For the use of Registered Oncologist only

Acalabrutinib 100mg **Capsules**

Calquence ®

Abbreviated Prescribing Information

QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 100mg acalabrutinib.

PHARMACEUTICAL FORM

Capsule, hard Size 1 hard gelatine capsule with a yellow body and blue cap, marked in black ink with 'ACA 100 mg'

Therapeutic indications

CALQUENCE (acalabrutinib) is indicated for the treatment of patients with mantle cell lymphoma (MCL) who have received at least one prior therapy.

CALQUENCE is indicated for the treatment of patients with chronic lymphocytic leukaemia (CLL)/small lymphocytic lymphoma (SLL).

Posology and method of administration

Treatment with CALQUENCE should be initiated and supervised by a physician experienced in the use of anticancer therapies.

Posology

MCL

The recommended dose of CALQUENCE for the treatment of MCL is 100 mg (1 capsule) twice daily.

CLL

The recommended dose of CALQUENCE for the treatment of CLL is 100 mg (1 capsule) twice daily, either as monotherapy or in combination with obinutuzumab. Refer to the obinutuzumab prescribing information for recommended obinutuzumab dosing information.

Doses should be separated by approximately 12 hours.

Treatment with CALQUENCE should continue until disease progression or unacceptable toxicity.

Missed Dose

If a patient misses a dose of CALQUENCE by more than 3 hours, instruct the patient to take the next dose at its regularly scheduled time. Extra capsules of CALQUENCE should not be taken to make up for a missed dose.

Dose Adjustments

Adverse Reactions

Temporarily interrupt CALQUENCE to manage a Grade ≥ 3 non-haematological treatment-related adverse reaction, Grade 3 thrombocytopenia with significant bleeding, Grade 4 thrombocytopenia, or Grade 4 neutropenia lasting longer than 7 days. Upon resolution of the adverse reaction to Grade 1 or baseline (recovery), restart CALQUENCE as recommended in Table 1.

Special patient populations

Elderly (≥ 65 years)

No dose adjustment is necessary based on age.

Renal Impairment
No dose adjustment is recommended in patients with mild to moderate renal impairment (eGFR greater than or equal to 30 mL/min/1.73m2 as estimated by MDRD (modification of diet in renal disease equation)). The pharmacokinetics and safety of CALQUENCE in patients with severe renal impairment (eGFR less than 29 mL/min/1.73m2) or end-stage renal disease have not been studied.

Hepatic Impairment
No dose adjustment is recommended in patients with mild or moderate hepatic impairment (Child-Pugh A, Child-Pugh B, or total bilirubin between 1.5-3 times the upper limit of normal [ULN] and any AST). It is not recommended to administer CALQUENCE in patients with severe hepatic impairment (Child-Pugh C or total bilirubin >3 times ULN and any AST).

Severe Cardiac Disease
Patients with severe cardiovascular disease were excluded from CALQUENCE clinical studies.

Paediatric and adolescents
The safety and efficacy of CALQUENCE in children and adolescents aged less than 18 years have not been established.

Contraindications

None.

Special warnings and special precautions for use

Haemorrhage

Serious haemorrhagic events, including fatal events, have occurred in patients with haematologic malignancies (n=1040) treated with CALQUENCE monotherapy. Major haemorrhage (Grade 3 or higher bleeding events, serious, or any central nervous system events) occurred in 3.6% of patients, with fatalities occurring in 0.1% of patients. Overall, bleeding events including bruising and petechiae of any grade occurred in 46% of patients with haematological malignancies.

Patients receiving antithrombotic agents may be at increased risk of haemorrhage. Use caution with antithrombotic agents and consider additional monitoring for signs of bleeding when concomitant use is medically necessary. Consider the benefit-risk of withholding CALQUENCE for at least 3 days pre- and post-surgery.

Infections

Serious infections (bacterial, viral or fungal), including fatal events have occurred in patients with hematologic malignancies (n=1040) treated with CALQUENCE monotherapy. Grade 3 or higher infections occurred in 18% of these patients. The most frequently reported Grade 3 or higher infection was pneumonia. Infections due to hepatitis B virus (HBV) reactivation, aspergillosis, and progressive multifocal leukoencephalopathy (PML) have occurred.

