PACKAGE LEAFLET: Information for the patient

AVACYN

Solution for infusion – 400 mg / 250 ml

(Moxifloxacin hydrochloride)

Read this leaflet carefully before you start taking this medicine.

- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:

1. WHAT AVACYN IS AND WHAT IT IS USED FOR

Avacyn contains the active substance moxifloxacin hydrochloride, which belongs to a group of antibiotics called fluoroquinolones.

It works by killing bacteria that cause infection, if it is caused by bacteria that are susceptible to moxifloxacin.

Avacyn is used in adults for treating the following bacterial infections:

- infection of the lungs acquired outside the hospital (community acquired pneumonia);
- infection of the skin and soft tissues.

Your doctor may have given you Avacyn for another purpose. Ask your doctor if you want to know why you were given Avacyn.

2. BEFORE YOU TAKE AVACYN

Do not take Avacyn if you:

- are hypersensitive to moxifloxacin hydrochloride, other quinolones or any of the excipients of this medicine;
- are pregnant or breast-feeding;
- are under 18 years old;
- have a history of tendon disease / disorder related to quinolone treatment;
- were born with or have had any condition with abnormal heart rhythm;
- have salt imbalance in the blood (low levels of potassium or magnesium in the blood);
- have a very slow heart rhythm (bradycardia);
- suffer from heart failure;
- have a history of abnormal heart rhythm;
- are taking other drugs that prolong the QT interval;
- have a severe liver disease or transaminases level 5 times higher than the upper normal limit.

Take special care with Avacyn

You should not take fluoroquinolone / quinolone antibacterial medicines, including Avacyn, if you have experienced any serious adverse reaction in the past when taking a quinolone or fluoroquinolone. In this situation, you should inform your doctor as soon as possible.

- Avacyn can **change your heart's ECG**, especially if you are female or if you are elderly. If you are currently taking any **medicine that decreases your blood potassium levels**, consult your doctor before Avacyn is administered.
- If you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking moxifloxacin, talk to your doctor before taking this medicinal product.
- If you suffer from **epilepsy** or a condition which makes you likely to have **convulsions**, tell your doctor before Avacyn is administered.
- If you have or have ever had any **mental health problems**, consult your doctor before Avacyn is administered.

- If you suffer from **myasthenia gravis**, using Avacyn may worsen the symptoms of your disease. If you think you are affected, consult your doctor immediately.
- If you are diabetic talk to your doctor, because you may experience a risk of change in blood sugar levels with moxifloxacin.
- If you or any member of your family have **glucose-6-phosphate dehydrogenase deficiency** (a rare hereditary disease), inform your doctor, who will advise whether Avacyn is suitable for you.
- Avacyn should be taken with intravenous route only, and should not be administered with intraarterial route.

Inform your doctor also before taking Avacyn:
- if you have been diagnosed with an enlargement or "bulge" of a large blood vessel (aortic aneurysm or large vessel peripheral aneurysm);
- if you have experienced a previous episode of aortic dissection (a tear in the aorta wall);
- if you have a family history of aortic aneurysm or aortic dissection or other risk factors or predisposing conditions (e.g. connective tissue disorders such as Marfan syndrome, or vascular Ehlers-Danlos syndrome, or vascular disorders such as Takayasu arteritis, giant cell arteritis, Behcet's disease, high blood pressure, or known atherosclerosis).

If you feel sudden, severe pain in your abdomen, chest or back, go immediately to an emergency room.

When using Avacyn:
- if you experience **palpitations or irregular heart beat** during the period of treatment, you should inform your doctor immediately; he/she should perform an ECG to measure your heart rhythm;
- the **risk of heart problems** may increase with the increase of the dose and the speed of the perfusion into your vein;
- there is a rare chance that you may experience a **severe, sudden allergic reaction** (an anaphylactic reaction/shock) even with the first dose, with symptoms that may include: tightness in the chest, feeling dizzy, feeling sick or faint, or experience dizziness on standing

(orthostatic hypotension); **if this happens, treatment with moxifloxacin solution for infusion has to be discontinued immediately;**

