receiving FACTIVE, the majority of rashes were maculopapular and of mild to moderate severity; 7% of the rashes were reported as severe, and severity appeared to correlate with the extent of the rash. In 68% of the subjects reporting a severe rash and approximately 25% of all those reporting rash, >60% of the body surface area was involved; the characteristics of the rash were otherwise indistinguishable from those subjects reporting a mild rash. The histopathology was consistent with the clinical observation of uncomplicated exanthematous morbilliform eruption. Approximately 11% of the rashes were described as being "urticaria-like". There were no documented cases of hypersensitivity syndrome or findings suggestive of angioedema or other serious cutaneous reactions.

The majority of rashes (81.9%) occurred on days 8 through 10 of the planned 10 day course of FACTIVE; 2.7% of rash events occurred within one day of the start of dosing. The median duration of rash was 6 days. The rash resolved without treatment in the majority of subjects. Approximately 19% received antihistamines and 5% received steroids, although the therapeutic benefit of these therapies is uncertain.

In the second part of this study after a 4 to 6 week wash out period, subjects developing a rash on FACTIVE were treated with ciprofloxacin (n=136) or placebo (n=50); 5.9% developed rash when treated with ciprofloxacin and 2.0% developed rash when treated with placebo. The cross sensitization rate to other fluoroquinolones was not evaluated in this clinical study. There was no evidence of sub-clinical sensitization to FACTIVE on a second exposure (i.e., subjects who had not developed a rash to FACTIVE in the first part of the study were not at higher risk of developing a rash to FACTIVE with a second exposure).

There was no relationship between the incidence of rash and systemic exposure (Cmax and AUC) to either gemifloxacin or its major metabolite, N-acetyl gemifloxacin.

REFERENCES:
1. Clinical and Laboratory Standards Institute. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically-Seventh Edition. Clinical and Laboratory Standards Institute document M7-A7, Vol. 26, No. 2, CLSI, Wayne, PA, January 2006.
2. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Disk Susceptibility Tests-Ninth Edition. Clinical and Laboratory Standards Institute document M2-A9, Vol. 26, No. 1, CLSI, Wayne, PA, January 2006.

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MEDICATION GUIDE
FACTIVE® [FAC-tiv]
(gemifloxacin)
320mg Tablets

Read the Medication Guide that comes with FACTIVE® before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking to your healthcare provider about your medical condition or your treatment.

What is the most important information I should know about FACTIVE?
FACTIVE belongs to a class of antibiotics called fluoroquinolones. FACTIVE can cause side effects that may be serious or even cause death. If you get any of the following serious side effects, get medical help right away. Talk with your healthcare provider about whether you should continue to take FACTIVE.

1. Tendon rupture or swelling of the tendon (tendinitis)
   - Tendon problems can happen in people of all ages who take FACTIVE.
     Tendons are tough cords of tissue that connect muscles to bones.
     - Symptoms of tendon problems may include: Pain, swelling, tears and inflammation of tendons including the back of the ankle (Achilles), shoulder, hand, or other tendon sites.
   - The risk of getting tendon problems while you take FACTIVE is higher if you:
     - are over 60 years of age
     - are taking steroids (corticosteroids)
     - have had a kidney, heart or lung transplant.

     Tendon problems can happen in people who do not have the above risk factors when they take FACTIVE.
   - Other reasons that can increase your risk of tendon problems can include:
     - physical activity or exercise
     - kidney failure
     - tendon problems in the past, such as in people with rheumatoid arthritis (RA).
   - Call your healthcare provider right away at the first sign of tendon pain, swelling or inflammation. Stop taking FACTIVE until tendinitis or tendon rupture has been ruled out by your healthcare provider. Avoid exercise and using the affected area. The most common area of pain and swelling is the Achilles tendon at the back of your ankle. This can also happen with other tendons.
   - Talk to your healthcare provider about the risk of tendon rupture with continued use of FACTIVE. You may need a different antibiotic that is not a fluoroquinolone to treat your infection.
   - Tendon rupture can happen while you are taking or after you have finished taking FACTIVE. Tendon ruptures have happened up to several months after patients have finished taking their fluoroquinolone.
   - Get medical help right away if you get any of the following signs or symptoms of a tendon rupture:
     - hear or feel a snap or pop in a tendon area
     - bruising right after an injury in a tendon area
     - unable to move the affected area or bear weight

2. Worsening of myasthenia gravis (a disease which causes muscle weakness). Fluoroquinolones like FACTIVE may cause worsening of myasthenia gravis symptoms, including muscle weakness and breathing problems. Call your healthcare provider right away if you have any worsening muscle weakness or breathing problems.

See the section "What are the possible side effects of FACTIVE?" for more information about side effects.

