boletim de FARMACOVIGILÂNCIA

VOLUME 24
NUMBER 12
DECEMBER 2020

Chloroquine/hydroxychloroquine – risk of psychiatric disorders

Chloroquine and hydroxychloroquine are authorised in several EU countries for the treatment of various autoimmune conditions such as rheumatoid arthritis and lupus, as well as for malaria prophylaxis. Though these products have been in off label use by some in the treatment of COVID-19, they are not approved for this indication.

The risk of psychiatric disorders including suicidal ideation was already known; these undesirable effects are indeed already listed in the SPCs and PLs of some of the products containing chloroquine and hydroxychloroquine as rare or of unknown frequency.

Following information provided by the Spanish medicines agency concerning six cases of psychiatric disorders in **COVID-19** patients who had received **higher** than authorised **doses of hydroxychloroquine**, EMA triggered an assessment of all available data. This assessment has confirmed that there is a causal nexus between the use of products containing chloroquine and hydroxychloroquine and the risk of psychiatric disorders. At its November 2020 meeting the **PRAC**, which is the committee at EMA in charge of assessing and monitoring the safety of medicinal products for human use, has recommended that the SPCs be updated.

Patients on these medicines who present with symptoms such as irrational thoughts, anxiety, hallucinations, delirium or depression (including self-harm or suicidal thoughts), should contact a physician promptly.

Reminder

When prescribing these medicines, the following should also be considered:

- risk of heart rhythm disturbances, namely in the context of pre-existing cardiac conditions, hypokalaemia, hypomagnesaemia and/or concomitant use of QT interval prolonging drugs
- risk of seizures due to neuronal injury secondary to liver impairment and hypoglycaemia

Márcia Silva

INDEX CARD

Director: Fátima Canedo
Editor: Rui Pombal
Contributors: Adriana Gamboa, Ana Severiano, Ana Sofia Martins, Cristina Mousinho, Fátima Bragança, Fátima Hergy, Magda Pedro, Márcia Silva, Patrícia Catalão, Sílvia Duarte
Publishing Assistant: Inocência Pinto
Advisory Board: Conselho Diretivo do INFARMED, I.P.
INFARMED – Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.
Parque de Saúde de Lisboa, Av. do Brasil, N.º 53, 1749-004 Lisboa
Phone: +351 217 987 100
E-mail: farmacovigilancia@infarmed.pt
Design and production: Letras & Sinais, Comunicação e Imagem, Lda.
ISSN: 0873-7118

Alerts and News at the Infarmed website

For news and publications, just use thirty seconds of your time and register here!

REPÚBLICA PORTUGUESA SAÚDE
SNS SERVIÇO NACIONAL DE SAÚDE
Infarmed Autoridade Nacional do Medicamento e Produtos de Saúde, I.P.

2020: key points

- **ABIRATERONE** Due to a potential pharmacokinetic interaction, administration of abiraterone (for the treatment of prostatic cancer) together with oral antidiabetic agents can be associated with a risk of hypoglycaemia. **BolFVG2-2020**

ADMINISTRATION ISSUES AND MEDICATION ERRORS

- **INSULINE** Cutaneous amyloidosis can be a class adverse effect of insulin. It is thought that this risk can be reduced, similarly to lipodystrophy, by constantly changing the injection site. **BolFVG6-2020**

- **LEUPRORELIN** The reconstitution and administration of leuprorelin should be undertaken by healthcare professionals who are familiar with those procedures. The risk of medication errors with the administration devices increases with the number of procedure steps and may potentially result in lack of efficacy from subtherapeutic doses. **BolFVG9-2020**

- **METHOTREXATE** An alert card and restricting prescription to physicians who are experienced in the use of this medicinal product, are measures put in place to reinforce prevention of accidental overdosing in the treatment of autoimmune conditions, namely through daily instead of weekly administration. **BolFVG5-2020**

- **ANTICOAGULANTS, DIRECT ORAL** DOACs maintain a favourable benefit-risk profile within their authorised indications. Elderly patients who are older than 75 years have a well-known increased risk of haemorrhage which does not by itself imply any dosing adjustments. **BolFVG3-2020**

- **BUPROPION + NALTREXONE** The safety and tolerability of this association should be assessed at regular intervals. In addition to neuropsychiatric contraindications, cardiovascular factors should also be taken into consideration, including arterial hypertension and its management. **BolFVG2-2020**

