Ictastan 200 mg/245 mg film-coated tablets

(Emtricitabine/Tenofovir disoproxil)

GUIDE FOR
HEALTHCARE PROFESSIONALS

HIV renal educational brochure for adults

This is a risk minimisation material provided by
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For further information, please refer to the
Summary of Product Characteristics (SPC) available at www.hpra.ie or
www.accord-healthcare.ie.

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HIV renal educational brochure for adults

This brochure includes a creatinine clearance slide ruler to address renal and bone toxicity, and dosing recommendations for this population.

HIV-positive patients are at increased risk of renal impairment, requiring baseline and subsequent renal monitoring.[1] For those adult patients on emtricitabine/tenofovir disoproxil based regimens specific recommendations are detailed below.

Important Points to Consider:

- ✓ There is an increased risk of renal disease in HIV infected patients associated with tenofovir disoproxil containing products such as Ictastan 200 mg/245 mg film-coated tablets.
- ✓ Always check the patient's baseline renal function by way of creatinine clearance before initiating emtricitabine/tenofovir disoproxil therapy.
- ✓ During emtricitabine/tenofovir disoproxil therapy, renal function (creatinine clearance and serum phosphate) should be assessed regularly (after two to four weeks of treatment, after three months of treatment and every three to six months thereafter in patients without renal risk factors) (see Table 1).
- ✓ Patients at risk of renal impairment require more frequent monitoring of renal function.
- ✓ In patients with renal impairment, emtricitabine/tenofovir disoproxil should only be used if the potential benefits of treatment outweigh the potential risks, and the daily dose of emtricitabine /tenofovir disoproxil may need to be adjusted (see Table 2) or the dosing interval may need to be prolonged.
- ✓ If serum phosphate is < 1.5 mg/dl or creatinine clearance decreases during therapy to < 50 ml/min then renal function should be re-evaluated within one week. Consider interrupting emtricitabine/tenofovir disoproxil if creatinine clearance is confirmed as < 50 ml/min or if serum phosphate decreases to < 1.0 mg/dl.
- ✓ Also consider interrupting treatment with emtricitabine/tenofovir disoproxil in case of progressive decline of renal function when no other cause has been identified.
- ✓ In patients with a creatinine clearance of 30-49 ml/min, dose interval adjustment of the emtricitabine/tenofovir disoproxil therapy is important.
- ✓ Emtricitabine/Tenofovir disoproxil is not recommended for patients with severe renal impairment (creatinine clearance < 30 ml/min).
- ✓ The use of emtricitabine/tenofovir disoproxil therapy should be avoided with concomitant or recent use of nephrotoxic medicinal products. If emtricitabine/tenofovir disoproxil is used with nephrotoxic medicinal products, renal function should be closely monitored according to the recommended schedule.

Emtricitabine and Tenofovir disoproxil renal safety profile

Emtricitabine and tenofovir are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion. In tenofovir disoproxil clinical studies and post-marketing safety surveillance, renal failure (rare), renal impairment, elevated creatinine, hypophosphataemia and proximal tubulopathy (including Fanconi syndrome) have been reported.

In some patients proximal renal tubulopathy has been associated with myopathy (rare), osteomalacia (rare) (manifested as bone pain and infrequently contributing to fractures), rhabdomyolysis (uncommon), muscle weakness (uncommon), hypokalaemia (uncommon) and hypophosphataemia (very common).[2]

Monitoring of renal function

The recommendations for monitoring renal function in patients without renal risk factors prior to and during treatment with Ictastan 200 mg/245 mg film-coated tablets are provided in Table 1. In patients at risk for renal impairment a more frequent monitoring of renal function is required.

Table 1: Monitoring of renal function in patients without renal risk factors.[2]

	Prior to Ictastan therapy	During the first 3 months of Ictastan therapy	> 3 months on Ictastan therapy
Frequency	At baseline	At 2 - 4 weeks of treatment and after 3 months of treatment	Every 3 - 6 months
Parameter	Creatinine clearance	Creatinine clearance and serum phosphate	Creatinine clearance and serum phosphate

If serum phosphate is < 1.5 mg/dl (0.48 mmol/l) or creatinine clearance is decreased to < 50 ml/min in any patient receiving emtricitabine/tenofovir disoproxil, renal function should be re-evaluated within 1 week, including measurements of blood glucose, blood potassium and urine glucose concentrations. Consideration should also be given to interrupting treatment with emtricitabine / tenofovir disoproxil in patients whose creatinine clearance decreased to < 50 ml/min or decreases in serum phosphate to < 1.0 mg/dl (0.32 mmol/l), or in case of progressive decline of renal function when no other cause has been identified. [2]

Use of emtricitabine/tenofovir disoproxil should be avoided with concurrent or recent use of a nephrotoxic medicinal product and drugs secreted by the same pathway; if concomitant use is unavoidable, renal function must be monitored weekly.