What is FACTIVE?
FACTIVE is a fluoroquinolone antibiotic medicine used to treat certain infections caused by certain germs called bacteria in adults 18 years or older. It is not known if FACTIVE is safe and works in children under 18 years of age. Children have a higher chance of getting bone, joint, or tendon (musculoskeletal) problems such as pain or swelling while taking fluoroquinolone antibiotic medicines.

Sometimes infections are caused by viruses rather than by bacteria. Examples include viral infections in the sinuses and lungs, such as the common cold or flu. Antibiotics including FACTIVE do not kill viruses.

Call your healthcare provider if you think your condition is not getting better while you are taking FACTIVE.

Who should not take FACTIVE?
Do not take FACTIVE if you have ever had a severe allergic reaction to an antibiotic known as a fluoroquinolone, or are allergic to any of the ingredients in FACTIVE. Ask your healthcare provider if you are not sure. See the list of ingredients in FACTIVE at the end of this Medication Guide.

What should I tell my healthcare provider before taking FACTIVE?
See "What is the most important information I should know about FACTIVE?"

Tell your healthcare provider about all your medical conditions, including if you:

- have tendon problems
- have a disease that causes muscle weakness (myasthenia gravis)
- have central nervous system problems (such as epilepsy)
- have nerve problems
- have or anyone in your family has an irregular heartbeat, especially a condition called "QT prolongation"
- have low blood potassium (hypokalemia) or magnesium (hypomagnesemia)
- have a slow heart beat (bradycardia)
- have a history of seizures
- have kidney problems. You may need a lower dose of FACTIVE if your kidneys do not work well.
- have rheumatoid arthritis (RA) or other history of joint problems
- are pregnant or planning to become pregnant. It is not known if FACTIVE will harm your unborn child.
- are breast-feeding or planning to breast-feed. It is not known if FACTIVE passes into breast milk. You and your healthcare provider should decide whether you will take FACTIVE or breast-feed.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal and dietary supplements. FACTIVE and other medicines can affect each other causing side effects. Especially tell your healthcare provider if you take:

- an NSAID (Non-Steroidal Anti-Inflammatory Drug). Many common medicines for pain relief are NSAIDs. Taking an NSAID while you take FACTIVE or other fluoroquinolones may increase your risk of central nervous system effects and seizures. See "What are the possible side effects of FACTIVE?"
- a blood thinner (warfarin, Coumadin®, Jantoven®)
- a medicine to control your heart rate or rhythm (antiarrhythmics) See "What are the possible side effects of FACTIVE?"

- an anti-psychotic medicine
- a tricyclic antidepressant
- a water pill (diuretic)
- probenecid (Probalan, Col-Probenecid)
- a steroid medicine. Corticosteroids taken by mouth or by injection may increase the chance of tendon injury. See "What is the most important information I should know about FACTIVE?"
- Certain medicines may keep FACTIVE from working correctly. Take FACTIVE either 2 hours before or 3 hours after taking these products:
  - an antacid, multivitamin, or other product that contains magnesium, aluminum, iron, or zinc
  - sucralfate (Carafate®).
  - didanosine (Videx®, Videx EC®).

Ask your healthcare provider if you are not sure if any of your medicines are listed above.

Know the medicines you take. Keep a list of your medicines and show it to your healthcare provider and pharmacist when you get a new medicine.

How should I take FACTIVE?

- Take FACTIVE exactly as prescribed by your healthcare provider.
- Take FACTIVE at about the same time each day.
- FACTIVE tablets should be swallowed.
- FACTIVE can be taken with or without food.
- FACTIVE should not be taken with dairy products (like milk or yogurt) or calcium-fortified juices alone, but may be taken with a meal that contains these products.
- Drink plenty of fluids while taking FACTIVE. Do not skip any doses, or stop taking FACTIVE even if you begin to feel better, until you finish your prescribed treatment, unless:
  - you have tendon effects (see "What is the most important information I should know about FACTIVE?"),
  - you have a serious allergic reaction (see "What are the possible side effects of FACTIVE?"), or your healthcare provider tells you to stop.
- This will help make sure that all of the bacteria are killed and lower the chance that the bacteria will become resistant to FACTIVE. If this happens, FACTIVE and other antibiotic medicines may not work in the future.
- If you miss a dose of FACTIVE, take it as soon as you remember. Do not take more than 1 dose of FACTIVE in one day.
- If you take too much, call your healthcare provider or get medical help immediately.

What should I avoid while taking FACTIVE?

- FACTIVE can make you feel dizzy and lightheaded. Do not drive, operate machinery, or do other activities that require mental alertness or coordination until you know how FACTIVE affects you.
- Avoid sunlamps, tanning beds, and try to limit your time in the sun. FACTIVE can make your skin sensitive to the sun (photosensitivity) and the light from sunlamps and tanning beds. You could get severe sunburn, blisters or swelling of your skin. If you get any of these symptoms while taking FACTIVE, call your healthcare provider right away. You should use sunscreen and wear a hat and clothes that cover your skin if you have to be in sunlight.