- Avacyn may cause **a rapid and severe inflammation of the liver** which could lead to life-threatening liver failure; please contact your doctor before you continue the treatment if you suddenly start to feel unwell or notice yellowing of the whites of the eyes, dark urine, itching of the skin, a tendency to bleed or disturbances of thought or wakefulness;
- serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, and acute generalised exanthematous pustulosis (AGEP) have been reported with the use of moxifloxacin; SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk; also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur; these serious skin rashes are often preceded by fever and/or flu-like symptoms; the rashes may progress to widespread peeling of the skin and life-threatening complications or be fatal; AGEP appears at the initiation of treatment as a red, scaly widespread rash with bumps under the skin and blisters accompanied by fever; the most common location: mainly localized on the skin folds, trunk, and upper extremities; **if you develop a serious rash or another of these skin symptoms, stop taking moxifloxacin and contact your doctor or seek medical attention immediately;**
- quinolone antibiotics, including Avacyn, may cause **convulsions**; if this happens, treatment with Avacyn has to be discontinued;
- you may rarely experience **symptoms of nerve damage (neuropathy)** such as: pain, burning, numbness and/or weakness especially in the feet and legs or hands and arms; if this happens, stop taking Avacyn and inform your doctor immediately in order to prevent the development of potentially irreversible condition;
- you may experience **mental health problems** even when taking quinolone antibiotics, including Avacyn, for the first time; in very rare cases, depression or mental health problems have led to suicidal thoughts and self-injurious behaviour such as suicide attempts; if you develop such reactions, treatment with Avacyn has to be discontinued;
- you may develop **diarrhoea** whilst taking, or after taking antibiotics, including Avacyn; if this becomes severe or persistent, or you notice that your stool contains blood or mucus, you should stop using Avacyn immediately and consult your doctor; in this situation, you should not take medicines that stop or slow down bowel movement;

- Avacyn may cause rarely **pain and swelling in the joints and inflammation or rupture of your tendons**; your risk is increased if you are elderly (above 60 years of age), have received an organ transplant, have kidney problems or if you are being treated with corticosteroids; inflammation and ruptures of tendons may occur within the first 48 hours after starting treatment and even up to several months after stopping the therapy; at the first sign of pain or inflammation of a tendon (for example in your ankle, wrist, elbow, shoulder or knee), stop using Avacyn, contact your doctor and rest the affected limb(s); avoid any unnecessary exercise, as this might increase the risk of a tendon rupture;
- if you are elderly with existing **kidney problems,** take care that your fluid intake is sufficient because dehydration may increase the risk of kidney failure;
- if your **eyesight becomes impaired** or if your eyes seem to be otherwise affected, consult an eye specialist immediately;
- fluoroquinolone antibiotics may cause an increase of your blood sugar levels above normal levels (hyperglycemia), or lowering of your blood sugar levels below normal levels (hypoglycaemia), potentially leading to loss of consciousness (hypoglycaemic coma) in severe cases (see section 4. Possible side effects); if you suffer from diabetes, your blood sugar should be carefully monitored;
- quinolone antibiotics may make your **skin** become more **sensitive to sunlight or UV light**; you should avoid prolonged exposure to sunlight or strong sunlight and should not use a sunbed or any other UV lamp while using Avacyn;
- there is limited experience on use of sequential intravenous/oral moxifloxacin for the treatment of infection of the lungs (pneumonia) acquired outside the hospital.

The efficacy of moxifloxacin in the treatment of severe burns, infections of deep tissue and diabetic foot infections with osteomyelitis (infections of the bone marrow) has not been established.

<u>Prolonged, disabling and potentially irreversible serious side effects</u>

Fluoroquinolone / quinolone antibacterial medicines, including moxifloxacin, have been associated with very rare but serious side effects, some of them being long lasting (continuing months or years), disabling or potentially irreversible. This includes tendon, muscle and joint

pain of the upper and lower limbs, difficulty in walking, abnormal sensations such as pins and needles, tingling, tickling, numbness or burning (paraesthesia), sensory disorders including impairment of vision, taste and smell, and hearing, depression, memory impairment, severe fatigue, and severe sleep disorders. If you experience any of these side effects after taking Avacyn, contact your doctor immediately prior to continuing treatment. You and your doctor will decide on continuing the treatment considering also an antibiotic from another class.

Children and adolescents

This medicine must not be administered to children and adolescents under the age of 18, because efficacy and safety have not been established for this age group.

