SUMMARY OF PRODUCT CHARACTERISTICS

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

ASPICAM, 15 mg, tablets

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

One tablet contains meloxicam 15 mg (*Meloxicamum*).

Excipient with known effect: lactose monohydrate 256.80 mg.

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Tablet

Round, biconvex, light yellow tablets.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Short- term symptomatic treatment of exacerbations of osteoarthritis.
Long- term symptomatic treatment of rheumatoid arthritis.
Long- term symptomatic treatment of ankylosing spondylitis.

4.2 Posology and method of administration

Oral use.

Adolescents over 15 years and adults usually use:

Short-term symptomatic treatment of exacerbations of osteoarthritis: 7.5 mg per day.
If necessary, in the absence of improvement, the dose may be increased to 15 mg per day.

Long- term symptomatic treatment of rheumatoid arthritis: 15 mg per day.

Long- term symptomatic treatment of ankylosing spondylitis: 15 mg per day.

(See also below ‘Special populations’).

According to therapeutic response, the dose may be reduced to 7.5 mg per day.

DO NOT EXCEED THE DOSAGE 15 mg per day.

The daily dose of Aspicam should be taken as a single dose with a meal, with water or other liquid.
Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to receive therapeutic effect (see section 4.4).

Special Populations

Elderly patients and patients with increased risks for adverse reaction (see section 5.2)
The recommended dose for long- term treatment of rheumatoid arthritis or ankylosing spondylitis in elderly patients is 7.5 mg per day. Patients with increased risks for adverse reactions should start treatment with 7.5 mg per day (see section 4.4).

Renal impairment (see section 5.2)
In dialysis patients with severe renal failure, the dose should not exceed 7.5 mg per day.
No dose reduction is required in patients with mild to moderate renal impairment (i.e. patients with a creatinine clearance of greater than 25 ml/min). For patients with non-dialysed severe renal failure – see section 4.3.

Hepatic impairment (see section 5.2)
No dose reduction is required in patients with mild to moderate hepatic impairment. For patients with severely impaired liver function– see section 4.3.

Children and adolescents
The medicine is contraindicated in children and adolescents aged under 15 years.

4.3 Contraindications

The medicinal product is contraindicated in the following situations:

- pregnancy and lactation (see section 4.6);
- hypersensitivity to meloxicam or to any of the excipients listed in section 6.1, or other non-steroidal anti-inflammatory drugs (NSAIDs).
  Aspicam should not be given to patients who have developed signs of asthma, nasal polyps, angioneurotic oedema or urticaria following the administration of acetylsalicylic acid or other NSAIDs;
- active, or history of recurrent peptic ulcer
- severely impaired liver function;
- non-dialysed severe renal failure;
- gastrointestinal bleeding, cerebrovascular bleeding or other bleeding disorders;
- perforation or gastrointestinal bleeding, related to previous NSAIDs therapy;
- severe heart failure.

4.4 Special warnings and precautions for use

Gastrointestinal effects
Any history of oesophagitis, gastritis and/or peptic ulcer must be sought in order to ensure their total cure before starting treatment with meloxicam. Attention should routinely be paid to the possible onset of a recurrence in patients treated with meloxicam and with a past history of this type.

Patients with a history of gastrointestinal disorder or disease (ulcerative colitis, Crohn's disease), should be monitored for the possibility of gastrointestinal disorders, especially bleeding (see section 4.8).

As with other non-steroidal anti-inflammatory drugs, there have been reports of gastrointestinal bleeding, ulceration and/or perforation (in some cases with fatal outcome). These types of undesirable effects can occur at any time during meloxicam treatment, with or without warning symptoms or a previous history of serious GI events.

GI bleeding, ulceration and/or perforation usually have more severe sequelae in elderly patients (see section 4.8).

In patients with a history of ulcer (particularly if complicated with haemorrhage or perforation), as in the elderly, the risk of GI bleeding, ulceration or perforation increases with increasing dose. In such patients, and also for patients requiring concomitant low dose acetylsalicylic acid, or other drugs likely to increase gastrointestinal risk, should commence treatment on the lowest dose available. Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered.

