls in blood pressure, this should be carried out under hospital supervision.

Elderly
Dosage requirements may be reduced, especially in patients with impaired renal function.

Paediatric population
There is no paediatric experience with atenolol and for this reason it is not recommended for use in children.

Method of administration: Oral

4.3 Contraindications

ANTIPRESS-50 (atenolol) should not be used in the presence of:

1. Sinus bradycardia, or bradycardia of other origin
2. Second and third degree A-V block

3. Sick sinus syndrome
4. Right ventricular failure secondary to pulmonary hypertension
5. Uncontrolled heart failure
6. Cardiogenic shock
7. Hypotension
8. Severe peripheral arterial disorders
9. Anesthesia with agents that produce myocardial depression
10. Pheochromocytoma, in the absence of alpha-blockade
11. Metabolic acidosis
12. Known hypersensitivity to the product

4.4 Special warnings and precautions for use

WARNINGS

Cardiac Failure

Special caution should be exercised when administering atenolol to patients with a history of heart failure. Sympathetic stimulation is a vital component supporting circulatory function in congestive heart failure and inhibition with beta blockade always carries the potential hazard of further depressing myocardial contractility and precipitating cardiac failure. Atenolol acts selectively without abolishing the inotropic action of digitalis on the heart muscle. However, the positive inotropic action of digitalis may be reduced by the negative inotropic effect of atenolol when the two drugs are used concomitantly. The effects of beta-blockers and digitalis are additive in depressing A-V conduction. In patients without a history of cardiac failure, continued depression of the myocardium over a period of time can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of impending cardiac failure, patients should be fully digitalised and/or given a diuretic and the response observed closely. If cardiac failure continues, despite adequate digitalisation and diuretic therapy, atenolol therapy should be immediately withdrawn.

Abrupt Cessation of Therapy with atenolol

Patients with angina should be warned against abrupt discontinuation of atenolol. There have been reports of severe exacerbation of angina and of myocardial infarction or ventricular arrhythmias occurring in patients with angina pectoris, following abrupt discontinuation of beta-blocker therapy. The last two complications may occur with or without preceding exacerbation of angina pectoris.

Therefore, when discontinuation of atenolol is planned in patients with angina pectoris, the dosage should be gradually reduced over a period of about two weeks and the patient should be carefully observed and advised to limit physical activity to a minimum. The same frequency of administration should be maintained. In situations of greater urgency, atenolol should be discontinued stepwise over a shorter time and under closer

observation. If angina markedly worsens or acute coronary insufficiency develops, it is recommended that treatment with atenolol be reinstituted promptly, at least temporarily.

Oculomucocutaneous Syndrome

Various skin rashes and conjunctival xerosis have been reported with beta-blockers, including atenolol. A severe syndrome (oculomucocutaneous syndrome) whose signs include conjunctivitis sicca and psoriasiform rashes, otitis, and sclerosing serositis has occurred with the chronic use of one beta-adrenergic blocking agent (practolol). This syndrome has not been observed with atenolol or any other such agent. However, physicians should be alert to the possibility of such reactions and should discontinue treatment in the event that they occur.

Prinzmetal's Angina

Atenolol may increase the number and duration of angina attacks in patients with Prinzmetal's angina due to unopposed alpha-receptor mediated coronary artery vasoconstriction. Atenolol, therefore, should only be used in these patients with the utmost care.

Sinus Bradycardia

Severe sinus bradycardia may occur with the use of atenolol treatment from unopposed vagal activity remaining after blockade of beta1-adrenergic receptors; in such cases, dosage should be reduced.

Thyrotoxicosis

In patients with thyrotoxicosis, possible deleterious effects from long-term use of atenolol have not been adequately appraised. Beta-blockade may mask the clinical signs of continuing hyperthyroidism or its complications and give a false impression of improvement. Therefore, abrupt withdrawal of atenolol may be followed by an exacerbation of the symptoms of hyperthyroidism, including thyroid storm.

Pregnancy

Atenolol can cause fetal harm when administered to a pregnant woman. 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 fetal injury cannot be excluded. Administration of atenolol, starting in the second trimester of pregnancy, has been associated with the birth of infants that are small for gestational age. Studies in humans have shown that transplacental passage of atenolol does occur in pregnant women, with fetal drug serum levels equal to those of the mother. In a limited number of patients who were given the drug during the last trimester of pregnancy, low birth weight, neonatal hypoglycemia, bradycardia in the fetus/newborn, and placental insufficiency were observed. Neonates born to mothers who are receiving atenolol at parturition or breast-feeding may be at risk for hypoglycemia and bradycardia. Caution should be exercised when atenolol is administered during pregnancy or to a woman who is breast-feeding.

