



COMPOSITION

Arsenor Tablet: Each film coated tablet contains Apremilast INN 10 mg.

Arsenor 30 Tablet: Each film coated tablet contains Apremilast INN 30 mg.

PHARMACOLOGICAL INFORMATION

Therapeutic Class: Antirheumatic Agent

PHARMACOLOGICAL ACTION

Description

The active ingredient in Arsenor tablets is Apremilast. Apremilast is a phosphodiesterase 4 (PDE4) inhibitor. Apremilast is known chemically as N-[2-[(1S)-1-(3-ethoxy-4-methoxyphenyl)-2-(methylsulfonyl)ethyl]-2,3-dihydro-1,3-dioxo-1H-isoindol-4-yl]acetamide. Its empirical formula is $C_{22}H_{24}N_2O_7S$ and the molecular weight is 460.5.

Mechanism of Action

Apremilast is an oral small-molecule inhibitor of phosphodiesterase 4 (PDE4) specific for cyclic adenosine monophosphate (cAMP). PDE4 inhibition results in increased intracellular cAMP levels. The specific mechanism(s) by which Apremilast exerts its therapeutic action in psoriatic arthritis patients is not well defined.

CLINICAL INFORMATION

Therapeutic Indications

- **Psoriatic Arthritis**
Apremilast is indicated for the treatment of adult patients with active psoriatic arthritis.
- **Psoriasis**
Apremilast is indicated for the treatment of patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.

Dosage

Dosage in Psoriatic Arthritis and Psoriasis

The recommended initial dosage titration of Apremilast from Day 1 to Day 5 is shown in below table. Following the 5-day titration, the recommended maintenance dosage is 30 mg twice daily taken orally starting on Day 6. This titration is intended to reduce the gastrointestinal symptoms associated with initial therapy.

Apremilast can be administered without regard to meals. Do not crush, split or chew the tablets.

Dosage Titration Schedule

Day 1		Day 2		Day 3		Day 4		Day 5		Day 6	
AM	PM	AM	PM	AM	PM	AM	PM	AM	PM	AM	PM
10 mg		10 mg		10 mg	20 mg	20 mg	20 mg	20 mg	30 mg	30 mg	30 mg

AM = Morning, PM = Evening

Dosage Adjustment in Patients with Severe Renal Impairment

Apremilast dosage should be reduced to 30 mg once daily in patients with severe renal impairment (creatinine clearance (CL_{cr}) of less than 30 ml per minute estimated by the Cockcroft-Gault equation).

For initial dosage titration in this group, it is recommended that Apremilast be titrated using only the AM (morning) schedule listed in above table and the PM (evening) doses is skipped.

Side Effects

- **Psoriatic Arthritis:** The most common adverse reactions ($\geq 5\%$) are diarrhea, nausea and headache
- **Psoriasis:** The most common adverse reactions ($\geq 5\%$) are diarrhea, nausea, upper respiratory tract infection and headache, including tension headache.

Contraindications

Apremilast is contraindicated in patients with a known hypersensitivity to Apremilast or to any of the excipients in the formulation.

Drug interactions

Use with strong Cytochrome P450 enzyme inducers (e.g., Rifampin, Phenobarbital, Carbamazepine, Phenytoin) is not recommended because loss of efficacy may occur.

Precautions

Depression: Advise patients, their caregivers and families to be alert for the emergence or worsening of depression and if such changes occur to contact their healthcare provider. Carefully weigh risks and benefits of treatment with Apremilast in patients with a history of depression.

Weight Decrease: Monitor weight regularly. If unexplained or clinically significant weight loss occurs, evaluate weight loss and consider discontinuation of Apremilast.

Pregnancy

Pregnancy Category: C

Nursing Mothers

It is not known whether Apremilast or its metabolites are present in human milk; however Apremilast was detected in milk of lactating mice.

Because many drugs are present in human milk, caution should be exercised when Apremilast is administered to a nursing woman.

Pediatric Use

The safety and effectiveness of Apremilast in pediatric patients less than 18 years of age have not been established.

Geriatric Use

No overall differences were observed in the efficacy and safety in elderly subjects ≥ 65 years of age and younger adult subjects < 65 years of age in the clinical trials.

Patients with Impaired Renal Function

Apremilast pharmacokinetics were not characterized in subjects with mild (creatinine clearance of 60-89 mL per minute estimated by the Cockcroft-Gault equation) or moderate (creatinine clearance of 30-59 mL per minute estimated by the Cockcroft-Gault equation) renal impairment.

The dose of Apremilast should be reduced to 30 mg once daily in patients with severe renal impairment (creatinine clearance of less than 30 mL per minute estimated by the Cockcroft-Gault equation).

Hepatic Impairment

Apremilast pharmacokinetics were characterized in subjects with moderate (Child Pugh B) and severe (Child Pugh C) hepatic impairment. No dose adjustment is necessary in these patients.

Overdosage

In case of overdose, patients should seek immediate medical help. Patients should be managed by symptomatic and supportive care should there be an overdose.

PHARMACEUTICAL INFORMATION

Storage Conditions

Store in a cool and dry place, away from light. Keep out of the reach of children.

Presentation & Packaging

Arsenor Tablet: Each commercial box contains 30 tablets in Alu-Alu blister pack.

Arsenor 30 Tablet: Each commercial box contains 20 tablets in Alu-Alu blister pack.

Manufactured By

BEACON[®]
Pharmaceuticals PLC

Bhaluka, Mymensingh, Bangladesh