Pharmaceutical opinion : **Interaction between anagelsics and anti-HCVs**

Patient : \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_ DOB \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ Telephone : \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

After analyzing your patient's file, I noticed a problem with his medication.

**Glecaprevir/Pibrentasvir (Maviret)**  and Fentanyl (Fentora)

**Interaction mechanism :** An increase in analgesics adverse effects may occur following co-administration with the anti-HCV drugs mentioned above. Fentanyl is a CYP 3A4 substrate that is inhibited by some anti-HCVs.

***Glecaprevir/Pibrentasvir (Maviret) and Fentanyl***

Additional information:

Glecaprevir/Pibrentasvir (Maviret) is a weak inhibitor of CYP 3A4. Administration with midazolam did not show a clinically significant increase.

Administration with fentanyl has not been studied, but since fentanyl has a narrow therapeutic index, concomitant use especially with illicit fentanyl use could have serious consequences for the patient. Indeed, high concentrations of fentanyl following drug interactions are associated with a risk of respiratory distress and death.

Possible therapeutic options:

***Fentanyl :***

\* Fentanyl not recommended with CYP 3A4 inhibitors according to the product monograph \*

*If the patient is already on fentanyl and treatment with Glecaprevir/Pibrentasvir (Maviret) is started.*

* Stop the fentanyl patch (ideally 48 hours before starting antiretrovirals) and, 8 hours after stopping fentanyl, start the replacement analgesic (morphine or hydromorphone) with 60-75% of the converted dose of fentanyl.
* If the fentanyl patch cannot be replaced by morphine or hydromorphone, ideally remove the patch that is in place, wait 8 hours, then start with a reduced dose of fentanyl (suggested to decrease to 50% of the dose) and monitor closely to assess tolerance and titrate the dose.

*If fentanyl is added to an already existing treatment with Glecaprevir/Pibrentasvir (Maviret).*

* Start with the lowest possible dose and titrate according to tolerance and efficacy.
* Alternative :
	+ Hydromorphone
	+ Morphine

*Patients currently under treatment with this combination and tolerating it.*

* Closely monitor side effects.

**Alternatives or in addition.**

* Tylenol, NSAIDs or co-analgesia.

**Follow up :**

* Monitor the effectiveness of analgesics.
* Monitor toxicity (miosis, euphoria, dysphoria, drowsiness, confusion, excessive sedation, decreased alertness, hallucinations, dizziness, bradycardia, myoclonus, hypotension, prolonged or recurrent respiratory depression) of analgesics.
* Watch for withdrawal symptoms (“craving”, irritability, myalgia, muscle spasms, redness, abdominal pain, nausea, vomiting, diarrhea, diaphoresis, tearing, rhinorrhea, mydriasis, yawning, piloerection, tachycardia, tremors).

Do not hesitate to contact us for additional information.
In collaboration,

Pharmacist : \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Telephone : \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_​ Fax : \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

As a prescription, date and sign:

Date : \_\_\_\_\_/\_\_\_\_\_/\_\_\_\_\_ Signature and licence : \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_