Patients with a history of GI toxicity with NSAIDs, particularly when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment. Caution is advised in patients receiving concomitant medications which could increase the risk of ulceration or bleeding, such as oral glucocorticoids, anticoagulants such as warfarin, selective serotonin reuptake inhibitors, or platelet-inhibiting drugs such as acetylsalicylic acid.

When GI bleeding or ulceration occurs the treatment should be withdrawn.

Skin reactions
Severe life-threatening hypersensitivity reactions such as anaphylactic reactions and serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, may occur in association with the use of NSAIDSs, including oxicams. Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Meloxicam should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity and patients must be closely monitored.

Parameters of liver and renal function
As with most NSAIDs, occasional increases in serum transaminase levels, increases in serum bilirubin or other liver function parameters, as well as increases in serum creatinine and blood urea nitrogen as well as other laboratory disturbances, may be reported.
The majority of these instances involved transitory and slight abnormalities. Should any such abnormality prove significant or persistent, the administration of meloxicam should be stopped and appropriate investigations undertaken.

Renal impairment
NSAIDs inhibit the synthesis of renal prostaglandins, which are responsible for maintaining renal perfusion in patients with reduced renal blood flow and circulating blood volume. NSAIDs use may lead to decompensation of latent renal failure. However, after withdrawing the treatment, renal function will reverse. This risk is present in all elderly patients, patients with congestive heart failure, liver cirrhosis, nephrotic syndrome, renal failure or lupus nephropathy, hepatic dysfunction as well as patients taking ACE inhibitors, angiotensin-II antagonists, sartans, diuretics or undergoing extensive surgery leading to hypovolemia. Careful monitoring of diuresis and renal function is required in such patients during treatment.
In rare instance NSAIDs may be the cause of interstitial nephritis, glomerulonephritis, renal medullary necrosis or nephrotic syndrome.

Sodium, potassium and water retention
Sodium, potassium and water retention, as well as impaired natriuretic effects of diuretics, may occur with NSAIDs. Consequently, cardiac failure or hypertension may be precipitated or exacerbated in susceptible patients as a result (see sections 4.2 and 4.3). Clinical monitoring is therefore necessary for patients with hypertension or heart failure, especially at the beginning of meloxicam treatment. A decrease of the antihypertensive effect of antihypertensive drugs can occur (see section 4.5).

Hyperkalaemia
Hyperkalaemia may occur especially in patients with diabetes mellitus or during concomitant therapy, which may also increase potassium levels. Regular monitoring of potassium values should be performed in such cases.

Cardiovascular and cerebrovascular effects
Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention. Fluid retention and oedema have been reported in association with NSAID therapy.

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 meloxicam.

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

Elderly
The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation which may be fatal

Adverse reactions are often less well tolerated in elderly, fragile or weakened individuals, who therefore require careful monitoring. As with other NSAIDs, particular caution is required in the elderly, in whom renal, hepatic and cardiac functions are frequently impaired.

Other warnings and precautions
The recommended maximum daily dose should not be exceeded in case of insufficient therapeutic effect, nor should an additional NSAID therapy including cyclooxygenase-2 selective inhibitors be used. This may increase the toxicity while therapeutic advantage has not been proven. If there is no improvement after a few days of treatment, the clinical benefit of treatment should be reassessed.

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular effects).

Meloxicam, as any other NSAID may mask symptoms of an underlying infectious disease.

Meloxicam should not be used in children and adolescents aged under 15 years.

Excipients
The product contains lactose. It should not be used in patients with rare hereditary galactose intolerance, lactase deficiency (Lapp type) or glucose-galactose malabsorption.

4.5 Interaction with other medicinal products and other forms of interaction

Interaction studies have only been performed in adults.

Pharmacodynamic interactions

Other non-steroidal anti-inflammatory drugs (NSAIDs) and acetylsalicylic acid ≥ 3g/d
The concomitant use of several NSAIDs may increase the risk of ulceration and bleeding due to synergistic effects. Combination of meloxicam with other NSAIDs is not recommended (see section 4.4).