A higher risk of renal impairment has been reported in patients receiving tenofovir disoproxil in combination with a ritonavir or cobicistat boosted protease inhibitor. Close monitoring of renal function is required in these patients. In patients with renal risk factors, the co-administration of tenofovir disoproxil with a boosted protease inhibitor should be carefully evaluated. [2]

Cases of acute renal failure after initiation of high dose or multiple non-steroidal anti-inflammatory drugs (NSAIDs) have been reported in patients treated with tenofovir disoproxil and with risk factors for renal dysfunction. If emtricitabine/tenofovir disoproxil is co-administered with an NSAID, renal function should be monitored adequately. [2]

Use in Renal Impairment

Emtricitabine and tenofovir are eliminated by renal excretion and the exposure to emtricitabine and tenofovir increases in patients with renal dysfunction. There are limited data on the safety and efficacy of emtricitabine/tenofovir disoproxil in patients with moderate and severe renal impairment (creatinine clearance < 50 ml/min) and long-term safety data has not been evaluated for mild renal impairment (creatinine clearance 50-80 ml/min). Therefore, in patients with renal impairment emtricitabine/tenofovir disoproxil should only be used if the potential benefits of treatment are considered to outweigh the potential risks. Patients with renal impairment may require close monitoring of renal function. Dose interval adjustments are recommended for patients with creatinine clearance between 30 and 49 ml/min. These dose adjustments have not been confirmed in clinical studies and the clinical response to treatment should be closely monitored in these patients.

The dosing interval adjustment guidelines for patients with creatinine clearance < 80 ml/min taking Ictastan 200 mg/245 mg film-coated tablets is shown in Table 2.

Mild renal impairment (creatinine clearance 50-80 ml/min)

Limited data from clinical studies support once daily dosing of emtricitabine and tenofovir disoproxil in patients with mild renal impairment.

Moderate renal impairment (creatinine clearance 30-49 ml/min)

Administration of emtricitabine and tenofovir disoproxil every 48 hours is recommended, based on modelling of single-dose pharmacokinetic data for emtricitabine and tenofovir disoproxil in non-HIV infected subjects with varying degrees of renal impairment.

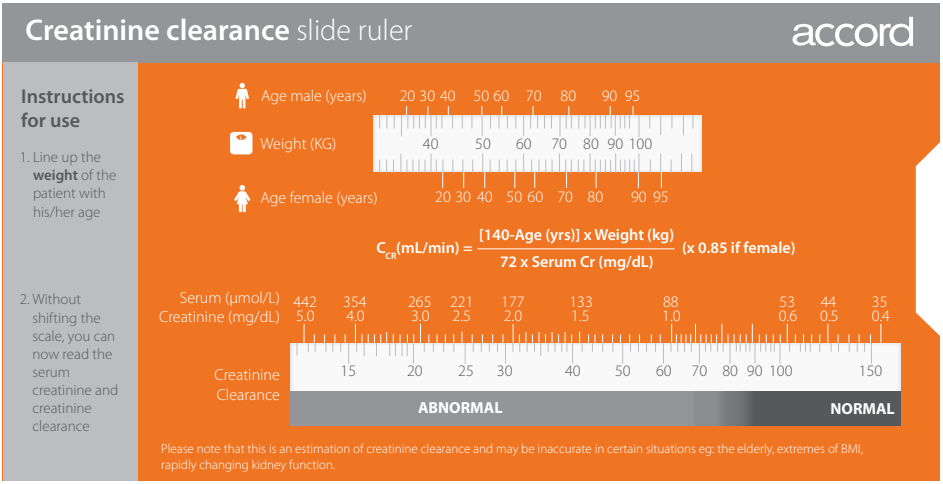
Severe renal impairment (creatinine clearance < 30 ml/min) and haemodialysis patients

Emtricitabine and tenofovir disoproxil is not recommended for patients with severe renal impairment (creatinine clearance < 30 ml/min) and in patients who require haemodialysis because appropriate dose reductions cannot be achieved with the combination tablet.

Table 2: Dosing interval adjustments for patients with renal impairment. [2]

Creatinine clearance	Dosing interval
50–80 (ml/min)	Administration of Ictastan 200 mg/245 mg film-coated tablets every 24 hours (no adjustment required).
30–49 (ml/min)	Administration of Ictastan 200 mg/245 mg film-coated tablets every 48 hours.
< 30 (ml/min)	Ictastan 200 mg/245 mg film-coated tablets are not recommended.
Haemodialysis patients	Ictastan 200 mg/245 mg film-coated tablets are not recommended.

Creatinine clearance slide ruler



References

1. Gupta SK et al Clin Infect Dis 2005;40:1559-1585

2. Ictastan 200 mg/245 mg film-coated tablets summary of product characteristics

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Earlsfort Terrace, IRL – Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517; Website: www.hpra.ie; E-mail: medsafety@hpra.ie.

Adverse reactions can also be reported to Medical Information at Accord Healthcare Ltd. via E-mail: medinfo@accord-healthcare.com; Tel: +44 (0) 1271 385 257; or by completing the online form at www.accord-healthcare.ie/drug-reaction-report.

By reporting side effects you can help provide more information on the safety of Ictastan 200 mg/245 mg film-coated tablets.

Further information

Additional electronic copies of this material are available at www.hpra.ie.
Additional hard copies of this material can be requested by contacting Actavis Ireland Ltd, a subsidiary of Accord Healthcare Ltd., Euro House, Euro Business Park, Little Island, Cork, T45 K857, Ireland; www.accord-healthcare.ie/medical-information-form; Tel: (0)21 461 9040; Fax: (0)21 461 9049.

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