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Newsletter

Medication Safety Warnings/Concerns

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A number of cases of patients who develop severe side effects from fluoroquinolone antibiotics have recently been reported in the local media. Medicine regulatory agencies from across the world, including the American Food and Drug Administration (FDA), and the European Medicines Agency (EMA), continuously monitor the side effects of medication and vaccines.

Because it's not possible to predict all of a drug's effects during clinical trials, monitoring safety issues after drugs get on the market is critical. Usually, when important new risks are uncovered, the risks are added to the drug's labelling and the public is informed of the new information through letters, public health advisories, and other educational materials. In some cases, the use of the drug must be substantially limited. And in rare cases, the drug must be withdrawn from the market.

In this document we have highlighted some of the FDA warnings regarding medication used during the treatment of infections published since 2006, in reverse chronological order.

2018

FDA warns about increased risk of ruptures or tears in the aorta blood vessel with fluoroquinolone antibiotics in certain patients.

Healthcare professionals should avoid prescribing fluoroquinolone antibiotics to patients who have an aortic aneurysm or are at risk for an aortic aneurysm, such as patients with peripheral atherosclerotic vascular diseases, hypertension, certain genetic conditions such as Marfan syndrome and Ehlers-Danlos syndrome, and elderly patients. Prescribe fluoroquinolones to these patients only when no other treatment options are available.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM628757.pdf

FDA reinforces safety information about serious low blood sugar levels and mental health side effects with fluoroquinolone antibiotics – requires label changes.

Healthcare professionals should be aware of the potential risk of hypoglycaemia sometimes resulting in coma, occurring more frequently in the elderly and those with diabetes taking an oral hypoglycaemic medicine or insulin. Alert patients of the symptoms of hypoglycaemia and carefully monitor blood glucose levels in these patients. Discuss with them how to treat themselves if they have symptoms of hypoglycaemia. Inform patients about the risk of psychiatric adverse reactions, including agitation, delirium, disorientation, nervousness, and attention and memory impairment, which can occur after just one dose of a fluoroquinolone.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM612834.pdf

FDA warns about increased risk of cancer relapse with long-term use of azithromycin antibiotic after donor stem cell transplant.

Healthcare professionals should not prescribe long-term azithromycin for prophylaxis of bronchiolitis obliterans syndrome to patients who undergo donor stem cell transplants because of the increased potential for cancer relapse and death.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM615731.pdf

FDA review finds additional data supports the potential for increased long-term risks with antibiotic clarithromycin in patients with heart disease.

Healthcare professionals should be aware of these significant risks, and weigh the benefits and risks of clarithromycin before prescribing it to any patient, particularly in patients with heart disease, even for short periods. Consider using other available antibiotics. Advise patients with heart disease of the signs and symptoms of cardiovascular problems, regardless of the medical condition for which you are treating them with clarithromycin.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM597723.pdf

FDA limits packaging for anti-diarrhoea medicine loperamide to encourage safe use.

Healthcare professionals should be aware that using much higher than recommended doses of loperamide, either intentionally or unintentionally, can result in serious cardiac adverse events, including QT interval prolongation, Torsades de Pointes or other ventricular arrhythmias, syncope, and cardiac arrest. In cases of abuse, individuals often use other drugs together with loperamide in attempts to increase its absorption and penetration across the blood-brain barrier, inhibit loperamide metabolism, and enhance its euphoric effects. Some individuals are taking high doses of loperamide to treat symptoms of opioid withdrawal. If loperamide toxicity is suspected, promptly discontinue the drug and start necessary therapy. For some cases of abnormal heart rhythms in which drug treatment is ineffective, electrical pacing or cardioversion may be required.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM594394.pdf

2017

FDA warns about rare but serious allergic reactions with the skin antiseptic chlorhexidine gluconate.