Diuretics
Concomitant administration with NSAIDs may cause severe renal impairment, especially in dehydrated patients. Patients receiving concomitant meloxicam and diuretics should be adequately hydrated. Renal function should be checked before starting treatment (see section 4.4).

Oral anticoagulants
There is an increased risk of bleeding due to inhibition of platelet function and damage to the gastrointestinal mucosa. The concomitant use of NSAIDs and oral anticoagulants is not recommended (see section 4.4).
Careful monitoring of the International Normalized Ratio (INR) is required if it proves impossible to avoid such combination.

Thrombolytics, antiplatelet drugs
Increased risk of bleeding, via inhibition of platelet function and damage to the gastroduodenal mucosa.

Selective serotonin reuptake inhibitors (SSRIs)
Increased risk of gastrointestinal bleeding (see section 4.4).

ACE inhibitors and Angiotensin-II Antagonists
NSAIDs (including acetylsalicylic acid ≥ 3g/d) and Angiotensin-II antagonists exert a synergistic effect on reducing glomerular filtration. This effect may be increased in renal impairment. In elderly and/or dehydrated patients, concomitant use of these drugs may lead to acute renal failure by directly affecting glomerular filtration. Monitoring of renal function at the beginning of therapy is recommended as well as adequately hydrated. In addition, combination therapy may reduce the antihypertensive effect of ACE inhibitors and angiotensin-II receptor antagonists, leading to a reduction in the effectiveness of treatment (due to inhibition of vasodilatory prostaglandin synthesis).

Other antihypertensive drugs (e.g. Beta-blockers)
As for the latter, a decrease of the antihypertensive effect of beta-blockers (due to inhibition of prostaglandins with vasodilatory effect) can occur.

Cyclosporine
Nephrotoxicity of calcineurin inhibitors may be enhanced by NSAIDs via renal prostaglandin mediated effects. During combined treatment renal function is to be measured. A careful monitoring of the renal function is recommended, especially in the elderly.

Corticosteroids
An increased risk of bleeding or gastrointestinal ulceration is possible.

Intrauterine devices
NSAIDs have been reported to decrease the efficacy of intrauterine devices. A decrease of the efficacy of intrauterine devices by NSAIDs has been previously reported but needs further confirmation.

<u>Pharmacokinetic interactions (effect of meloxicam on the pharmacokinetics of other drugs)</u>

Lithium
NSAIDs have been reported to increase blood lithium levels (via decreased renal excretion of lithium), which may reach toxic values. The concomitant use of lithium and NSAIDs is not recommended (see section 4.4). If this combination appears necessary, lithium plasma concentrations should be monitored carefully during the initiation, adjustment and withdrawal of meloxicam treatment.

Methotrexate
NSAIDs can reduce the tubular secretion of methotrexate thereby increasing the plasma concentrations of methotrexate. For this reason, for patients on high dosages of methotrexate (more than 15 mg/week) the concomitant use of NSAIDs is not recommended (see section 4.4).
The risk of an interaction between NSAID preparations and methotrexate, should be considered also in patients on low dosage of methotrexate, especially in patients with impaired renal function. In case combination treatment is necessary blood cell count and the renal function should be monitored. Caution should be taken in case both NSAID and methotrexate are given within 3 days, in which case the plasma level of methotrexate may increase and cause increased toxicity.

Although the pharmacokinetics of methotrexate (15mg/week) were not relevantly affected by concomitant meloxicam treatment, it should be considered that the haematological toxicity of methotrexate can be amplified by treatment with NSAID drugs – see above (see section 4.8).

Pharmacokinetic interactions (effect of other drugs on the pharmacokinetics of meloxicam)

Cholestyramine
Cholestyramine accelerates the elimination of meloxicam by interrupting the enterohepatic circulation so that clearance for meloxicam increases by 50% and the half-life decreases to 13±3 hours. This interaction is of clinical significance.

