PATIENT INFORMATION LEAFLET

SCHEDULING STATUS S4

MOXIFLOXACIN 400 mg/250 mL FRESENIUS

Solution for infusion

Moxifloxacin

Sugar free

Read all of this leaflet carefully before you are given MOXIFLOXACIN FRESENIUS

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse, or other healthcare provider.

What is in this leaflet

1. What MOXIFLOXACIN FRESENIUS is and what it is used for

MOXIFLOXACIN FRESENIUS is used to treat a bacterial infection of the lungs (where the infection was contracted outside a hospital), and severe bacterial infections of the skin, skin tissues and inside your belly (abdomen) where therapy with other appropriate antibiotics have failed, cannot be used, or cannot be tolerated.

2. What you need to know before you are given MOXIFLOXACIN FRESENIUS

You should not receive MOXIFLOXACIN FRESENIUS

- If you are hypersensitive (allergic) to moxifloxacin, any other quinolone antibiotic or any of the other ingredients of MOXIFLOXACIN FRESENIUS (listed in section 6).
- If you have previously experienced side effects with the use of quinolone/fluoroquinolone antibiotics relating to your joints, muscles, ligaments, nerves, central nervous system (brain), epilepsy or mental health (psychiatric disorder).
- If you have severe liver disease, e.g. liver cirrhosis.
- If you are pregnant or breastfeeding your baby (see section “Pregnancy and breastfeeding”).
- If you were born with or have:
    - Any condition with abnormal heart rhythm whether related to QT time prolongation or not (seen on ECG, electrical recording of the heart)
    - A salt imbalance in the blood (especially low levels of potassium or magnesium in the blood)
    - A very slow heart rhythm (called ‘bradycardia’)
    - A weak heart (heart failure)
    - A history of abnormal heart rhythms
- If you are taking other medicines that result in abnormal heart rate or rhythm tracing (ECG) e.g. prolongation of the “QT time”.
- 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 aortic wall).
- If you have been diagnosed with leaking heart valves (heart valve regurgitation).
- If you have a family history of aortic aneurysm or aortic dissection or congenital heart valve disease, or other risk factors or predisposing conditions (e.g. connective tissue

disorders such as Marfan syndrome, or Ehlers-Danlos syndrome, Turner syndrome, Sjogren's syndrome [an inflammatory autoimmune disease], or vascular disorders such as Takayasu arteritis, giant cell arteritis, Bechet's disease, high blood pressure, or known atherosclerosis, rheumatoid arthritis [a disease of the joints] or endocarditis [an infection of the heart].

- If you have myasthenia gravis (abnormal muscle fatigue leading to weakness and in serious cases paralysis).
- **If you or your child are younger than 18 years.**
- If you have moderate to severe impairment of your kidney function and are treated with ACE inhibitors/angiotensin-receptor blockers. Ask your doctor if you are not sure.

Warnings and precautions

Take special care with MOXIFLOXACIN FRESENIUS

- MOXIFLOXACIN FRESENIUS can cause certain changes in the ECG (electronic recording of the heart), especially if you are female or if you are elderly. If you are currently taking other medicines that can reduce your blood potassium levels. If you experience heart palpitations or an irregular heartbeat at any time during treatment, please tell your doctor immediately. If necessary, he/she will then perform an ECG, to determine the pattern of your heartbeat.
- Inform your doctor of any other medicines when taken concurrently with MOXIFLOXACIN FRESENIUS, including over-the-counter/ non-prescription medicines.
- MOXIFLOXACIN FRESENIUS may cause hypersensitivity (allergic) reactions (an anaphylactic reaction/shock), even with the first dose which may be life-threatening or cause life-threatening shock. Discontinue MOXIFLOXACIN FRESENIUS at the first sign of a skin rash or other signs (tightness in the chest, feeling dizzy, feeling sick or faint, or experience dizziness on standing) indicative of an allergic reaction. In these cases, MOXIFLOXACIN FRESENIUS must be discontinued immediately, and appropriate medical treatment be instituted.

- If you feel sudden, severe pain in your abdomen, chest or back, which can be symptoms of aortic aneurysm and dissection, go immediately to an emergency room. Your risk may be increased if you are being treated with systemic corticosteroids.
- If you start experiencing a rapid onset of shortness of breath, especially when you lie down flat in your bed, or you notice swelling of your ankles, feet or abdomen, or a new onset of heart palpitations (sensation of rapid or irregular heartbeat), you should inform a doctor immediately.
- MOXIFLOXACIN FRESENIUS may cause a rapid and severe inflammation of the liver which could lead to life- threatening liver failure (including fatal cases). Please tell your doctor before you continue treatment if you develop signs such as rapidly feeling unwell and/or being sick associated with yellowing of the whites of the eyes, dark urine, itching of the skin, a tendency to bleed.
- **Serious skin reactions:**

  Tell your doctor **before receiving MOXIFLOXACIN FRESENIUS** if you have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking moxifloxacin.