What are the possible side effects of FACTIVE?

FACTIVE can cause side effects that may be serious or even cause death. See "What is the most important information I should know about FACTIVE?"

Other serious side effects of FACTIVE include:

- Central Nervous System effects
  Seizures have been reported in people who take fluoroquinolone antibiotics, including FACTIVE. Tell your healthcare provider if you have a history of seizures. Ask your healthcare provider whether taking FACTIVE will change your risk of having a seizure. Central Nervous System (CNS) side effects may happen as soon as after taking the first dose of FACTIVE. Talk to your healthcare provider right away if you get any of these side effects, or other changes in mood or behavior:
  - feel dizzy
  - seizures
  - hear voices, see things, or sense things that are not there (hallucinations)
  - feel restless
  - tremors
  - feel anxious or nervous
  - confusion
  - depression
  - trouble sleeping
  - feel more suspicious (paranoia)
  - suicidal thoughts or acts
  - nightmares
- Serious allergic reactions
  Allergic reactions can happen in people taking fluoroquinolones, including FACTIVE, even after only one dose. Stop taking FACTIVE and get emergency medical help right away if you get any of the following symptoms of a severe allergic reaction:
  - hives
  - trouble breathing or swallowing
  - swelling of the lips, tongue, face
  - throat tightness, hoarseness
  - rapid heartbeat
  - faint
- Yellowing of the skin or eyes

Stop taking FACTIVE and tell your healthcare provider right away if you get yellowing of your skin or white part of your eyes, or if you have dark urine. These can be signs of a serious reaction to FACTIVE (a liver problem).

- Skin rash
  Skin rash may happen in people taking FACTIVE. Stop taking FACTIVE at the first sign of a skin rash and call your healthcare provider. Skin rash may be a sign of a more serious reaction to FACTIVE. Rash happens more often with FACTIVE in:
  - women, especially women who take hormone replacement therapy
  - people under 40 years of age
  - people who take FACTIVE for longer than 5 days.
- Serious heart rhythm changes (QT prolongation and torsades de pointes)
  Tell your healthcare provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you faint. FACTIVE may cause a rare heart problem known as prolongation of the QT interval. This condition can cause an abnormal heartbeat and can be very dangerous. The chances of this happening are higher in people:
  - who are elderly
  - with a family history of prolonged QT interval
  - with low blood potassium (hypokalemia)
  - who take certain medicines to control heart rhythm (antiarrhythmics).
- Intestine infection (Pseudomembranous colitis)
  Pseudomembranous colitis can happen with most antibiotics, including FACTIVE. Call your healthcare provider right away if you get watery diarrhea, diarrhea that does not go away, or bloody stools. You may have stomach cramps and a fever. Pseudomembranous colitis can happen 2 or more months after you have finished your antibiotic.
- Changes in sensation and possible nerve damage (Peripheral Neuropathy)
  Damage to the nerves in arms, hands, legs, or feet can happen in people taking fluoroquinolones, including FACTIVE. Talk with your healthcare provider right away if you get any of the following symptoms of peripheral neuropathy in your arms, hands, legs, or feet:
  - pain
  - burning
  - tingling
  - numbness
  - weakness

FACTIVE may need to be stopped to prevent permanent nerve damage.

- Sensitivity to sunlight (photosensitivity)
  See "What should I avoid while taking FACTIVE?"
- Joint problems

The most common side effects of FACTIVE include:

- diarrhea
- rash
- nausea
- headache
- stomach pain
- vomiting
- dizziness

These are not all the possible side effects of FACTIVE. Tell your healthcare provider about any side effect that bothers you, or that does not go away.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

How should I store FACTIVE?

- Store FACTIVE at 59º - 86ºF (15º to 30ºC)
- Keep FACTIVE away from light

Keep FACTIVE and all medicines out of the reach of children.

Reference ID: 3030736

General Information about FACTIVE

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use FACTIVE for a condition for which it is not prescribed. Do not give FACTIVE to other people, even if they have the same symptoms that you have. It may harm them.

This Medication Guide summarizes the most important information about FACTIVE. If you would like more information about FACTIVE, talk with your healthcare provider. You can ask your healthcare provider or pharmacist for information about FACTIVE that is written for healthcare professionals. For more information go to www.FACTIVE.com or call 1-888-661-9260.

What are the ingredients in FACTIVE?

- Active ingredient: gemifloxacin
- Inactive ingredients: crospovidone, hydroxypropyl methycellulose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, povidone, titanium dioxide.

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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