Atenolol has been shown to produce a dose-related increase in embryo/fetal resorptions in rats at doses equal to or greater than 50 mg/kg/day or 25 or more times the maximum recommended human dose.

PRECAUTIONS

Bronchospastic Disorders

Patients with bronchospastic diseases should, in general, not receive beta-blockers. Due to the relative beta1-selectivity of atenolol, atenolol may be used with caution in patients with bronchospastic disease who do not respond to, or cannot tolerate, other antihypertensive treatment. Since beta1-selectivity is not absolute, a beta2-stimulating agent should be administered concomitantly, the lowest possible dose of atenolol should be used.

Despite these precautions, the respiratory status of some patients may worsen, and, in such cases, atenolol should be withdrawn.

First Degree Heart Block

Due to its negative effect on A-V conduction time, atenolol should be used with caution in patients with first degree block.

Peripheral Arterial Circulatory Disorders

Atenolol may aggravate less severe peripheral arterial circulatory disorders (see CONTRAINDICATIONS).

Anaphylaxis - Epinephrine and Beta-Blockers

There may be increased difficulty in treating an allergic type reaction in patients on beta blockers. In these patients, the reaction may be more severe due to pharmacological effects of beta-blockers and problems with fluid changes. Epinephrine should be administered with caution since it may not have its usual effects in the treatment of anaphylaxis. On the one hand, larger doses of epinephrine may be needed to overcome the bronchospasm, while on the other, these doses can be associated with excessive alpha adrenergic stimulation with consequent hypertension, reflex bradycardia and heart-block and possible potentiation of bronchospasm. Alternatives to the use of large doses of epinephrine included vigorous supportive care such as fluids and the use of beta agonists including parenteral salbutamol or isoproterenol to overcome bronchospasm, and norepinephrine to overcome hypotension.

Diabetes and Patients Subject to Hypoglycemia

Atenolol should be administered with caution to patients subject to spontaneous hypoglycemia, or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic blockers may mask the premonitory signs (e.g. tachycardia) and symptoms of acute hypoglycemia.

Impaired Renal Function

Atenolol should be used with caution in patients with impaired renal function.

When renal function is impaired, clearance of atenolol is closely related to the glomerular filtration rate; however, significant accumulation does not occur until the creatinine clearance falls below;

35 mL/min/1.73m^2.

Elective or Emergency Surgery

It is not advisable to withdraw beta-adrenoceptor blocking drugs prior to surgery in the majority of patients. However, care should be taken when using atenolol with anaesthetic agents such as those which may depress the myocardium. Vagal dominance, if it occurs, may be corrected with atropine (1-2 mg IV).

Some patients receiving beta-adrenergic blocking agents have been subject to protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported.

In emergency surgery, since atenolol is a competitive inhibitor of beta-adrenergic receptor agonists, its effects may be reversed, if necessary, by sufficient doses of such agonists as isoproterenol or norepinephrine.

Ethnic Populations

Atenolol appears to be effective and well-tolerated in most ethnic populations, although the responses may be less in black patients than in Caucasians.

Use in Lactating Women

In humans, there is a significant accumulation of atenolol in the breast milk of lactating women. Neonates born to mothers who are breastfeeding may be at risk for hypoglycemia and bradycardia. If the use of atenolol is considered essential, then mothers should stop nursing.

Use in Children

There is no experience with atenolol in the treatment of pediatric age groups.

Activities Requiring Mental Alertness

Use of atenolol is unlikely to result in any impairment of the ability of patients to drive or operate machinery. However, it should be taken into account that dizziness or fatigue may occur.

Geriatric Use

Clinical studies of atenolol did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between elderly and younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic renal, or cardiac function, and concomitant diseases or other drug therapy.

4.5 Interaction with other medicinal products and other forms of interaction

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 daysbefore 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. (Also see prescribing information for clonidine).

Reserpine or Guanethidine

Patients receiving catecholamine-depleting drugs, such as reserpine or guanethidine, should be closely monitored because the added beta-adrenergic blocking action of atenolol may produce anexcessive reduction of sympathetic activity. Atenolol should not be combined with other beta- blockers.

Antiarrhythmic Agents

Class I anti-arrhythmic drugs (e.g. disopyramide) and amiodarone may have potentiating effect onatrial-conduction time and induce negative inotropic effect.