- **CIPROTERONE ACETATE** Risk of meningiomas, especially in association with higher doses and prolonged periods of time (namely longer than 5 years and in daily doses ≥ 50 mg). Once clinical improvement is achieved, the lowest effective dose should be used. **BolFVG10-2020**

- **FLUOROQUINOLONES (SYSTEMIC OR INHALATIONAL)** In patients with risk factors for mitral and aortic valve regurgitation, these antibiotics should only be used following careful benefit-risk assessment and consideration of therapeutic alternatives. **BolFVG10-2020**

- **GENOTOXIC MEDICINES**

  Recommended duration of post-treatment contraception:
  Females: 5 half-lives + 6 months
  Males: 5 half-lives + 90 days
  BolFVG4-2020

2020: key points

INTERACTIONS

- **MACROGOL** As for other osmotic laxatives, ischaemic colitis may occur in association with macrogol in colonoscopy preps. This laxative should therefore be used with caution in patients with known risk factors for ischaemic colitis or when stimulant laxatives (e.g., bisacodyl, sodium picosulfate) are taken concomitantly. **BollFVG6-2020**

- **MIRTAZAPINE** Recently confirmed adverse reactions: DRESS syndrome (in addition to the already known risk of SJS-TEN spectrum reactions); amnesia. In either case mirtazapine should be promptly discontinued. **BollFVG7-2020**

- **SOFOSBUVIR** At least for the first two weeks of treatment with sofosbuvir, during concomitant administration of **AMIODARONE** and for the first few months after discontinuation of the latter, all patients should undergo cardiac monitoring – risk of bradycardia and heart block. **BollFVG5-2020**

- **REMDESIVIR** Adverse reactions listed in the SPC: raised transaminases, headache, nausea, rash, hypersensitivity, infusion-related reactions. Slower infusion (which can take as long as 120 minutes) may prevent anaphylactic-like reactions, including hypotension, bradycardia, dyspnoea, etc. Renal toxicity is an important identified risk included in the product's Risk Management Plan and is under intensive monitoring. However, a causal relation between remdesivir and acute kidney injury has not been found. **BollFVG8-2020** **BollFVG11-2020**

- **THIAZIDE, THIAZIDE-LIKE DIURETICS AND ASSOCIATIONS** The presence of the sulphonamide group can be associated with an imbalance of the prostaglandin-thromboxane metabolism resulting in increased transudation through the eye's choroidal capillaries. This idiosyncratic ocular choroidal effusion can cause visual field defects, transient myopia or even acute closed angle glaucoma with attending risk of blindness. **BollFVG4-2020**

- **TOFACITINIB** A review of the recommendations of use of this product has resulted in updated posology and warnings. These updates are to do with evidence of an increased, dose-dependent risk of deep vein thrombosis and serious venous thromboembolic phenomena, as well as of increased mortality associated with cardiovascular events, infections and malignant neoplasms. **BollFVG1-2020**

What do they mean?

ADR	Adverse Drug Reaction
EMA	European Medicines Agency
MA	Marketing Authorization
PIL	Patient Information Leaflet
PRAC	Pharmacovigilance Risk Assessment Committee (EMA)
SPC	Summary of Product Characteristics

Communications to Healthcare Professionals published in the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Materials? Online publication date
5-aminolevulinic acid Gliolan	**Physicians:** neurosurgeons who have received training on this product and who are qualified to use it	Use in case of surgery postponement/delay and information on fluorescence in low-grade gliomas 04-12-2020
Metamizole Dolocalma, Metamizol Vitória, Nolotil	**Physicians:** general/family medicine, internal medicine, general surgery, neurology, oncology, orthopaedic surgery, paediatrics, rheumatology, dentistry **Pharmacists:** hospital	Risk of liver injury 15-12-2020

Compiled by Patrícia Catalão

Educational Materials published in the Infomed product information webpage

Click on the links.

INN Medicinal product	Target	Materials? Online publication date
Nitric oxide VasoKINOX	**Healthcare professionals:** intensive care physicians and nurses	Guide 22-12-2020
Nivolumab Opdivo	**Patients**	Alert ard 15-12-2020

Compiled by Patrícia Catalão

Portal **RAM**

Notificação de Reações Adversas a Medicamentos

Report an adverse drug reaction here.
Find answers to your questions about the ADR Portal here.