Prescription chlorhexidine gluconate mouthwashes and oral chips used for gum disease already contain a warning about the possibility of serious allergic reactions in their labels. Advise patients to seek immediate medical attention if they experience any symptoms of an allergic reaction when using these products. Consider using alternative antiseptics such as povidone-iodine, alcohols, benzalkonium chloride, benzethonium chloride, or parachlorometaxylenol.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM539059.pdf

2016

FDA warns that prescribing of ketoconazole oral tablets for unapproved uses including skin and nail infections continues – linked to patient death.

Healthcare professionals should use ketoconazole tablets only to treat serious fungal infections when no other antifungal therapies are available. Skin and nail fungal infections in otherwise healthy persons are not life-threatening, and so the risks associated with oral ketoconazole outweigh the benefits. Other treatment options are available over-the-counter and by prescription, but are also associated with risks that should be weighed against their benefits. The death of a patient due to liver failure has been linked with oral ketoconazole prescribed for a fungal nail infection.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM501983.pdf

FDA advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections; warns about disabling side effects that can occur together.

The FDA is advising that the serious side effects associated with fluoroquinolones generally outweigh the benefits for patients with acute sinusitis, acute bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options. Healthcare professionals should stop systemic fluoroquinolone treatment immediately if a patient reports serious side effects, and switch to a non-fluoroquinolone antibiotic to complete the patient's treatment course.

The labels of fluoroquinolone medications already have a Boxed Warning for tendinitis, tendon rupture, and worsening of myasthenia gravis. The labels also include warnings about the risks of peripheral neuropathy and central nervous system effects. Other serious risks associated with fluoroquinolones are described in the labels, such as cardiac, dermatologic, and hypersensitivity reactions.

References: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM500591.pdf and
https://www.fda.gov/downloads/Drugs/DrugSafety/UCM513019.pdf

FDA to review study examining use of oral fluconazole in pregnancy.

The current FDA drug label states that data available from studies in people do not suggest an increased risk of problems during pregnancy or abnormalities in developing foetuses when women are exposed to a single 150 mg dose of oral fluconazole to treat vaginal yeast infections. However, high doses of oral fluconazole (400 – 800 mg per day) taken by pregnant women for much longer than a single dose have resulted in reports of abnormalities at birth. In the Danish study, most of the oral fluconazole use appeared to be one or two doses of 150 mg.

References: Molgaard-Nielsen D et al. Association between use of oral fluconazole during pregnancy and risk of spontaneous abortion and stillbirth. JAMA 2016; 315(1): 58 – 67 and
https://www.fda.gov/downloads/Drugs/DrugSafety/UCM497705.pdf

2015

FDA evaluating the potential risks of using codeine cough-and-cold medicines in children.

Children, especially those who already have breathing problems, may be more susceptible to these serious side effects, including slow and laboured breathing. In 2013, FDA warned against using codeine in children who recently had surgery to remove their tonsils and/or adenoids. In April 2015, the EMA announced that codeine must not be used to treat coughs and colds in children under 12 years, and that codeine is not recommended in children and adolescents between 12 and 18 years who have breathing problems, including those with asthma and other chronic breathing problems.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM453228.pdf

2014

FDA approves label changes for antibacterial doripenem describing increased risk of death for ventilated patients with pneumonia.

Doripenem is not approved to treat any type of pneumonia, and the revised label also includes a new warning about this unapproved use. Healthcare professionals should consider whether the benefits of doripenem treatment are likely to exceed its potential risks in patients who develop pneumonia while on ventilators. Doripenem is still considered safe and effective for its FDA-approved indications, i.e. treatment of adults with complicated intra-abdominal infections and complicated urinary tract infections, including pyelonephritis.

Reference: Kollef MH, et al. A randomized trial of 7-day doripenem versus 10-day imipenem-cilastatin for ventilator-associated pneumonia. Crit Care 2012, 16(6): R218.

2013

FDA approves label changes for antimalarial drug mefloquine hydrochloride due to risk of serious psychiatric and nerve side effects.

The mefloquine drug label already states that mefloquine should not be prescribed to prevent malaria in patients with major psychiatric disorders or with a history of seizures. The changes to the mefloquine drug label better describe the possibility of persistent neurologic (vestibular) adverse effects after mefloquine is discontinued and the possibility of permanent vestibular damage.