Calcium Channel Blockers

Combined use of beta-blockers and calcium channel blockers with negative inotropic effects can lead to prolongation of S-A and A-V conduction, particularly in patients with impaired ventricularfunction, conduction abnormalities, or diminished cardiac output. This may result in severe hypotension, bradycardia and cardiac failure. Concomitant therapy with dihydropyridines, e.g., nifedipine, may increase the risk of hypotension, and cardiac failure may occur in patients with latent cardiac insufficiency.

Digitalis Glycosides

Digitalis glycosides may potentiate the bradycardia of beta1-blockade.

Non-Steroidal Anti-Inflammatory Agents

The concomitant use of non-steroidal anti-inflammatory agents may blunt the antihypertensiveeffects of beta-blockers.

Anaesthetic Agents

Anaesthetics can produce a hypotensive state with associated reflex tachycardia. Since beta- blockade will inhibit reflex tachycardia, the hypotensive potential of anaesthetic agents is increasedwith concomitant use of atenolol. The anaesthetist should be informed and the choice of anaestheticshould be an agent with as little negative inotropic activity as possibl.

Fingolimod

Concomitant use of fingolimod with beta blockers may potentiate bradycardic effects and is not recommended. Where such co-administration is considered necessary, appropriate monitoring attreatment initiation, i.e. at least overnight monitoring, is recommended.

4.5 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, since beta-blockers, in general, have been associated
with a decrease in placental perfusion which may result in intra-uterine deaths, immature and premature deliveries.

Lactation
Atenolol is excreted in human milk, and consequently caution should be exercised when Atenolol is administered to a nursing mother.

4.7 Effects on ability to drive and use machines

Atenolol has no or negligible influence on the ability to drive and use machines.
However, it should be taken into account that occasionally dizziness or fatigue may occur.

4.8 Undesirable effects

The most serious adverse reactions encountered are congestive heart failure, A-V block and bronchospasm. Bronchospasm may occur in patients with bronchial asthma or a history of asthmaticcomplaints.
The most common adverse reactions reported in clinical trials with oral atenolol in 2500 patients arebradycardia (3%), dizziness (3%), vertigo (2%), fatigue (3%), diarrhea (2%) and nausea (3%).
Adverse reactions occurring with an incidence of less than 1%, grouped by system, are as follows:

Cardiovascular
Heart failure deterioration (see WARNINGS)
Heart block
Palpitations
Lengthening of P-R interval
Chest pain

Light-headedness
Postural hypotension which may be associated with syncope
Raynaud's phenomenon
Intermittent claudication, or worsening of pre-existing intermittent claudication
Leg pain and cold extremities
Edema

Respiratory
Dyspnea, wheeziness
Cough
Bronchospasm

Central Nervous System
Faintness
Ataxia
Tiredness
Lethargy
Nervousness
Depression
Drowsiness
Vivid dreams
Insomnia
Paresthesia
Headache
Tinnitus
Mood Changes
Visual disturbances
Psychoses and hallucinations

Gastrointestinal
Constipation
Anorexia
Abdominal discomfort, indigestion

Miscellaneous
Skin rash
Itchy and/or dry eyes
Psoriasiform skin reactions
Exacerbation of psoriasis
Decreased exercise tolerance

Alopecia
Epistaxis
Flushes
Impotence, decreased libido
Sweating
General body aches
Thrombocytopenia and purpura

Post-Marketing Experience

During the post-marketing experience with atenolol, cold extremities, gastrointestinal disturbances and fatigue were commonly reported. The following have been reported in temporal relationship tothe use of the drug: elevated liver enzymes and/or bilirubin, headache, confusion, nightmares, impotence, Peyronie's disease, psoriasiform rash or exacerbation of psoriasis, purpura, reversible alopecia and thrombocytopenia. Rare cases of hepatic toxicity including intrahepatic cholestasis have been reported. Atenolol, like other beta blockers, has been associated with the development ofantinuclear antibodies (ANA) and lupus syndrome.

In a long-term, well-controlled trial of 1,627 elderly patients with systolic hypertension, theincidence of dry mouth was significantly higher in patients taking atenolol (12.2%).

