SUMMARY OF THE PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICNAL PRODUCT

BACTIGRAM 750 mg tablets with modified release formulation

2. QUALITATIVE AND QUANTITATIVE CMPOSITION

One tablet contains:
Attive substance:
Cefaclor monohydrate equal to Cefaclor 750 mg
Excipients:
Mannitol
For the complete list of excipients, see paragraph 6.1

3. PHARMACEUTICAL FORM

Tablets with modified release formulation

4. CLINICAL INFORMATION

4.1. Therapeutic information

BACTIGRAM 750 mg tablets with modified release formulation is indicated for the treatment of particularly severe forms of the following infections: :

- acute bronchitis and re-acutisation of chronic bronchitis;
- pharyngitis and tonsillitis;
- infections of the skin and soft tissues;
- non complicated infections of the low urinary tract

4.2. Dosage and administration method

BACTIGRAM is administered orally and can be taken independently of meals. The concomitant food assumption increases the absoption of BACTIGRAM (see Pharmacokynetics). The tablets must be taken whole. Do not break, crush or chew them.
The following dosage scheme can be followed:
- Pharyngitis, tonsillitis and infections of the skin and soft tissues: 750 mg 2 times per day.
- Non complicated infections of the low urinary tract: 750 mg 2 times per day.
- Bronchitis: 750 mg 2 times per day.

In the treatment of infections from S. Pyogenes (streptococci of the A group), the therapy with BACTIGRAM should last 10 days.

4.3. Contraindications

Hypersensitivity to the active principle or to any excipients and to other cephalosporins or penicillins (see par. 4.4).

4.4.Special warnings and use 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 or other drugs 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 (including anaphylaxis).
There are 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.

In the case of allergic reactions to BACTIGRAM, the administration of the drug must be interrupted.
Treatment with broad-band antibiotics, including BACTIGRAM, alters the normal bacterial flora of the colon and determines an increase of clostrides. Various studies have demonstrated that a toxin produced by the Clostridium difficile is the main cause for severe diarrhea associated with antibiotic therapy, including pseudomembranous cholitis. This diagnosis must therefore be taken into careful consideration in patients who develop diarrhea during therapy with these antibiotics.
As with other antibiotics, during treatment with BACTIGRAM, the possible insurgence of resistant microorganisms which could lead to a superinfection must be taken into consideration as well as the adoption of suitable measures.
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).
Pediatric use – The effectiveness and the tolerability in children have not been clearly ascertained.
BACTIGRAM is administered orally and can be taken independently of meals. The tablets should be taken full and therefore not broken, crushed or chewed.

4.5. Interactions with other drugs and other forms of interaction

The absorbption of BACTIGRAM decreases if within one hour from the antibiotic assumption antiacids containing magnesium hydroxide or aluminium are administered. H2-blockers do not alter BACTIGRAM absorption speed and quantity.
Similarly to other b-lactamic antibiotics, the excretion of BACTIGRAM through the kidneys is inhibited by the administration of probenicid; in the course of clinical studies no significant interactions with other drugs were observed.

4.6. Pregnancy and breastfeeding

No specific and well controlled studies were carried out on pregnant women and, as studies on animal reproduction are not always predictive of human response, this drug should only be administered during pregnancy in case of effective need.
The use of BACTIGRAM during labor and delivery has not been studied; therefore the drug should only be given if it is needed.

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.

Important information about some of the excipients:
This medicinal product contains mannitol and may therefore have a mild laxative effect.

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 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.
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.
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.).
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.
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 BACTIGRAM may include nausea, vomit, gastric disturbances and diarrhea.,
Treatment: the intestinal absorption could be reduced by induced vomit, gastrogavage or the administration of active carbon. Forced diuresis, peritoneal dialysis, heamodialysis or haemoperfusion have not shown to accelerate the elimination of BACTIGRAM.

5. PHARMACOLOGICAL PROPERTIES
5.1. Pharmacodynamical properties
Pharmacotherapeutic category: antibiotic for oral use belonging to the cephalosporin class – ATC Code J01DC04
BACTIGRAM exerts its bactericidal action by binding to specific essential proteins of the bacteric wall and by inducing the inhibition of the wall synthesis.
BACTIGRAM shows a wide spectrum antibacterial activity in vitro. It is active against staphilococci (including the S. aureus strains which produce penicillinase), streptococci, Haemophilus sp., Moraxella (branhamella) catarrhalis (including the strains producing b-lactamase) and against the greatest part of commonly isolated Gram-negative bacilli.
Serratia sp., Pseudomonas sp., Acinetobacter calcoaceticus, indole-positive Proteus, meticillin resistano enterococci and stafilococci are usually resistent to BACTIGRAM in vitro.

5.2. Pharmacokynetic properties
After oral administration, BACTIGRAM is well absorbed by the gastro-intestinal tract: it can be taken independently of meal, however food can increase its systemic bioavailability. When BACTIGRAM is taken within one hour after the meal, the bioavailability is 91-94% compared to the one of BACTIGRAM.

After fasting administration, bioavailability was 77% of BACTIGRAM and the average blood counts are lower (21-34%) and were reached 45-60 minutes earlier.
The concomitant assumption of H2-blockers does not influence the absorption speed and quantity.
The administration of antiacids containing magnesium hydroxie or aluminium one hour after the assumption of BACTIGRAM does not alter its absorption speed, but causes a decrease in bioavalability (17%).
After administering doses of 375 mg and 750 mg to patients with a full stomach within 2,5-3 hours, haematic peaks of respectively 4 and 11 mg/ml were observed. No accumulation was observed when administering the drug twice a day.
In healthy subjects, the plasmatic half-life corresponds to about 1 hour independently of the pharmaceutical form.
Elderly subjects (age > 65 anni) with normal creatininaemia values show a higher haematic peak and a higher AUC due to the slightly reduced kidney function which do not have any apparent clinical significance.
It is therefore not necessary to change the drug dosage in elderly subjects with normal kidney function
There is no evidence that BACTIGRAM is matabolised by the human organism.

5.3. Pre-clinical safety data
Pre-clinical pharmacological studies with BACTIGRAM were carried out on mice, rats, guinea pigs and dogs.
No significant pharmacological effects were observed after the administration of multiple doses which were much higher than the ones therapeutically recommended. No “dosis-correlated” alterations were observed in terms of behaviour, body temperature and nervous system function.
No mutagenic and teratogenic effects and no effects on reproduction were observed.

6. PHARMACEUTICAL INFORMATION
6.1. List of excipients
BACTIGRAM 750 mg tablets with modified release formulation contains:
hypromellose, mannitol, povidone, magnesium stearate, colloidal silica, propylene glycol, titanium dioxide.

6.2. Incompatibility
Not applicable

6.3. Shelf life
3 years.

6.4. Special storage precautioins
Keep at a temperature not higher than 25°C

6.5. Nature and content of the container
BACTIGRAM 750 mg tablets with modified release formulation - 6 tablets: 1 blister-pack containing 6 tablets

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 750 mg tablets with modified release formulation – 6 tablets: DAN 034619039

9. DATE OF THE FIRST AUTHORISATION/AUTHORISATION RENEWAL

Renewal date: December 2011

10. TEXT REVIEW DATE

March 2017