No clinically relevant pharmacokinetic drug-drug interactions were detected with respect to the concomitant administration of antacids, cimetidine and digoxin.

4.6 Pregnancy and lactation

Fertility
The use of meloxicam may adversely affect female fertility and it is not recommended for women who are planning to become pregnant. For women who have difficulties conceiving or who are undergoing investigation of infertility, consideration should be given to stopping treatment with meloxicam.

Pregnancy
Inhibition of prostaglandin synthesis may adversely affect the pregnancy and/or the embryo or foetal development. Data from epidemiological studies suggest an increased risk of miscarriage and of cardiac and gastrointestinal malformation after use of a prostaglandin synthesis inhibitor in early pregnancy. The absolute risk for cardiovascular malformation was increased from less than 1 %, up to approximately 1.5 %. The risk is believed to increase with dose and duration of therapy.

In animals, the lethal dose to the foetus was higher than the clinically used doses. An increased incidence of various congenital malformations, including cardiovascular malformations, has been observed in animals treated with prostaglandin synthesis inhibitors during the organogenesis period.

Meloxicam should be avoided in women during the first two trimesters of pregnancy.

In the final three months of pregnancy, all prostaglandin synthesis inhibitors may damage the foetus:
- circulatory system (pulmonary hypertension with premature closure of the ductus arteriosus),
- kidneys (which can lead to the development of renal failure with oligohydramnios).

All prostaglandin synthesis inhibitors administered to women in the third trimester of pregnancy may:
- cause prolonged bleeding time in both mothers and new-borns as well as anti-aggregation effects, even after using very low doses of the drug,
- inhibit uterine contractility. This effect on the uterus was associated with an increased incidence of dystocia and delayed delivery in animals.

Consequently, meloxicam is contraindicated during the third trimester of pregnancy.

Breastfeeding
NSAIDs are known to pass into mother's milk. Administration therefore is not recommended in women who are breastfeeding.

4.7 Effects on ability to drive and use machines

There are no specific studies on the ability to drive and use machinery of Aspicam. On the basis of the pharmacodynamic profile and reported adverse drug reactions, it is likely to have no or negligible influence on the ability to drive and use machinery. However, when visual disturbances or drowsiness,

vertigo or other central nervous system disturbances occur, it is advisable to refrain from driving and operating machinery.

4.8 Undesirable effects

a) General description

The following are side effects that may be causally related to meloxicam. The incidence of these adverse reactions is based on relevant clinical trial data, regardless of causation. This information comes from clinical studies in 3750 patients who were treated with meloxicam tablets or capsules at 7.5 mg or 15 mg daily oral doses for up to 18 months (mean treatment duration 127 days).

Adverse drug reactions that have come to light as a result of reports received in relation to administration of the marketed product are included.

Adverse reactions have been ranked under headings of frequency using the following convention:

Very common:	≥ 1/10
Common:	≥ 1/100, < 1/10
Uncommon:	≥ 1/1000, < 1/100
Rare:	≥ 1/10000, < 1/1000
Very rare:	< 1/10000, including single cases
Not known:	cannot be estimated from the available data

b) Summary of adverse reactions

Blood and lymphatic system disorders

Common:	anaemia
Uncommon:	blood count abnormal: leukopenia, thrombocytopenia, agranulocytosis (see section c)

Immune system disorders

Rare:	anaphylactic or anaphylactoid reaction

Psychiatric disorders

Rare:	mood altered, insomnia and nightmares

Nervous system disorders

Common:	dizziness, headache
Uncommon:	vertigo, tinnitus, drowsiness
Rare:	confusion

Eye disorders

Rare:	visual disturbance including blurred vision

Cardiac disorders

Uncommon:	palpitations, cardiac failure

Vascular disorders

Uncommon:	blood pressure increased (see section 4.4), flushing

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), see section 4.4.
Oedema, hypertension and heart failure have been reported in association with NSAID treatment.