  When receiving MOXIFLOXACIN FRESENIUS, serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, and acute generalised exanthematous pustulosis (AGEP) and Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) have been reported with the use of moxifloxacin as in MOXIFLOXACIN FRESENIUS.

  - 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.

- DRESS appears initially as flu-like symptoms and a rash on the face then an extended rash with a high body temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes.

- If you develop a serious rash or another of these skin symptoms, you should contact your doctor immediately and treatment with MOXIFLOXACIN FRESENIUS must be stopped.

- Convulsions (fits) have been reported with the use of MOXIFLOXACIN FRESENIUS and you should not receive MOXIFLOXACIN FRESENIUS if you have a history of this condition or continue with treatment if you get fits while receiving MOXIFLOXACIN FRESENIUS.
- If you develop diarrhoea while receiving MOXIFLOXACIN FRESENIUS, your treatment will be stopped. In this situation, you should not receive or use medicines that stop or slow down bowel movement (see section “You should not receive MOXIFLOXACIN FRESENIUS”).
- MOXIFLOXACIN FRESENIUS can cause tendon (ligament) pain, inflammation (tendinitis) or tendon tearing, during treatment and up to several months after discontinuing MOXIFLOXACIN FRESENIUS treatment. The Achilles tendon (the heel tendon) is most frequently affected. The risk of inflammation and tearing of tendons is increased if you are elderly or if you are currently treated with corticosteroids. At the first sign of any pain or inflammation of the tendon, discontinue treatment; rest and refrain from exercise; and tell your doctor immediately. The recovery process of your tendons, muscles and joints may take weeks or months and full recovery to your pre-treatment status may not occur (see section ”You should not receive MOXIFLOXACIN FRESENIUS”).
- Tell the doctor or laboratory staff that you are receiving MOXIFLOXACIN FRESENIUS if you have to provide a blood or urine sample.
- MOXIFLOXACIN FRESENIUS may interfere with the interpretation of diagnostic culture tests for tuberculosis.

- Your skin may become sensitive to sunlight or UV light when receiving MOXIFLOXACIN FRESENIUS. Avoid prolonged exposure to sunlight and do not use tanning beds or any other UV lamp while receiving MOXIFLOXACIN FRESENIUS. If a sunburn-like reaction or skin eruptions occur, contact your doctor (see section 4, Possible side effects).
- You may experience symptoms of neuropathy such as pain, burning, tingling, numbness and/or weakness in your limbs. If this happens, treatment with MOXIFLOXACIN FRESENIUS should be stopped and you should contact your doctor immediately. The recovery process of your nerve condition may take weeks or months and full recovery to your pre-treatment condition may not occur (see section ”You should not receive MOXIFLOXACIN FRESENIUS**).**
- You may experience mental health problems when receiving MOXIFLOXACIN FRESENIUS for the first time.

  Depression or mental health problems can progress to thoughts of suicide or suicide attempts. If this happens, treatment with MOXIFLOXACIN FRESENIUS should be stopped and you should contact your doctor immediately (see section “You should not receive MOXIFLOXACIN FRESENIUS”).
- If you suffer from myasthenia gravis (type of muscle weakness) you should not receive MOXIFLOXACIN FRESENIUS as it may worsen your disease (see section: “You should not receive MOXIFLOXACIN FRESENIUS”).
- Consult your doctor before receiving MOXIFLOXACIN FRESENIUS if you are diabetic, because you may experience a risk of change in blood sugar levels with MOXIFLOXACIN FRESENIUS.

  MOXIFLOXACIN FRESENIUS may cause an increase of your blood sugar levels above normal levels (hyperglycaemia) 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.

- If you have moderate to severe impairment of your kidney function, or if you are elderly and are treated with ACE inhibitors/angiotensin-receptor blockers to control your blood pressure as this may cause further injury to your kidneys (see section “You should not receive MOXIFLOXACIN FRESENIUS:). Your kidney function will be checked before and during treatment if you are receiving fluoroquinolone antibiotics and ACE inhibitors/angiotensin-receptor blockers to control your blood pressure.

