

SUMMARY OF PRODUCT CHARACTERISTICS

1. Name of the medicinal product:

Brand Name: PIROZEN 20

Generic Name: Piroxicam Capsules BP 20 mg

2. Qualitative and Quantitative composition:

Composition:

Each hard gelatin capsule
contains Piroxicam BP 20 mg
Excipients Q.S

Excipients of known concern: lactose

For a full list of excipients see section 6.1.

3. Pharmaceutical Form: Solid dosage form (Capsule)

4. Clinical Particulars:

4.1 Therapeutic indications

Piroxicam is indicated for symptomatic relief of osteoarthritis, rheumatoid arthritis, or ankylosing spondylitis.

4.2 Posology and method of administration

The maximum recommended daily dose is 20mg.
Undesirable effects may be minimized by using the minimum effective dose for the shortest duration necessary to control symptoms. The benefit and tolerability of treatment should be reviewed within 14 days. If continued treatment is considered necessary, this should be accompanied by frequent review. Given that piroxicam has been shown to be associated with an increased risk of gastrointestinal complications, the need for possible combination therapy with gastroprotective agents (e.g. misoprostol or proton pump inhibitors) should be carefully considered, in particular for elderly patients.

4.3 Contraindications

Hypersensitivity to the active substance(s) or to any of the excipients.

4.4 Special warnings and precautions for use

Undesirable effects may be minimized by using the minimum effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular (CV) risks below).

The clinical benefit and tolerability should be re-evaluated periodically and treatment should be immediately discontinued at the first appearance of cutaneous reactions or relevant gastrointestinal events.

Gastrointestinal (GI) Effects, Risk of GI Ulceration, Bleeding, and Perforation
NSAIDs, including piroxicam, can cause serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach, small intestine or large intestine, which can be fatal.

NSAID exposures of both short and long duration have an increased risk of serious GI events. Administration of doses of greater than 20 mg per day carries an increased risk of GI side effects. Evidence from observational studies suggests that piroxicam may be associated with a high risk of serious gastrointestinal toxicity, relative to other NSAIDs. These serious adverse events can occur at any time, with or without warning symptoms, in patients treated with NSAIDs.

Patients with significant risk factors for serious GI events should be treated with piroxicam only after careful consideration.

The possible need for combination therapy with gastro-protective agents (e.g. misoprostol or proton pump inhibitors) should be carefully considered.

Serious GI Complications

Identification of at-risk subjects: The risk for developing serious GI complications increases with age. Age over 70 years is associated with high risk of complications. The administration to patients over 80 years should be avoided.

Patients taking concomitant oral corticosteroids, selective serotonin reuptake inhibitors (SSRIs) or anti-platelet agents such as low-dose acetylsalicylic acid as well as those ingesting excessive amounts of alcohol are at increased risk of serious GI complications. As with other NSAIDs, the use of piroxicam in combination with protective agents (e.g. misoprostol or proton pump inhibitors) must be considered for these at-risk patients.

Patients and physicians should remain alerted for signs and symptoms of GI ulceration and/or bleeding during piroxicam treatment. Patients should be asked to report any new or unusual abdominal symptom during treatment. If

a gastrointestinal complication is suspected during treatment, piroxicam should be discontinued immediately and additional clinical evaluation and treatment should be considered. Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and/or cerebrovascular disease should only be treated with piroxicam after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular (CV) events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Clinical trial and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for Piroxicam. The relative increase of this risk appears to be similar in those with or without known CV disease or CV risk factors. However, patients with known CV disease or CV risk factors may be at greater risk in terms of absolute incidence, due to their increased rate at baseline.

Piroxicam should be used with caution in patients with a history of bronchial asthma. Poor Metabolisers of CYP2C9

Substrates

Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be administered piroxicam with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.

Sodium

This medicine contains less than 1 mmol sodium (23 mg) per capsule, that is to say essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

Antacids: Concomitant administration of antacids had no effect on piroxicam plasma levels. Anti-coagulants: NSAIDs, including piroxicam, may enhance the effects of anticoagulants, such as warfarin. Therefore, the use

of piroxicam with concomitant anticoagulant such as warfarin should be avoided.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs):
Increased risk of gastrointestinal bleeding.