Neurologic side effects include vertigo, dizziness, loss of balance and tinnitus, and may persist for months to years after mefloquine discontinuation. Patients who experience vestibular symptoms often have concomitant psychiatric symptoms such as confusion, depression, anxiety and paranoia.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM362232.pdf

FDA warns about the risk of potentially fatal heart rhythms with the use of azithromycin.

Healthcare professionals should consider the risk of Torsades de Pointes and fatal arrhythmia when considering treatment options with azithromycin or alternative antibacterial drugs.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/UCM343347.pdf

2012

FDA warns about cefepime and risk of seizure in patients not receiving dosage adjustments for kidney impairment.

Non-convulsive status epilepticus has been reported with cefepime. Most cases occurred in patients with renal impairment for whom the dosage was not appropriately adjusted.

Reference: https://www.fda.gov/Drugs/DrugSafety/ucm309661.htm

2011

FDA updates information about the drug interaction between linezolid and serotonergic psychiatric medications.

The FDA is providing additional information about the reports of serotonin syndrome. Not all serotonergic psychiatric drugs have an equal capacity to cause serotonin syndrome with linezolid. Most cases from the FDA's Adverse Event Reporting System (AERS) of serotonin syndrome with linezolid occurred in patients taking specific serotonergic psychiatric drugs, namely a selective serotonin re-uptake inhibitor (SSRI) or a serotonin and noradrenaline re-uptake inhibitor (SNRI).

Reference: https://www.fda.gov/Drugs/DrugSafety/ucm276251.htm

2010

FDA reiterates concerns regarding the increased risk of death with tigecycline compared to other antibiotics used to treat similar infections.

The FDA is reminding healthcare professionals of an increased mortality risk associated with the use of the intravenous antibacterial tigecycline (Tygacil) compared to that of other drugs used to treat a variety of serious infections. The increased risk was determined using a pooled analysis of clinical trials. The cause of the excess death in these trials is often uncertain, but it is likely that most deaths in patients with these severe infections were related to progression of the infection. The increased risk was seen most clearly in patients treated for hospital-acquired pneumonia, especially ventilator-associated pneumonia, but was also seen in patients with complicated skin and skin structure infections, complicated intra-abdominal infections, and diabetic foot infections.

Reference: https://www.fda.gov/Drugs/DrugSafety/ucm224370.htm

FDA warns about eosinophilic pneumonia associated with the use of daptomycin.

Healthcare professionals should closely monitor patients being treated with daptomycin (Cubicin) for the development of eosinophilic pneumonia. In 2007, pulmonary eosinophilia was added to the Adverse Reactions, Post-Marketing Experience section of the daptomycin product label. Since then, the Agency has reviewed published case reports of daptomycin-associated eosinophilic pneumonia, and conducted a review of post-marketing adverse event reports from the FDA's AERS.

Reference:
https://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm220273.htm

2006

FDA issues advisory about telithromycin and hepatotoxicity

The FDA described rare but serious side effects, including three cases of severe hepatotoxicity, attributed to telithromycin (Ketek). In this context, the FDA asked the advisory committee to weigh the risk-to-benefit ratio of telithromycin in acute bacterial sinusitis and acute bacterial exacerbations of chronic bronchitis. Severe liver damage, in some cases leading to a liver transplant or death, has happened in people treated with telithromycin. Severe liver damage has happened during treatment, even after a few doses, or right after treatment with telithromycin has ended.

Reference: https://www.fda.gov/downloads/Drugs/DrugSafety/ucm088615.pdf

In conclusion

Both prescription and over-the-counter medication have risks as well as benefits. Before prescribing any medication, the risks and benefits need to be considered, and discussed with the patient. Ask your patient about any other medications, including vitamins and herbal supplements, to determine if there will be any deleterious interactions. Discuss with your patient whether they are willing to accept the potential risks in order to get the benefit of that particular medication.

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