QUINOLONE TOXICITY SUPPORT UK

www.quintoxsupport.co.uk

Dear Doctor,

On March 21st 2019 the MHRA issued a DSU, DDL and (unusually) a CAS to ensure that all healthcare providers (HCPS) were aware of new warnings and restrictions concerning the fluoroquinolone class of antibiotic. They also issued a patient information leaflet which was designed to help inform patients and to encourage discussion between patient and doctor until such time as the product information leaflet contained in the packaging was updated.

These publications warned that the side effects to any of the fluoroquinolones could be "disabling and potentially long-lasting or irreversible" and list the following as examples:
"tendinitis or tendon rupture, muscle pain, muscle weakness, joint pain, joint swelling, peripheral neuropathy, and central nervous system effects".

The frequency of these severe adverse reactions is stated as being very rare although the MHRA add that under-reporting is likely (their own estimate is that only 10% of side effects are reported). The Yellow Card figures show an average of 28.7 new reports of serious adverse reactions have been received every month since March 2019 when the above warnings were issued), which (at 10%) possibly indicates that 287 people per month have been seriously (potentially irreversibly) harmed for the last two and a half years – or over 8,600 since the new warnings were issued. The total number of reported reactions currently stands at 23,581 which (at 10%) might indicate nearer to 240,000 people have been affected by a fluoroquinolone in the UK.
https://yellowcard.mhra.gov.uk/iDAP/

Many HCPs interpret the term "very rare" as meaning that they will never see an example of side effects to a fluoroquinolone and so deny a patient presenting with typical symptoms. Many HCPs believe the fluoroquinolone will have 'left the body after 3 weeks' and no longer be able to cause side effects despite the above warnings and the SmPC stating that:
"Very rare cases of prolonged (continuing months or years), disabling and potentially irreversible serious adverse drug reactions affecting different, sometimes multiple, body systems (musculoskeletal, nervous, psychiatric and senses) have been reported.…".

Please do be aware that, if your patient has been prescribed a course of any of the fluoroquinolone class in the previous 6 months (possibly to a year), his/her neuropathy, tendon/muscle pain, gut or psychiatric or other problems could well stem from the antibiotic.

These new warnings were the result of the 2017/18 EMA (European Medicines Agency) Review into the potential dangers of fluoroquinolone side effects. A Public Hearing also took place in June 2018, which was only the second (and last) time the EMA had held such an event.
The full Assessment Report from the Review can be found at:
https://www.ema.europa.eu/en/documents/referral/quinolone-fluoroquinolone-article-31-referral-assessment-report_en.pdf
which documents the non-clinical aspects of fluoroquinolones, namely their mechanisms of action. Both the EMA and MHRA say it is not "helpful" to discuss with HCPs how the bactericidal action of fluoroquinolones is achieved but, given there is no known treatment for the side effects, you may be interested to know that their conclusion was that the "Potential mechanisms of toxicity" are "multifactorial" and "oxidative stress and mitochondrial toxicity have been outlined in the majority of studies"
(Full paragraph below and on p. 7 of the Assessment Report).
You may be aware that the MHRA have issued other DSUs with regard to fluoroquinolones i.e. in

2008, 2012, 2014, 2018 (risk of aortic dissection) , 2019 (mentioned above), May 2019 (risk of hypoglycaemia and mental health problems), and Dec 2020 (risk of heart valve regurgitation). With regard to advice about treatment for the side effects to fluoroquinolones, the MHRA have stated that “It is not the role of the MHRA to advise on clinical practice or provide detailed treatment information as only the individual patient’s HCPs are in possession of the patient’s clinical data, including any concurrent diseases and any other medications they may be taking, in order to formulate treatment plans which are tailored appropriately for each individual. In terms of providing clinical guidance, the National Institute for Health and Care Excellence (NICE) has this responsibility.”

What this paragraph fails to address is the fact that there is no known treatment, and whether a patient recovers or not is largely down to his/her underlying health. NICE have no clinical guidance for the treatment of these side effects, their only advice is the same as the MHRA’s which is to stop fluoroquinolone treatment at the first sign of side effects. This is very often too late for most sufferers and, contrary to the popular belief of many HCPs, the pains do not stop once the tablets have been stopped. The pains, in fact, generally get much worse and, for some sufferers, never stop.

Thank you for your time,

Miriam Knight
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Full wording of paragraph: “Conclusion on non-clinical aspects
Potential mechanisms of toxicity underlying the above described symptoms have been found to be multifactorial in a number of non-clinical studies. Among those mechanisms, oxidative stress and mitochondrial toxicity have been outlined in the majority of studies and MAHs´ responses. However, other possible mechanisms as highlighted above such as inhibition of cell proliferation and migration, reduced extracellular matrix, enhanced MMPs expression, apoptosis, ischemia and chelating properties of (fluoro)quinolones may be involved.”

Section 2.2 p. 7 EMA PRAC Assessment Report (2019)
https://www.ema.europa.eu/en/documents/referral/quinolone-fluoroquinolone-article-31-referral-assessment-report_en.pdf