Other medicines and MOXIFLOXACIN FRESENIUS

Always tell your healthcare provider if you are taking any other medicine. (This includes all complementary or traditional medicines.)

- If you are receiving MOXIFLOXACIN FRESENIUS and other medicines that affect your heart, there is an increased risk for altering your heart rate or rhythm. Therefore, you must tell your doctor, if you are taking any of the medicines that belong to the group of anti-dysrhythmics (medicines to treat your heart rhythm abnormalities), antipsychotics (used for schizophrenia), tricyclic antidepressants, some antimicrobials (that belong to the group of macrolides)
- 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, corticosteroids (medicines to treat inflammation or suppress your immune (defence) system), or amphotericin B) or medicines that may cause a slow heart rate because these medicines can also increase the risk of developing serious heart rhythm disturbances while receiving MOXIFLOXACIN FRESENIUS.
- If you take NSAIDs (nonsteroidal anti-inflammatory medicines), used for pain and inflammation. Examples include ibuprofen, indomethacin, diclofenac. You are more likely to have a fit (seizure) if these medicines are taken with MOXIFLOXACIN FRESENIUS.
- If you take digoxin (used to control some heart problems). When used simultaneously, moxifloxacin increased the effect of digoxin. Your doctor may want to monitor you more closely.

- If you are currently taking oral anti-coagulants (e.g. warfarin, a medicine that prevents blood clotting), it may be necessary for your doctor to monitor your blood clotting times.
- Tell your doctor if you are on treatment with ACE inhibitors/angiotensin-receptor blockers used to control your blood pressure as this may cause further injury to your kidneys.
- If you are taking glibenclamide (an antidiabetic medicine), tell your doctor, as moxifloxacin may reduce the effect of glibenclamide and your doctor may want to monitor you more closely.

Pregnancy, breastfeeding and fertility

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other health care provider for advice before receiving MOXIFLOXACIN FRESENIUS.

Pregnancy

If you are pregnant, you should not receive MOXIFLOXACIN FRESENIUS. Safety during pregnancy has not been established. Joint injuries have been reported with quinolone type medicines, which include moxifloxacin (as in MOXIFLOXACIN FRESENIUS).

In animal studies toxic effects on reproduction have been reported.

Breastfeeding

If you are receiving MOXIFLOXACIN FRESENIUS, you should not breastfeed your baby, as moxifloxacin is excreted in human breastmilk. Moxifloxacin, as in MOXIFLOXACIN FRESENIUS has been shown to cause lesions in the cartilage (connective tissue) between weight-bearing joints of young animals.

Fertility

No information available.

Driving and using machines

MOXIFLOXACIN FRESENIUS may affect your ability to drive and operate machinery. MOXIFLOXACIN FRESENIUS may make you feel dizzy or light-headed, you may experience a sudden, transient loss of vision or you may faint for a short period.

MOXIFLOXACIN FRESENIUS contains sodium

MOXIFLOXACIN FRESENIUS contains 747,5 mg (32,5 mmol) sodium (as acetate and as sulphate). If you are on a controlled-salt diet, please inform your doctor immediately.

3. How to use MOXIFLOXACIN FRESENIUS

MOXIFLOXACIN FRESENIUS is a solution for infusion.

Your doctor will prescribe the correct dose for your condition.

The duration of your treatment will be determined by your doctor. MOXIFLOXACIN FRESENIUS will be administered into one of your veins.

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

If you receive more MOXIFLOXACIN FRESENIUS than you should

Since a healthcare provider will administer MOXIFLOXACIN FRESENIUS, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

If you miss a dose of MOXIFLOXACIN FRESENIUS

Since a healthcare provider will administer MOXIFLOXACIN FRESENIUS, it is unlikely that the dose will be missed.

If you stop using MOXIFLOXACIN FRESENIUS

You should always consult your doctor before deciding to interrupt the course of treatment or stop receiving MOXIFLOXACIN FRESENIUS altogether.

4. Possible side effects

MOXIFLOXACIN FRESENIUS can have side effects.

Not all side effects reported for MOXIFLOXACIN FRESENIUS are included in this leaflet. Should your general health worsen or if you experience any untoward effects while receiving MOXIFLOXACIN FRESENIUS, please consult your healthcare provider for advice.