Aspirin and other Non-Steroidal Anti-Inflammatory Drugs: Piroxicam, like other non-steroidal anti-inflammatory drugs decreases platelet aggregation and prolongs bleeding time. This effect should be kept in mind when bleeding times are determined.

As with other NSAIDs, the use of piroxicam together with acetylsalicylic acid or concomitant use with other NSAIDs, including other piroxicam formulations, must be avoided, since data are inadequate to show that combinations produce greater improvement than that achieved with piroxicam alone; moreover, the potential for adverse reactions is enhanced. Human studies have shown that concomitant use of piroxicam and acetylsalicylic acid reduces the plasma piroxicam concentration to about 80% of the usual value.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma glycoside levels.

Ciclosporin, Tacrolimus: possible increased risk of nephrotoxicity when NSAIDs are given with ciclosporin or tacrolimus.

Cimetidine: Results of two separate studies indicate a slight but significant increase in absorption of piroxicam following cimetidine administration but no significant changes in elimination rate constants or half-life. The small increase in absorption is unlikely to be clinically significant.

Corticosteroids: increased risk of gastrointestinal ulceration or bleeding.

Digoxin, Digitoxin: Concurrent therapy with piroxicam and digoxin, or piroxicam and digitoxin, did not affect the plasma levels of either drug.

Anti-hypertensives including diuretics, angiotensin-converting enzyme (ACE) inhibitors, angiotensin II antagonists (AIIA) and beta-blockers:

NSAIDs can reduce the efficacy of diuretics and other anti-hypertensive drugs including ACE inhibitors, AIIA and beta-blockers. In patients with impaired renal function (e.g. dehydrated patients or elderly patients with the renal function compromised), the co-administration of an ACE inhibitor or an AIIA and/or diuretics with a cyclo-oxygenase inhibitor can increase the deterioration of the renal function, including the possibility of acute renal failure, which is usually reversible.

The occurrence of these interactions should be considered in patients taking piroxicam with an ACE inhibitor or an AIIA and/or diuretics. Therefore, the concomitant administration of these drugs should be done with caution, especially in elderly patients. Patients should be adequately hydrated and the need to monitor the renal function should be assessed in the beginning of the concomitant treatment and periodically thereafter.

Highly protein-bound drugs: Piroxicam is highly protein-bound and therefore might be expected to displace other protein-bound drugs. The physician should closely monitor patients for change when administering Piroxicam to patients on highly protein-bound drugs.

Lithium: Non-steroidal anti-inflammatory drugs, including Piroxicam, have been reported to increase steady state plasma lithium levels. It is recommended that these levels are monitored when initiating, adjusting and discontinuing Piroxicam.

Piroxicam, like other non-steroidal anti-inflammatory drugs, may interact with the following drugs / classes of therapeutic agents

4.6 Fertility, pregnancy and lactation

NSAIDs should not be used during the first two trimesters of pregnancy or labour unless the potential benefit to the patient outweighs the potential risk to the foetus. Piroxicam is not recommended for use in nursing mothers

4.7 Effects on ability to drive and use machines

Not available

4.8 Undesirable effects

The most adverse reactions are nausea and dizziness.

Reporting of suspected adverse reactions:

Healthcare professionals are requested to report any suspected adverse reactions via the national Pharmacovigilance Electronic Reporting Systems to the respective national regulatory authorities.

4.9 Overdose

In the event of overdosage with Piroxicam, supportive and symptomatic therapy is indicated. Studies indicate that administration of activated charcoal may result in reduced re-absorption of piroxicam, thus reducing the total amount of active drug available.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Piroxicam is a non-steroidal anti-inflammatory agent which also possesses analgesic and antipyretic properties. Oedema, erythema, tissue proliferation, fever and pain can all be inhibited in laboratory animals by the administration of piroxicam. It is effective regardless of the aetiology of the inflammation. While its mode of action is not fully understood, independent studies in vitro as well as in vivo have shown that piroxicam interacts at several steps in the immune and inflammation responses through:

Inhibition of prostanoid synthesis, including prostaglandins, through a reversible inhibition of the cyclo-oxygenase enzyme.