Respiratory, thoracic and mediastinal disorders

Rare:	asthma in individuals allergic to acetylsalicylic acid or other NSAIDs

Gastrointestinal disorders

Common:	dyspepsia, nausea, vomiting, abdominal pain, constipation, flatulence, diarrhoea
Uncommon:	gastrointestinal haemorrhage, duodenal and gastric ulcer, oesophagitis, stomatitis (also ulcerative)
Rare:	gastrointestinal perforation, gastritis, colitis
Not known	pancreatitis

Gastrointestinal haemorrhage, ulceration or perforation may sometimes be severe and potentially fatal, especially in elderly (see section 4.4). Other side effects such as melaena, haematemesis or exacerbation of Crohn's disease may also occur.

Hepatobiliary disorders

Uncommon:	transient liver function disorder (e.g. raised transaminases or bilirubin)
Rare:	hepatitis

Skin and subcutaneous tissue disorders

Common:	pruritus, rash
Uncommon:	urticaria
Rare:	Stevens-Johnson syndrome, toxic epidermal necrolysis, angioedema, erythema multiforme, photosensitivity reaction

Renal and urinary disorders

Uncommon:	sodium and water retention, hyperkalaemia, renal function test abnormal – increased serum creatinine and/or serum urea
Rare:	renal failure (see section 4.4)

General disorders and administration site conditions

Common:	oedema including oedema of the lower limbs.

c) Information characterising individual serious and/or frequently occurring adverse reactions

Very rare cases of agranulocytosis have been reported in patients treated with meloxicam and other potentially myelotoxic drugs (see section 4.5).

d) Adverse reactions which have not been observed yet in relation meloxicam, but which are generally accepted as being attributable to other compounds in the class

Organic renal injury probably resulting in acute renal failure: very rare cases of interstitial nephritis, acute tubular necrosis, nephrotic syndrome, and papillary necrosis have been reported.

Reporting of suspected adverse reactions
Reporting of suspected adverse reactions after authorisation of the medicinal product is important. This allows continuous monitoring of the benefit/risk balance of the medicinal product. Healthcare

professionals are asked to report any suspected adverse reactions via the Pharmacovigilance Department of the Office for Registration of Medicinal Products, Medical Devices and Biocidal Products
Al. Jerozolimskie 181C, 02-222 Warsaw
tel.: + 48 22 49 21 301, fax: + 48 22 49 21 309
e-mail: ndl@urpl.gov.pl
Adverse reactions may also be reported to the marketing authorization holder.

4.9 Overdose

Symptoms

Symptoms following acute NSAID overdose are usually limited to lethargy, drowsiness, nausea, vomiting and epigastric pain, which are generally reversible with supportive care. Gastrointestinal bleeding can occur. Severe poisoning may result in hypertension, acute renal failure, hepatic dysfunction, respiratory depression, coma, convulsions, cardiovascular collapse and cardiac arrest. Anaphylactoid reactions have been reported with therapeutic ingestion of NSAID and may occur following an overdose.

Treatment

Patients should be managed with symptomatic and supportive care following an NSAID overdose. Accelerated removal of meloxicam by 4 g oral doses of cholestyramine given three times a day was demonstrated in a clinical trial.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Non-steroidal anti-inflammatory agents, oxicams.
ATC code: M01AC06

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) of the oxicam family.

It has anti-inflammatory, analgesic and antipyretic properties.

The anti-inflammatory activity of meloxicam has been proven in classical models of inflammation.

As with other NSAID, its precise mechanism of action remains unknown. However, there is at least one common mode of action shared by all NSAID (including meloxicam): inhibition of the biosynthesis of prostaglandins, known inflammation mediators.

5.2 Pharmacokinetic properties

Absorption
Meloxicam is well absorbed from the gastrointestinal tract, which is reflected by a high absolute bioavailability of 89% following oral administration.
Following single dose administration of meloxicam (tablet), mean maximum plasma concentrations achieved within 5-6 hours.
With multiple dosing, steady state conditions were reached within 3 to 5 days. Once daily dosing leads to drug plasma concentrations with a relatively small peak-trough fluctuation in the range of 0.4-1.0 μg/ml for 7.5 mg doses and 0.8-2.0 μg/ml for 15 mg doses, respectively (C_{min} and C_{max} at steady state, respectively). Maximum plasma concentrations of meloxicam at steady state, are achieved within five to six hours for tablets.