Consider prophylaxis in patients who are at increased risk for opportunistic infections. Monitor patients for signs and symptoms of infection and treat as medically appropriate

Cytopenia's

Treatment-emergent Grade 3 or 4 cytopenias, including neutropenia (21%), anaemia (10%) and thrombocytopenia (7%) based on laboratory measurements, occurred in patients with haematologic malignancies (n=1040) treated with CALQUENCE monotherapy

Second Primary Malignancies

Second primary malignancies, including non-skin cancers , occured in 12% of patients with haematologic malignancies (n=1040) treated with CALQUENCE monotherapy. The most frequent second primary malignancy was skin cancer, which occured in 7% of patients. Monitor patients for the appearance of skin cancers.

Atrial Fibrillation

In patients with haematologic malignancies (n=1040) treated with CALQUENCE monotherapy, Grade 3 atrial fibrillation/flutter occurred in 1% of patients, and Grade 1 or 2 in 3% of patients. Monitor for symptoms (e.g., palpitations, dizziness, syncope, chest pain, dyspnoea) of atrial fibrillation and atrial flutter and obtain an ECG as appropriate.

Pregnancy and lactation

CALQUENCE should not be used during pregnancy and women of childbearing potential should be advised to avoid becoming pregnant while receiving CALQUENCE. Breast-feeding mothers are advised not to breast-feed during treatment with CALQUENCE and for 2 days after receiving the last dose

Interaction with other medical products and other form of interactions.

CYP3A Inhibitors

Co-administration with a strong CYP3A inhibitor like ketoconazole and other molecules increase the Cmax and AUC. Patients taking strong CYP3A inhibitors with CALQUENCE should be monitored more closely for adverse reactions.

CYP3A Inducers

Co-administration of a strong CYP3A inducer decreased Cmax and AUC. Avoid St. John's wort which may unpredictably decrease acalabrutinib plasma concentrations.

Undesirable effects

Overall Summary of Adverse Drug Reactions

The overall safety profile of acalabrutinib is based on data from 1040 patients with hematologic malignancies receiving acalabrutinib monotherapy. The most common (≥ 20%) adverse drug reactions (ADRs) of any grade reported in patients receiving acalabrutinib were infection,headache, diarrhoea, bruising, musculoskeletal pain, nausea, fatigue, and rash. The most commonly reported (≥ 5%) Grade ≥ 3 adverse drug reactions were infection (17.6%), neutropenia (14.2%), and anaemia (7.8%). Dose reductions due to adverse events were reported in 4.2% of patients. Discontinuation due to adverse events were reported in 9.3% of the patients. The median dose intensity was 98.7%.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic properties

Mechanism of action

Acalabrutinib is a selective small-molecule inhibitor of BTK form a covalent bond with a cysteine residue in the BTK active site, leading to irreversible inactivation of BTK (IC50 ≤ 5 nM) with minimal off-target interactions. BTK is a signalling molecule of the B cell antigen receptor (BCR) and cytokine receptor pathways. In B cells, BTK signalling results in B-cell survival and proliferation, and is required for cellular adhesion, trafficking, and chemotaxis.

Pharmacokinetic properties

The pharmacokinetics (PK) of acalabrutinib were studied in healthy subjects and patients with B-cell malignancies. The median time to peak acalabrutinib plasma concentrations (Tmax) was 0.75 hours. The absolute bioavailability of CALQUENCE was 25%. The human plasma protein binding is 97.5% with volume of distribution is approximately 34L. Acalabrutinib is predominantly metabolized by CYP3A enzymes. The median terminal elimination half-life (t1/2) of acalabrutinib was 0.9 hours. The t1/2 of the active metabolite (ACP- 5862) was 6.9 hours.

Major route of drug elimination is by faeces (84%) followed by urine (12%). Less than 1% excreted as unchanged acalabrutinib.

PHARMACEUTICAL PARTICULARS

List of excipients

Capsule Content: microcrystalline cellulose, colloidal silicon dioxide, partially pregelatinized starch (maize), magnesium stearate (E572), and sodium starch glycolate (Type A).

Capsule Shell: gelatine, titanium dioxide (E171), yellow iron oxide (E172), and FD&C Blue 2 (Indigotine/Indigo carmine) (E132).

Printing Ink: Shellac, black iron oxide (E172), propylene glycol (E1520), ammonium hydroxide.

Incompatibilities

Not applicable

Special precautions for storage

This medicinal product does not require any special storage conditions.

Nature and contents of container

Aluminium/Aluminium blisters. Cartons of 2 x 6 capsules.

Instructions for use, handling and disposal

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

CALQUENCE ® is a trademark of AstraZeneca group of companies

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Version 02 dated 16th March 2020.

Please refer to Full prescribing information Version 2, dated 9th Dec 2019

Calquence API Version 2, 16th Sep 2020