HPRA
An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Ocaliva (obeticholic acid): Risk of serious liver injury in patients with pre-existing moderate or severe hepatic impairment – reminder of differential dosing recommendations

In the post-marketing setting, in patients with moderate to severe decreases in liver function, being treated for primary biliary cholangitis (PBC), serious liver injury and death have been reported when more frequent dosing of obeticholic acid than recommended was prescribed.

Liver related adverse reactions have occurred both early in treatment and after months of treatment. Due to this serious risk, prescribers are reminded of the following:

Advice to Healthcare Professionals

- The hepatic status of the patient must be assessed prior to treatment with obeticholic acid.
- The dose of obeticholic acid should be adjusted in patients with moderate to severe hepatic impairment (See Table 1 below), in line with the recommendations in section 4.2 of the Summary of Product Characteristics (SmPC).
- During treatment, all patients should be monitored for PBC progression through laboratory and clinical assessment to determine whether dosage adjustment is necessary.
- Patients at an increased risk of hepatic decompensation should be monitored closely, including those with laboratory evidence of worsening liver function or progression to cirrhosis.
- Dosing frequency should be reduced in patients who progress to advanced disease (i.e. from Child-Pugh Class A to Child-Pugh Class B or C).
- The approved product information (SmPC) has been updated to include this information.

Table 1: Dosing regimen by PBC patient population

Staging/ Classification	Non-cirrhotic or Child-Pugh Class A	Child-Pugh Class B or C or Decompensated Cirrhotic
Starting dosage	5mg once daily	5mg once weekly
Dosage titration	For patients who have not achieved an adequate reduction in alkaline phosphatase (ALP) and/ or total bilirubin after 6 months of treatment and the patient is tolerating obeticholic acid, titrate up to 10mg once daily.	For patients who have not achieved an adequate reduction in ALP and/or total bilirubin after 3 months of treatment and the patient is tolerating obeticholic acid, titrate up to 5mg twice weekly (at least 3 days apart) and subsequently to 10mg twice weekly (at least 3 days apart) based on response and tolerability.
Maximum dosage	10mg once daily	10mg twice weekly (at least 3 days apart)

Key Message

- Patients with pre-existing moderate or severe liver impairment who are taking obeticholic acid are at risk of serious liver injury; adequate dose reduction in these patients is therefore essential.
- Hepatic status should be evaluated prior to and during treatment with obeticholic acid. Patients with moderate to severe hepatic impairment should have their doses of obeticholic acid adjusted– see SmPC.
- All patients should be monitored for PBC progression with laboratory and clinical assessment and the need for dose adjustment should be evaluated at regular intervals.
- This medicine is subject to additional monitoring requirements and healthcare professionals are requested to report any suspected adverse reactions associated with its use to the HPRA via the available options (www.hpra.ie).

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