Taking other medicines

Concomitant treatment with other medicines may affect or be affected by Avacyn.
Please contact your doctor or pharmacist if you are taking or have recently taken other medicines, including those obtained without a prescription.
Do not forget to inform your doctor for the treatment with Avacyn if you take any other medicine during treatment.
If you are using Avacyn and other medicines that affect your heart, there is an increased risk for altering your heart rhythm, therefore, do not use Avacyn together with:

- medicines that belong to the group of anti-arrhythmics (e.g. quinidine, hydroquinidine, disopyramide, amiodarone, sotalol, dofetilide, ibutilide);
- antipsychotics (e.g. phenothiazines, pimozide, sertindole, haloperidol, sultopride);
- tricyclic antidepressants;
- some antimicrobials (e.g. saquinavir, sparfloxacin, intravenous erythromycin, pentamidine, antimalarials, particularly halofantrine);
- some antihistamines (e.g. terfenadine, astemizole, mizolastine);
- several other medicines (e.g. cisapride, intravenous vincamine, bepridil and diphemanil).

You must tell your doctor if you are taking other medicines that can lower your blood potassium levels (e.g. some diuretics, some laxatives and enemas [large doses] or corticosteroids [anti-inflammatory drugs], amphotericin B) or cause a slow heart rate because these can also increase the risk of serious heart rhythm disturbances while using Avacyn.

If you are currently taking oral anti-coagulants (e.g. warfarin), it may be necessary for your doctor to monitor your blood clotting times (INR).

Taking Avacyn with food and drinks

The effect of Avacyn is not influenced by food, including dairy products.

Pregnancy and breastfeeding

Do not use Avacyn if you are pregnant or breastfeeding.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before using this medicine.

Animal studies do not indicate that your fertility will be impaired by using this medicine.

Driving and using machines

Avacyn may make you feel dizzy and you may experience a sudden transient loss of vision, or you might faint for a short period. If you are affected in this way, do not drive or operate machinery.

Important information about some of the excipients of Avacyn

This medicinal product contains 787 mg (approximately 34 mmol) sodium in one bottle of 250 ml solution for infusion.

To be taken into consideration by patients on a controlled sodium diet.

3. HOW TO TAKE AVACYN

Avacyn will always be given to you by a doctor or healthcare professional.

The recommended dose for adults is one bottle once daily.

Avacyn is for intravenous use. Your doctor should ensure that the infusion is given at a constant flow over 1 hour.

No adjustment of the dose is required in elderly patients, patients with a low bodyweight or in patients with kidney problems.

Your doctor will decide on the duration of your treatment with Avacyn.

In some cases your doctor may start your treatment with Avacyn solution for infusion and then continue your treatment with Avacyn tablets.

The duration of treatment depends upon the type of infection, and how well you respond to treatment **but the recommended durations of use are:**

- infection of the lungs (pneumonia) acquired outside the hospital, 7 - 14 days;
  most patients with pneumonia are switched to oral treatment with moxifloxacin tablets within 4 days;
- infections of the skin and soft tissue, 7 - 21 days;
  for patients with complicated skin and skin structure infections, the mean duration of intravenous treatment is approximately 6 days and the average overall duration of treatment (infusion followed by tablets) is 13 days.

It is important that you complete the course of treatment, even if you begin to feel better after a few days. If you stop using this medicine too soon, your infection may not be completely cured, the infection may return or your condition may get worse, and you may also create a bacterial resistance to the antibiotic. The recommended dose and duration of treatment should not be exceeded.

If you receive more Avacyn than you should

If you are concerned that you may have received too much Avacyn, contact your doctor immediately.

If you miss a dose of Avacyn

If you are concerned that you may have missed a dose of Avacyn, contact your doctor immediately.

If you stop using Avacyn

If the treatment with this medicine is stopped too soon, your infection may not be completely cured. Consult your doctor if you wish to stop the treatment with Avacyn solution for infusion or Avacyn film-coated tablets before the end of the course of treatment.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. POSSIBLE SIDE EFFECTS

Like all medicines, moxifloxacin can cause side effects, although not everybody gets them.
The **most serious side effects** observed during treatment with moxifloxacin are listed below.
If the following situations occur, **stop taking Avacyn and tell your doctor immediately as you may need urgent medical advice:**