Potential Adverse Reactions

The following adverse reactions have occurred with other beta-blockers but have not been reportedwith atenolol:

Cardiovascular:	Pulmonary edema, cardiac enlargement, hot flushes and sinus arrest
Central Nervous System:	Aggressiveness, anxiety, short term memory loss, and emotional Lability with slightly clouded sensorium.
Allergic:	Laryngospasm, status asthmaticus and fever combined with achingand sore throat.
Dermatological:	Exfoliative dermatitis
Ophthalmological:	Blurred vision, burning, and grittiness
Hematological:	Agranulocytosis
Gastrointestinal:	Mesenteric arterial thrombosis and ischemic colitis

4.9 Overdose

Limited information is available with regard to overdosage with ANTIPRESS-100 (atenolol) in humans. Overdosage with atenolol has been reported with patients surviving acute doses as high as5 g. One death was reported in a man who may have taken as much as 10 g acutely.

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

Treatment should be symptomatic and supportive and directed to the removal of any unabsorbed drug by induced emesis, or administration of activated charcoal. Atenolol can be removed from the general circulation by hemodialysis. Further consideration should be given to dehydration, electrolyte imbalance and hypotension by established procedures.
Other treatment modalities should be employed at the physician's discretion and may include:

Bradycardia: Atropine 1-2 mg intravenously. If there is no response to vagal blockade, give isoproterenol cautiously. In refractory cases, a transvenous cardiac pacemaker may be indicated. Glucagon in a 10 mg intravenous bolus has been reported to be useful. If required, this may be repeated or followed by an intravenous infusion of glucagon 1-10 mg/h depending on response. If no response to glucagon occurs or if glucagon is unavailable, a beta-adrenoceptor stimulant such as dobutamine 2.5 to 10 micrograms/kg/minute by intravenous infusion or isoproterenol 10 to 25 micrograms given as an infusion at a rate not exceeding5 micrograms/minute may be given, although larger doses may be required.
Heart block:(second or third degree): Isoproterenol or transvenous pacemaker.
Congestive Heart Failure: Digitalize the patient and administer a diuretic. Glucagon has been reported to be useful.
Hypotension: Vasopressors such as dopamine or norepinephrine.Monitor blood pressure continuously.
Bronchospasm: A $beta_2$-stimulant such as isoproterenol or terbutaline and/or intravenous aminophylline.
Hypoglycemia: Intravenous glucose.
Based on the severity of symptoms, management may require intensive support care and facilities for applying cardiac and respiratory support.

For management of a suspected drug overdose, contact your regional Poison Control CentreImmediately.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic Group: Beta-blocking agents
ATC Code: C07AB03
Beta-adrenergic blocking agents (hereafter called Beta-blockers) compete with Beta-adrenergic agonists for available Beta receptor sites. Unselective Beta- blockers inhibit the Beta1 receptors (located chiefly in cardiac muscle) and Beta2 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 Beta1 adrenoceptors. Beta1 selectivity has been confirmed by the inability of Atenolol to reverse the Beta2 mediated vasodilating effects of Epinephrine or Isoproterenol. This contrasts with the effect of nonselective Beta-blockers which completely reverse the vasodilating effects of Epinephrine.
Atenolol does not have membrane stabilising effects, little direct myocardial depressant activity and little or no intrinsic sympathomimetic activity.
Clinical response to Beta-blockade includes slowing of sinus heart rate, depressed AV conduction, decreased cardiac output at rest and on exercise, reduction of systolic blood pressure on exercise, reduction of both supine and standing blood pressure, inhibition of isoproterenol induced tachycardia and reduction of reflex orthostatic tachycardia.

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

No further data is presented given the well-known pre-clinical and clinical profile of Atenolol.

6. PHARMACEUTICAL PARTICULARS

6.1 List of Excipients

Maize Starch BP
Colloidal Anhydrous Silica BP
Microcrystalline Cellulose BP
Colour Sunset Yellow BP
Sodium Lauryl Sulphate BP
Purified Water BP
Magnesium Stearate BP
Purified Talc BP
Polacrilin Potassium BP

6.2 Incompatibilities

Not Applicable

6.3 Shelf Life

36 Months

6.4 Special Precautions for Storage

Store below 30ºC in a cool and dry place. Protect from heat, light and moisture.

KEEP OUT OF REACH OF CHILDREN.

6.5 Nature and Contents of Container

10 × 10 Alu-PVC Blister Pack.

6.6 Instructions for use and handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Ahmedabad
Gujarat, India.
E-mail: info@sagalabs.com
URL: www.sagalabs.com

8. NUMBER(S) IN THE NATIONAL REGISTER OF FINISHED PHARMACEUTICAL PRODUCTS

06872/08784/NMR/2021

9. DATE OF FIRSHT AUTHORISATION/RENEWAL OF THE AUTHORISATION

28/11/2021

10. DATE OF REVISION OF THE TEXT

01 April 2026