If any of the following happens, stop receiving MOXIFLOXACIN FRESENIUS and tell your doctor immediately:

- angioedema (rapid swelling of the skin and mucous membranes of the face, lips, tongue, or throat with difficulty to breathe)
- anaphylactic reaction/shock which is a severe sudden allergic reaction and is rapid in onset. Symptoms of anaphylactic reaction include: dizziness, feeling dizzy, sick or faint or experiencing dizziness when standing up), tightness in the chest, loss of consciousness, difficulty in breathing, swelling of the face, lips, tongue, throat and airways (breathing tubes), blueness of the skin, low blood pressure, heart failure, and can result in death;
- sudden severe pain in your chest, abdomen (tummy) or back;
- severe dizziness, fainting, fast or pounding heartbeats;
- sudden pain, snapping or popping sound, bruising, swelling, tenderness, stiffness, or loss of movement in any of your muscles, ligaments or joints;
- Cases of enlargement or weakening of the aortic wall or a tear in the aortic wall (aneurysms and dissections), which may rupture and may be fatal, and of leaking heart valves have been reported in patients receiving fluoroquinolones. See also section 2;
- loss of consciousness due to severe decrease in blood sugar levels (hypoglycaemic coma);
- diarrhoea that is watery or bloody;
- confusion, hallucinations, depression, unusual thoughts or behaviour;
- seizure (convulsions);

- pale or yellowed skin, dark coloured urine, fever, weakness;
- urinating less than usual or not at all;
- easy bruising or bleeding;
- numbness, tingling, or unusual pain anywhere in your body;
- the first sign of any skin rash, no matter how mild; or 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 (potentially life threatening);
- Syndrome associated with impaired water excretion and low levels of sodium (SIADH).

<u>Frequent side effects include</u>

- Infections caused by fungi (oral and vaginal infections/thrush caused by Candida)
- Anaemia (low red blood cell count), leukopenia (low white blood cell count), neutropenia (low numbers of special white blood cells – neutrophils), thrombocytopenia (decrease or increase of special cells necessary for blood clotting), prolonged prothrombin time or increased INR (decreased blood clotting)
- Allergic reactions, pruritus (itching), rash, urticaria (skin hives), blood eosinophilia (increased specialised white blood cells – eosinophils)
- Increased blood lipids/fats
- Anxiety reactions, restlessness/agitation
- Headache, dizziness, par- and dysesthesia (tingling sensation (pins and needles) and/or numbness), taste disorders or loss of taste, confusion and disorientation, sleep disorders, tremor (shaking), vertigo (sensation of dizziness, spinning or falling over), somnolence (sleepiness)
- Visual disturbances including double and blurred vision

- QT prolongation in patients with hypokalaemia (delayed electrical recovery time within the heart as shown by ECG in patients with low blood potassium level), QT prolongation (delayed electrical recovery time within the heart shown by ECG), palpitations (irregular heartbeat), tachycardia (fast heartbeat), vasodilatation (widening of blood vessels)
- Dyspnoea (difficulty in breathing including asthma)
- Nausea, vomiting, gastrointestinal and abdominal pain, diarrhoea, decreased appetite and food intake, constipation, dyspepsia (upset stomach, indigestion and/or heartburn), flatulence (wind), gastroenteritis (inflammation of the stomach), increased amylase (a special digestive enzyme in the blood)
- Increase in transaminases (a special liver enzyme in the blood), impaired liver function, including LDH increase (a special liver enzyme in the blood), increase of bilirubin in the blood, increase of gamma-glutamyl-transferase and/or alkaline phosphatase in the blood (special liver enzymes in the blood)
- Arthralgia (joint pain), myalgia (muscle pain)
- Dehydration (caused by diarrhoea or reduced fluid intake)
- Feeling unwell (predominantly weakness or tiredness), unspecific aches and pains such as back, chest, pelvic and extremities pains, sweating

<u>Less frequent side effects include</u>

- Abnormal thromboplastin level (special enzyme in the blood involved in blood coagulation), changes in prothrombin level and INR (increased or abnormal blood clotting)
- A drop in the number of red and white blood cells and platelets (pancytopenia)
- Anaphylactic reaction (severe, sudden allergic reaction for example difficulty in breathing, drop of blood pressure, fast pulse), angioedema (swelling of the face, lips, tongue, throat and airway), anaphylactic shock (which may be life-threatening)
- Blood-glucose disorders (high blood sugar – hyperglycaemia or low blood sugar - hypoglycaemia), hyperuricemia (increased blood uric acid)