- an abnormal fast heart rhythm (rare side effect);
- suddenly you start feeling unwell or notice yellowing of the whites of the eyes, dark urine, itching of the skin, a tendency to bleed or disturbances of thought or wakefulness (these can be signs and symptoms of fulminant inflammation of the liver, potentially leading to life-threatening liver failure (very rare side effect, fatal cases have been observed));
- serious skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis; these can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and can be preceded by fever and flu-like symptoms (very rare side effects, potentially life threatening);
- a red, scaly widespread rash with bumps under the skin and blisters accompanied by fever at the initiation of treatment (acute generalised exanthematous pustulosis) (frequency of this side effect is ‘not known’);
- syndrome associated with impaired water excretion and low levels of sodium (SIADH) (very rare side effect);
- loss of consciousness due to severe decrease in blood sugar levels (hypoglycaemic coma) (very rare side effect);
- inflammation of blood vessels (signs could be: red spots on your skin, usually on your lower legs or effects like: joint pain) (very rare side effect);
- a severe, sudden, generalised allergic reaction including very rarely a life-threatening shock (e.g. difficulty in breathing, drop of blood pressure, fast pulse) (rare side effect);
- swelling, including swelling of the airway (rare side effect, potentially life-threatening);
- convulsions (rare side effect);
- troubles associated with the nervous system such as: pain, burning, tingling, numbness and/or weakness in extremities (rare side effect);

- depression (in very rare cases leading to self-harm, such as suicidal ideations/thoughts, or suicide attempts) (rare side effect);
- insanity (potentially leading to self-harm, such as suicidal ideations/thoughts, or suicide attempts) (very rare side effect);
- severe diarrhoea containing blood and/or mucus (antibiotic associated colitis e.g.: pseudomembranous colitis), which in very rare circumstances, may develop into complications that are life-threatening (rare side effects);
- pain and swelling of the tendons (tendonitis) (rare side effect) or a tendon rupture (very rare side effect);
- muscle weakness, tenderness or pain and particularly, if at the same time, you feel unwell, have a high temperature or have dark urine; they may be caused by an abnormal muscle breakdown which can be life threatening and lead to kidney problems (a condition called rhabdomyolysis) (frequency of this side effect is 'not known').

In addition, if you notice:

- transient loss of vision (very rare side effect),
- discomfort or pain in the eyes, especially due to light exposure (very rare to rare side effect),

contact an eye specialist immediately.

If you have experienced life-threatening irregular heart beat (Torsade de Pointes) or stopping of heart beat while taking Avacyn (very rare side effects), **tell your treating doctor immediately and do not restart the treatment with Avacyn.**

A worsening of the symptoms of myasthenia gravis has been observed in very rare cases. If this happens, **consult your doctor immediately**.

If you suffer from diabetes and you notice that your blood sugar is increased or decreased (rare or very rare side effect), **inform your doctor**.

If you are elderly with existing kidney problems and you notice decrease in urine output, swelling in your feet or ankles, fatigue, nausea, drowsiness, shortness of breath or confusion (these can be signs and symptoms of kidney failure, a rare side effect), **consult your doctor.**

Other side effects which have been observed during treatment with moxifloxacin are listed below by how likely they occur:

Common (may affect up to 1 in 10 people):
nausea, diarrhoea, dizziness, stomach and abdominal ache, vomiting, headache, increase of a special liver enzyme in the blood (transaminases), infections caused by resistant bacteria or fungi e.g. oral and vaginal infections caused by *Candida*, pain or inflammation at injection site, change of the heart rhythm (ECG) in patients with low blood potassium level.

Uncommon (may affect up to 1 in 100 people):
rash, stomach upset (indigestion/heartburn), changes in taste (in very rare cases loss of taste), sleep problems (predominantly sleeplessness), increase of a special liver enzyme in the blood (gamma-glutamyl-transferase and/or alkaline phosphatase), low number of special white blood cells (leukocytes, neutrophils), constipation, itching, sensation of dizziness (spinning or falling over), sleepiness, wind, change of the heart rhythm (ECG), impaired liver function (e.g: increase of a special liver enzyme in the blood (LDH)), decreased appetite and food intake, low white blood cells count, back, chest, pelvic and extremities pain, increase of specific blood cells count necessary for blood clotting, sweating, increased specialised white blood cells count (eosinophils), anxiety, feeling unwell (predominantly weakness or tiredness), shaking, joint pain, palpitations, irregular and fast heart beat, difficulty in breathing e.g. asthmatic conditions, increase of a special digestive enzyme in the blood (amylase), restlessness / agitation, tingling sensation (pins and needles) and/or numbness, skin hives, widening of blood vessels, confusion and disorientation, decrease of specific blood cells count necessary for blood clotting, visual disturbances e.g. double and blurred vision, decreased blood clotting, increased blood lipids (fats), low red blood cell count, muscle pain, allergic reaction, increase of bilirubin in the blood, inflammation of a vein, inflammation of the stomach, dehydration, severe heart rhythm abnormalities, dry skin, angina pectoris.

