SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

BACTIGRAM 500 mg rigid capsules
BACTIGRAM 250 mg/5 ml granules for oral suspension

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

BACTIGRAM 500 mg hard capsules
One capsule contains:
Active substance
Cefaclor monohydrate equal to Cefaclor 500 mg

BACTIGRAM 250 mg/5 ml granules for oral suspension
5 ml suspension prepared as indicated contain:
Active substance
Cefaclor monohydrate equal to Cefaclor 250 mg

For the complete list of excipients, see paragraph 6.1

3. PHARMACEUTICAL FORM

BACTIGRAM 500 mg rigid capsules. Hard gelatine capsules.
BACTIGRAM 250 mg/5 ml granules for oral suspension. Granules for the preparation of an extemporaneous suspension for oral use.

4.- CLINICAL INFORMATION

4.1. Therapeutic indications

Cefaclor is indicated for the treatment of the following infections sustained by sensitive germs:

- Infections of the respiratory apparatus, including penumonia, bronchitis, re-acutisation of chronic bronchitis, pharyngitis and tonsillitis;
- otitis media;
- infections of the skin and soft tissues;
- infections of the urinary apparatus, including pielonephritis and cystitis;
- synusitis;
- gonococcic urethritis.

4.2.- Dosage and administration method

Cefaclor is administered orally.
Adults: the normal dosage for adults corresponds to 250 mg every 8 hours. In more serious infections or in infections caused by less sensitive germs, higher doses may be necessary. The maximum recommended dose is 2 g per day, even though doses of 4 g per day have been administered to normal subjects for 28 days without the occurance of unfavourable effects. In the treatment of acute gonococcic urethritis in both sexes a single 3 g administration of cefaclor associated, if necessary, with 1 g probenicid is recommended.
Children*:* the normal daily dosage for children corresponds to 20 mg/kg in fractioned doses administered every 8 hours.

In more serious infections, in otitis media and in infections caused by less sensitive germs, a dosage of 40 mg/kg up to a maximum daily dose of 1 g is recommended.

Alternative dosage: in otitis media and pharyngitis the total daily dose can be administered in fractioned doses every 12 hours.
See package leaflet for further details concerning the pediatric dosage.

4.3.- Contraindications
Hypersensitivity to the active principle or to any excipients.

4.4.-Special warnings and precautions
Before starting therapy with Cefaclor, we recommend to carefully evaluate the benefit/risk ratio for each single patient. In particular, we recommend to carry out a careful family and individual anamnesis concerning the occurrance of hypersensitivity reactions to this or other drugs.
It must be carefully evaluated if the patient has had hypersensitivity reactions to cephalosporins and penicillins in the past. Cephalosporin C derivatives should be administered with caution to penicillin-sensitive patients. Evidence exists of a partial crossed allergic reaction between penicillins and cephalosporins. It is therefore necessary to take suitable precautions to prevent undesired reactions.
There have been patients who have experienced serious reactions (anaphylaxis included) following the administration of penicillin or cephalosporin, mediated IgE reactions usually manifested a the cutaneous, gastroenteric, respiratory and cardio-circulatory level.
The symptoms may be: sudden and serious hypotension, pulse acceleration and slowdown, unusual tiredness or weakness, anxiety, agitation, dizziness, loss of consciousness, difficulty in breathing or swallowing, generalised itchiness especially on the soles of the feet and the palms of the hand, nettle rash with or without angioedema (swollen and itchy skin areas, most frequently localised at the extremes, external genitals and face, above all in the eye and lip areas) skin reddening, especially around the eyes, cyanosis, abundant perspiration, nausea, vomiting, cramp like abdominal pains, diarrhea.
The possible insurgence of pseudomembraneous cholitis in patients treated with broad spectrum antibiotics must be taken into careful consideration in patients who develop diarrhea during chemotherapy with antibiotics.

Use during pregnancy. There is no sufficient evidence of cefaclor tolerability during pregnancy.
Keep out of reach and sight of children.