Inhibition of neutrophil aggregation.

Inhibition of polymorphonuclear cell and monocyte migration to the area of inflammation. Inhibition of lysosomal enzyme release from stimulated leucocytes.

Reduction of both systemic and synovial fluid rheumatoid factor production in patients with seropositive rheumatoid arthritis.

5.2 Pharmacokinetic properties

Absorption

Piroxicam is well absorbed following oral or rectal administration. With food there is a slight delay in the rate but not the extent of absorption following administration. The plasma half-life is approximately 50 hours in man and stable plasma concentrations are maintained throughout the day on once-daily dosage. Continuous treatment with 20mg/day for periods of 1 year produces similar blood levels to those seen once steady state is first achieved.

Distribution:

Drug plasma concentrations are proportional for 10 and 20mg doses and

generally peak within 3 to 5 hours after medication. A single 20mg dose generally produces peak piroxicam plasma levels of 1.5 to 2 mcg/ml while maximum plasma concentrations, after repeated daily ingestion of 20mg piroxicam, usually stabilise at 3 to 8 mcg/ml. Most patients approximate steady state plasma levels within 7 to 12 days.

Treatment with a loading dose regimen of 40mg daily for the first 2 days followed by 20mg daily thereafter allows a high percentage (approximately 76%) of steady state levels to be achieved immediately following the second dose. Steady state levels, area under the curves and elimination half-life are similar to that following a 20mg daily dose regimen.

A multiple dose comparative study of the bioavailability of the injectable forms with the oral capsule has shown that after intramuscular administration of piroxicam, plasma levels are significantly higher than those obtained after ingestion of capsules during the 45 minutes following administration the first day, during 30 minutes the second day and 15 minutes the seventh day. Bioequivalence exists between the two dosage forms.

A multiple dose comparative study of the pharmacokinetics and the bioavailability of Piroxicam FDDF with the oral capsule has shown that after once daily administration for 14 days, the mean plasma piroxicam concentration time profiles for capsules and Piroxicam FDDF were nearly superimposable. There were no significant differences between the mean steady state C_{max} values, C_{min} values, T_{1/2}, or T_{max} values. This study concluded that Piroxicam FDDF (Fast Dissolving Dosage Form) is bioequivalent to the capsule after once daily dosing. Single dose studies have demonstrated bioequivalence as well when the tablet is taken with or without water.

Biotransformation:

Piroxicam is extensively metabolised and less than 5% of the daily dose is excreted unchanged in urine and faeces. Piroxicam metabolism is predominantly mediated via cytochrome P450 CYP 2C9 in the liver. One important metabolic pathway is hydroxylation of the pyridyl ring of the piroxicam side-chain, followed by conjugation with glucuronic acid and urinary elimination.

Patients who are known or suspected to be poor CYP2C9 metabolizers based on previous history/experience with other CYP2C9 substrates should be

administered piroxicam with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.

5.3 Preclinical safety data

Not Applicable

6. Pharmaceutical particulars

6.1 List of excipients

Maize starch

Lactose

Sodium Lauryl Sulphate

Colloidal Silicon Dioxide

Purified Talc

EHG Gelatin Capsule Scarlet/Scarlet capsules size "2"

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 Months

6.4 Special precautions for storage

Store at a temperature not exceeding 30°C. Protect from light & moisture.

This medicinal product does not require any special storage conditions.

6.5 Nature and contents of container

10 x 10 Capsules packed in Alu PVC blister packed in printed carton with insert.

6.6 Special precautions for disposal and other handling

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

7. Marketing Authorization Holder:

ZAIN PHARMA LIMITED

Plot No: 209/13741, Colchester Park,

Go-Down No.1, 2, 3, Off Mombasa

Road, Behind Nice And Lovely House,
P.O. Box: 100167-00101, Nairobi, Kenya

8. Marketing Authorization Number: --
H2025/CTD12274/26401

9. Date of first Authorization /renewal of the authorization:
2025 December 07

10. Date of revision of text:
2025 December 07