Rare (may affect up to 1 in 1,000 people):
muscle twitching, muscle cramps, hallucinations, high blood pressure, swelling (of the hands, feet, ankles, lips, mouth, throat), low blood pressure, kidney impairment (e.g. increase in specific

kidney laboratory test results like urea and creatinine), inflammation of the liver, inflammation of the mouth, ringing/noise in the ears, jaundice (yellowing of the whites of the eyes or yellowing of the skin), impairment of skin sensation, abnormal dreams, disturbed concentration, difficulty in swallowing, changes in smell sensation (e.g.: loss of smell), balance disorder and poor coordination (due to dizziness), partial or total loss of memory, hearing impairment including deafness (usually reversible), increased blood uric acid, emotional instability, impaired speech, fainting, muscle weakness.

Very rare (may affect up to 1 in 10,000 people):
inflammation of joints, abnormal heart rhythm, increase of skin sensitivity, a feeling of self-detachment (not being yourself), increased blood clotting, muscle rigidity, significant decrease of special white blood cells count (agranulocytosis), a drop in the number of red and white blood cells and platelets (pancytopenia).

The following symptoms have been observed more frequently in patients treated intravenously:
Common (may affect up to 1 in 10 people):

- increase in the level of a specific liver enzyme in the blood (gamma-glutamyl-transferase)

Uncommon (may affect up to 1 in 100 people):

- severe diarrhoea containing blood and/or mucus (antibiotic associated colitis) which in very rare circumstances may develop into complications that are life-threatening;
- abnormal, fast heart rhythm;
- hallucinations;
- low blood pressure;
- kidney impairment (incl. increase in specific kidney laboratory test results like urea and creatinine);
- kidney failure;
- swelling (of the hands, feet, ankles, lips, mouth, throat);
- convulsions.

Furthermore, there have been very rare cases of the following side effects reported following treatment with other quinolone antibiotics, which might possibly also occur during treatment with Avacyn: raised pressure in the skull (symptoms include: headache, visual problems including blurred vision, “blind” spots, double vision, loss of vision), increased blood sodium levels, increased blood calcium levels, a special type of reduced red blood cell count (haemolytic anaemia), increased sensitivity of the skin to sunlight or UV light.
Very rare cases of long lasting (up to months or years) or permanent adverse drug reactions, such as tendon inflammations, tendon rupture, joint pain, pain in the limbs, difficulty in walking, abnormal sensations such as pins and needles, tingling, tickling, burning, numbness or pain (neuropathy), depression, fatigue, sleep disorders, memory impairment, as well as impairment of hearing, vision, and taste and smell have been associated with administration of quinolone and fluoroquinolone antibiotics, in some cases irrespective of pre-existing risk factors.
If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist. When any of the above-mentioned side effects appears, the treatment with Avacyn should be discontinued and you should consult your doctor or pharmacist.

5. HOW TO STORE AVACYN

Keep this medicine out of the sight and reach of children!
Do not use this medicine after the expiry date which is stated on the label of the bottle and on the carton.
Do not store above 25ºC!
This product is for single use only. Any unused solution should be discarded.
Do not use this medicine if you notice any visible particulate matter or if the solution is cloudy.
Store in the original packaging to protect it from light!

6. FURTHER INFORMATION

What Avacyn 400 mg / 250 ml solution for infusion contains

The active substance is moxifloxacin hydrochloride.
Each bottle of 250 ml contains 400 mg moxifloxacin (as hydrochloride).
1 ml solution for infusion contains 1.6 mg moxifloxacin (as hydrochloride).

The excipients are: sodium chloride, hydrochloric acid or sodium hydroxide may be added for pH-adjustment, water for injection.

Content of the pack

Carton box with one glass bottle of 250 ml.

Marketing Authorisation Holder (MAH) and Manufacturer:

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