Continuous treatment for more than a year leads to the similar levels to those seen when steady state is reached for the first time. Extent of absorption for meloxicam following oral administration is not altered by concomitant food intake.

Distribution
Meloxicam is very strongly bound to plasma proteins, essentially albumin (99%).
Meloxicam penetrates into synovial fluid to give concentrations approximately half of those in plasma. Volume of distribution is low, on average 11 L. Inter-individual variation is the order of 30-40%.

Biotransformation
Meloxicam undergoes extensive hepatic biotransformation.
Four different metabolites of meloxicam were identified in urine, which are all pharmacodynamically inactive. The major metabolite, 5'-carboxymeloxicam (60% of dose), is formed by oxidation of an intermediate metabolite 5'-hydroxymethylmeloxicam, which is also excreted to a lesser extent (9% of dose). *In vitro* studies suggest that CYP 2C9 plays an important role in this metabolic pathway, with a minor contribution from the CYP 3A4 isoenzyme. The patient's peroxidase activity is probably responsible for the other two metabolites, which account for 16% and 4% of the administered dose respectively.

Elimination
Meloxicam is excreted predominantly in the form of metabolites and occurs to equal extents in urine and faeces. Less than 5% of the daily dose is excreted unchanged in faeces, while only traces of the parent compound are excreted in urine. The mean elimination half-life is about 20 hours. Total plasma clearance amounts on average 8 mL/min.

Linearity/non-linearity
Meloxicam demonstrates linear pharmacokinetics in the therapeutic dose range of 7.5 mg 15 mg following per oral administration.

Special populations

Hepatic or renal insufficiency
Neither hepatic, nor mild nor moderate renal insufficiency has a substantial effect on meloxicam pharmacokinetics. In terminal renal failure, the increase in the volume of distribution may result in higher free meloxicam concentrations, and a daily dose of 7.5 mg must not be exceeded (see section 4.2).
Meloxicam is contraindicated in patients with severe hepatic impairment and in non-dialysed patients with severe renal impairment (see section 4.3).

Elderly
Mean plasma clearance at steady state in elderly subjects was slightly lower than that reported for younger subjects.

5.3 Preclinical safety data

Preclinical studies in animals have shown that the damaging effect of meloxicam after long-term use of high doses is the same as for other NSAIDs: gastrointestinal ulcers and erosions, renal papillary necrosis. Reproductive studies in the rats have shown a decrease of ovulations and inhibition of implantations and embryotoxic effects (increase of resorptions) at maternotoxic dose levels at 1 mg/kg and higher.

The affected dose levels exceeded the clinical dose (7.5-15 mg) by a factor of 10 to 5-fold on a mg/kg dose basis (75 kg person). Foetotoxic effects of meloxicam at the end of gestation, shared by all prostaglandin synthesis inhibitors, have been described. No evidence has been found of any mutagenic effect, either *in vitro* or *in vivo*.

No carcinogenic risk has been found in the rat and mouse at doses far higher than those used clinically.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate
Povidone
Crospovidone
Magnesium stearate

6.2 Incompatibilities

Not applicable

6.3 Shelf life

3 years

6.4 Special precautions for storage

Store below 25°C.

6.5 Nature and contents of container

PVC/PVDC/Aluminium blisters in a carton box.

Pack sizes:
10 tablets
20 tablets
30 tablets
60 tablets

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. MARKETING AUTHORISATION HOLDER

Biofarm Sp. z o.o.,
13 Wałbrzyska St.
60-198 Poznań – Poland

8. MARKETING AUTHORISATION NUMBER

MA No.: 9975

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18 August 2003.

Date of latest renewal: 30 July 2014.

10. DATE OF REVISION OF THE TEXT

24.05.2017