ATTENTION: BACTIGRAM 250 mg/5 ml granules for oral suspension: 5 ml suspension contain 2,863 g of saccharose. The medicine is therefore contraindicated in cases of hereditary intolerance to fructose, glucose and galactose malabsorption syndrome and in saccharose-isomaltose deficiency.
In the case of allergic reactions to cefaclor, the administration of the drug must be interrupted and the patient suitably treated.
The prolonged use of cefaclor can give rise to a development of non-sensitive germs; if a bacterial super-infection arises during therapy, it must be treated suitably.
Cefaclor should be administrated carefully in patients with considerably reduced kidney functionality. In these cases, the dosage should be lower than the generally recommended one.

After the administration of cefaclor, it is possible to obtain falsely positive reactions to urinary glucose with Benedict, Fehling and Clinitest solutions, but not with Test Tape (glucose in urine enzymatic test, Lilly).
Broad spectrum antibiotics should be prescribed with caution in subjects with an anamnesis of intestinal disorders, in particular cholitis.

Instructions for use
BACTIGRAM ***250 mg / 5 ml granules for oral suspension***
- Shake well the vial before adding water to facilitate the dispersion of the granulate;
- Add water to the level indicated by the arrow on the label.
- Tap and shake well until the suspension is homogeneous; the volume will lower below the level indicated by the arrow.
- Add water again to return the volume to the level indicated by the arrow on the label.
- Shake well until you get a uniform suspension,

If prepared according to these instructions, 5 ml of the suspension will contain 250 mg of Cefaclor.
Shake the suspension well before each administration

4.5.- Interactions with other drugs and other forms of interactions
Similarly to other beta-lactamic antibiotics, the excretion of cefaclor through the kidneys is inhibited by the administration of probenicid.
It has been widely observed that the presence of food reduces and delays the maximum concentrations of cefaclor in blood without altering the total quantity present in urine.

4.6.- Pregnancy and breastfeeding
There is no sufficient evidence of cefaclor tolerability during pregnancy.
The drug should only be administered to pregnant women in the case of effective need and under medical supervision.
Small quantities of cefaclor have been found in breastmild after the administration of single 500 mg doses. As the effects of cefaclor in breast-fed babies is not known, caution is recommended in the use of this drug.

4.7.- Effects on the ability to drive vehicles and use machinery
BACTIGRAM does not affect the ability to drive vehicles or use machinery.

4.8.- Undesired effects
The adverse reactions considered as attributable to treatment with cefaclor are the following:
Hypersensitivity: Hypersensitivity reactions have been observed in 1,5% of the patients, including morbiliform eruptions (1 out of 100); itchiness, urticaria, and positive Coombs tests are observed in less than 1 patient out of 200 treated patients.
Generalised reactions have also been reported called “serum-similar illnesses” in association with the use of cefaclor. These are characterised by multiform erythema, skin eruptions and other manifestations affecting the skin, accompanied by arthritis and/or arthralgia with or without fever. They differentiate themselves from the classical serum illnesses as lymphadenopathy and proteinuria are rarely present and as there are no circulating immune complexes. Furthermore, until now there is no evidence of how the reaction sequence takes place.
While research is still under way, the “serum-similar illness” reactions seem to occur more often during and after a treatment cycle with cefaclor.