- Depression, hallucinations, feelings of not being yourself, psychotic reactions (potentially leading to self-harm, such as thought to kill oneself, or suicide attempts)
- Reduced skin sensation, smell disorders, abnormal dreams, disturbed coordination due to dizziness or vertigo (may lead to fall with injuries), seizures (fits), disturbed attention, impaired speech, amnesia (partial or total loss of memory), peripheral neuropathy and polyneuropathy (troubles associated with the nervous system such as pain, burning, tingling, numbness and/or weakness in extremities), increased sensitivity of the skin
- Temporary loss of vision
- Ringing in the ears (tinnitus), hearing impairment including deafness (usually reversible)
- Abnormal fast heart rhythm, syncope (fainting), high blood pressure, low blood pressure, unspecified abnormal heart rhythms, Torsade de Pointes (life-threatening irregular heartbeat), cardiac arrest (stopping of heartbeat)
- Dysphagia (difficulty in swallowing), stomatitis (inflammation of the mouth), antibiotic-associated colitis (severe diarrhoea containing blood and/or mucous, which may be life-threatening)
- Jaundice (yellowing of the whites of the eyes or skin), hepatitis (inflammation of the liver), severe inflammation of the liver (potentially leading to life-threatening liver failure)
- Tendinitis (pain and swelling of the tendons), increased muscle tone and cramping, muscular weakness, tendon rupture, arthritis (inflammation of joints), gait disturbance (caused by muscular, tendon or joint symptoms), worsening of the symptoms of myasthenia gravis
- Impairment or failure of the kidneys (due to dehydration)
- Oedema (swelling of the hands, feet, ankles, lips, mouth, throat)

<u>Not known (frequency cannot be estimated from the available data)</u>

- A red, scaly widespread rash with bumps under the skin and blisters accompanied by fever at the initiation of treatment (acute generalised exanthematous pustulosis)

- Widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (drug reaction with eosinophilia and systemic symptoms which is also known as DRESS or drug hypersensitivity syndrome)
- Increased sensitivity of the skin to sunlight or UV light (see also section 2, Warnings and precautions)
- Sharply demarcated, erythematous patches with/without blistering that develop within hours of administration of moxifloxacin and heals with post inflammatory residual hyperpigmentation; it usually recurs at the same site of the skin or mucous membrane upon subsequent exposure to moxifloxacin
- 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)

<u>The following side effects have been observed more frequently in patients treated with intravenously followed by oral treatment:</u>

- Increased gamma-glutamyl-transferase (liver enzyme in the blood), abnormal fast heart rhythm, low blood pressure, oedema (swelling of the hands, feet, ankles, lips, mouth or throat), antibiotic- associated colitis (severe diarrhoea containing blood and /or mucous), seizures (fits), hallucinations, impairment and failure of kidneys.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med

Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.

Healthcare providers are asked to report any suspected adverse drug reactions to the Holder of the Certificate of Registration at the following email address: safety.fksa@fresenius-kabi.com and to the relevant medicine's regulatory authority in the country where the product is marketed.

5. How to store MOXIFLOXACIN FRESENIUS

Store all medicines out of reach of children.

Store at or below 30 °C in the original packaging and protect from light (keep bags in their overwraps until required for use). Do not store below 15 °C. At temperatures below 15 ºC precipitation may occur, which will re-dissolve at room temperature (15℃ to 25℃). It is therefore recommended not to store the infusion solution in a refrigerator. Protect from light. Keep the flexibags in the overwrap/pouch or the bottles in the outer cartons until required for use.

MOXIFLOXACIN FRESENIUS should be inspected visually for particles prior to administration. Only clear solution free from particles should be used.

6. Contents of the pack and other information

What MOXIFLOXACIN FRESENIUS contains

The active substance is moxifloxacin. Each bag/bottle contains 400 mg of moxifloxacin (as hydrochloride).

The other ingredients are: Sodium acetate trihydrate, disodium sulphate, water for injection, sulphuric acid (for pH-adjustment). (See section "MOXIFLOXACIN FRESENIUS contains sodium").

What MOXIFLOXACIN FRESENIUS looks like and contents of the pack

MOXIFLOXACIN FRESENIUS is a clear, yellow solution.

Two packing systems are provided:

- 300 mL Polyolefin *(***Free***flex*®) bags with polypropylene port, sealed in aluminium foil overwrap.

- The ***KabiPac***® packaging system consists of a primary container of 250 mL low density polyethylene blow-fill-seal bottle. The container's head is protected by a secondary packaging closure, consisting of HDPE/LDPE.

Pack sizes: 1, 10, 20, 25 and 40.

Not all pack sizes may be marketed.

Holder of Certificate of Registration

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Access to the corresponding Professional Information

The professional information will be printed and packed with the product.