These reactions have been reported more frequently in children than adults: there has been an incidence of 1 out of 200 (0,5%) during a clinical study and of 2 out of 8.346 (0,024%) during other clinical works (the incidence in children corresponded to 0,055%) and, finally, of 1 out of 38,000 (0,003%) in the ambit of spontaneous events. Signs and symptoms occur a few days after starting the therapy and cease a few days after its conclusion.
Only rarely have these reactions lead to hospitalisation which has generally been very short (averagely from 2 to 3 days according the the "Post-Marketing Surveillance studies)
Patients who had been hospitalised showed slight to severe symptoms (more severe in children). Antihistamines and cortisonic drugs reduce the related signs and symptoms.
No severe cases were reported.
Serious hypersensitivity reactions, including the Steven-Johnson syndrome, epidermic toxic necrolysis and anaphylaxis were observed rarely.
Severe hypersensitivity reactions have been rarely observed, including the Steven-Johnson symdrome, epidermic toxic necrolysis and anaphylaxis.
Very rare cases with fatal outcome have been reported; the occurrance and the evolution of a serious anaphylactic reaction can be very rapid and therefore it is necessary to adopt all useful precautions to avoid it (see point 4.4).
Anaphylaxis can be observed more often in patients allergic to penicillin.
Gastroenteric effects: these are present in around 2.5% of patients, even with the appearance of diarrhea (1 out of 70 patients treated). Pseudomembranous cholitis can be observed during or after the treatment with antibiotics. Nausea and vomiting are rarely observed. Transitory hepatitis and cholestatic jaundice have been observed rarely with some kinds of penicillin and cephalosporin.
Other effects: angioedema, eosinophilia (1 out of 50 patients treated), genital itching, vaginal moniliasis, vaginitis (less than 1 out of 100), and rarely, thrombocytopenia and reversible, interstitial nephritis. Cases of haemolytic anaemia following treatment with cephalosporin have been reported.
Effects that cannot be attributed to the treatment with certainty:
Central nervous system: rarely reversible hyperactivity, restlessness, insomnia, mental confusion, hypertonia, hallucinations, sense of instability and swaying, sleepiness.
Transitory alterations of the haematochemical values have been reported. The following information is reported for clinical purposes even though their aetiology is still uncertain.
Alterations of the hepatic function: Slight increases in SGOT and SGPT values or in alkaline phosphatasis have been observed (1 out of 40).
Haematologic alterations: as with other betalactamic antbiotics, transitory lymphocytosis, leukopenia and rarely haemolytic anaemia, aplastic anaemia, agranulocytosis, and reversible neutropenia, which could possibly have a clinical significance, have been reported. There have been rare reports of increased prothrombin time, with or without clinical bleeding in patients that received cefaclor and Warfarin sodium.
Kidney alterations: Slight increases of azotemia or creatininaemia (less than 1 out of 500) or alterations of the urine test results (less than 1 out of 200) were reported.

Reporting suspected adverse reactions
Reporting suspected adverse reactions occurring after the authorization of the medicine is important, as it allows continuous monitoring of the benefit / risk ratio of the drug. Healthcare professionals are required to report any suspected adverse reactions via the national reporting system at http://www.agenziafarmaco.gov.it/en/responsabili.

4.9.- Overdose

Signs and symptoms: toxic symptoms deriving from an overdose of cefaclor may include nausea, vomit, gastric disturbances and diarrhea. The severity of epigastric disorders and of diarrhea depends the on the dosis taken. If other symptoms occur, they are probably secundary to the basic pathology, to an allergic reaction or to some other intoxication.

Treatment: always consider that an overdose may be caused by several drugs, by interactions beteween drugs and by the patient's particular pharmacokynetics. Gastrogavage is unnecessary if the patient has not ingested a dose 5 times higher than the recommended cefaclor dose.

The patient should be monitored carefully, especially checking the pulmonary ventilation and perfusion, vital signs, haemo-gas-analysis, serum electrolytes etc.

Intestinal absorption can be reduced by administering active carbon which, in many cases, is more efficacious than induced vomiting or gastrogavage; coals is therefore considered as an alternative treatment or in addition to gastric emptying. The repeated administration of active carbon can facilitate the elimination of other drugs that may have been taken. Carefully check the patients airways during gastric emptying and when using active carbon.

It is not known if forced diuresis, peritoneal dialysis, haemo-dialysis or haemo-perfusion with coal are beneficial to the patient in cases of cefaclor overdosage.

5.- PHARMACOLOGICAL PROPERTIES

5.1.- Pharmacodynamic properties

Pharmacodynamical properties

Pharmacotherapeutic category: antibiotic for oral use belonging to the cephalosporin class – ATC Code J01DC04

In-vitro tests have demonstrated that the bactericidal action of cephalosporin is exerted through the inhibition of the cell wall synthesis.

In vitro, cefaclor is active against the following microorganisms:

- Alpha-haemolitic and Beta-haemolitic streptococci
- Staphilococci, including the positive and negative coagulasis strains and those producing penicillinase
- Streptococcus (Diplococcus) pneumonite.
- Escherichia coli.
- Proteus mirabilis.
- Klebsiella sp.
- Moraxella (Branhamella) catarrhalis.
- Haemophilus influenzae, includine ampicillin-resistant strains.

Note: cefaclor is not active on Pseudomonas sp. and on the greates part of the enterococci-strains (Streptococcus faecalis), Enterobacter sp., indole-positive Proteus and Serratia. Some rare stafilococci strains are resistant to cefaclor.

5.2.- Pharmacokynetic properties

Cefaclor is well absorbed after oral administration, both in association with food and on an empty stomach. With doses of 250 mg, 500 mg and 1 g, the seric peaks observed after 30-60 minutes corresponded respectively to 7, 13 e 23 mcg/ml. About 60-85% of the drug is excreted, unvaried, in urine within 8 hours after administration.

During this time the maximum concentration in urine after the administration of 250 mg, 500 mg ed 1 g doses corresponded respectively to about 600, 900 e 1.900 mcg/ml.

Cefaclor is very well metabolised. The presence of food in the gastrointestinal tract dealys the absorption and reduces seric peaks. It does however not alter the total absorbed quantity of cefaclor.

5.3.- Pre-clinical safety data

Tests carried out on mice, rats, guinea pigs and dogs showed that the drug has a low toxicity. When administered to rats orally or intraperitoneally, DL50 values were higher than 5g/kg . Also dogs and monkeys could tolerate high drug doses (DL50 > 1g/kg) with occasional vomit and diarrhea events.
Cefaclor is neither teratogenic nor mutagenic.

6.- PHARMACEUTICAL INFORMATION

6.1.- List of excipients

BACTIGRAM 500 mg hard capsules

Maize starch, dimethicone, magnesium stearate (E572).
The capsule is constituted by: titanium dioxyde (E171), Indigotin (E132), gelatine.

BACTIGRAM 250 mg/5 ml granules for oral suspension

dimethicone, polysaccharide gum, starch, erythrosine E127 aluminium lacquer, strawberry aroma, lauryl-bisulphate, methylcellulose, saccharose.

6.2.- Incompatibility

Not Applicable

6.3.- Shelf life

*BACTIGRAM **500 mg hard capsules**: 2 years*
*BACTIGRAM **250 mg/5 ml granules for oral suspension**:3 years*
The use-by-date refers to the product in unopened packaging, correctly stored at a temperature not higher than 30°C

6.4.- Special storage precautioins

*BACTIGRAM **500 mg hard capsules***
Store at a temperature not higher than 30°C.
*BACTIGRAM **250 mg/5 ml granules for oral suspension***
No special storage precaution required.
Once prepared, the suspension must be kept in the refrigerator between 2° and 8° and used within 14 days.

6.5.- Nature and content of the container

*BACTIGRAM **500 mg hard capsules**:* Box containing 1 blister-pack with 8 capsules.
*BACTIGRAM **250 mg/5 ml granules for oral suspension**:* Box containing 1 yellow glass vial of 100 ml.

6.6.- Special precautions for disposal

No special precaution for disposal.
The unused medicinal product and any waste derived from it must be disposed of in compliance with local laws.

7.- MARKETING AUTHORISATION HOLDER

MAGIS FARMACEUTICI S.r.l. - Via Cefalonia, 70 – 25124 Brescia

8.- MARKETING AUTHORISATION NUMBER(S)

BACTIGRAM 500 mg hard capsules: MA n. 034619027
BACTIGRAM 250 mg/5ml granules for oral suspension: Ma n. 034619015

9.- DATE OF THE FIRST AUTHORISATION/AUTHORISATION RENEWAL

Renewal date: December 2011

10.- TEXT REVISION DATE

March 2017