ZEPATIER®▼ Elbasvir/Grazoprevir

PRESCRIBING INFORMATION
Refer to Summary of Product Characteristics before prescribing

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in Google Play or Apple App Store. Adverse events should also be reported to MSD UK (tel: 0208 1548000).
By clicking the above link you will leave the MSD website and be taken to the MHRA website.

PRESENTATION: film-coated tablet contains 50 mg of elbasvir and 100 mg of grazoprevir.

USES: Treatment of chronic hepatitis C (CHC) genotype 1a, 1b or 4 infection in adults and children aged ≥12 years of age and weighing ≥30 kg.

DOSAGE AND ADMINISTRATION: See SmPC for full details.
Treatment should be initiated and monitored by a physician experienced in the management of CHC. Recommended dose is one tablet once daily.

HCV genotype	Treatment and duration
1a	ZEPATIER for 12 weeks ZEPATIER for 16 weeks plus ribavirin should be considered in patients with baseline HCV RNA level >800,000 IU/ml and/or the presence of specific NS5A polymorphisms causing at least a 5-fold reduction in activity of elbasvir to minimise the risk of treatment failure.
1b	ZEPATIER for 12 weeks
4	ZEPATIER for 12 weeks ZEPATIER for 16 weeks plus ribavirin should be considered in patients with baseline HCV RNA level >800,000 IU/ml to minimise the risk of treatment failure.

No dose adjustment required in patients with mild, moderate, or severe renal impairment (including patients receiving haemodialysis or peritoneal dialysis). No dose adjustment required in children aged >12 years and weighing >30 kg.

CONTRA-INDICATIONS: Hypersensitivity; moderate or severe hepatic impairment (Child-Pugh B or C); co-administration with OATP1B inhibitors or CYP3A inducers or P-gp inducers.

PRECAUTIONS: Assess hepatic function prior to therapy, at treatment week 8, and as clinically indicated. For patients receiving 16 weeks of therapy, also assess hepatic function at week 12. Advise patients to seek medical advice immediately if they have fatigue, weakness, lack of appetite, nausea and vomiting, jaundice or discoloured faeces. Consider discontinuing therapy if ALT levels >10 x ULN. Discontinue therapy if ALT elevation is accompanied by signs or symptoms of liver inflammation, increased conjugated bilirubin, alkaline phosphatase, or INR. Not recommended in genotypes 2, 3, 5 and 6. Perform HBV screening in all patients before initiation of Zepatier treatment. HBV/HCV co-infected patients are at risk of HBV reactivation, and should be monitored and managed according to current clinical guidelines. Contains lactose and 69.85 mg of sodium per dose. Diabetics may have improved glucose control resulting in symptomatic hypoglycaemia after initiating HCV direct acting antiviral (DAA) treatment. Monitor glucose levels particularly for first 3 months and modify medication if necessary. Inform physician in charge of diabetic care when DAA therapy is initiated. *Drug interactions*: Co-administration with strong CYP3A inhibitors not recommended. Concentrations of dabigatran may increase when co-administered with elbasvir, with possible increased bleeding risk. Clinical and laboratory monitoring is recommended. When co-administered with vitamin K antagonists, monitor INR. When co-administered, the daily dose of atorvastatin, fluvastatin, lovastatin or simvastatin should not exceed 20 mg and the daily dose of rosuvastatin should not exceed 10 mg. When co-administered, monitor tacrolimus whole blood concentrations, changes in renal function, and for tacrolimus-associated adverse events. When co-administered, use with caution as dose adjustment of sunitinib may be required. *Children*: not indicated in children aged <12 years. *Pregnancy and*

lactation: Use in pregnancy only if the potential benefit justifies the potential risk to the foetus. When used with ribavirin, women of childbearing potential must use effective contraception during treatment and for a period post-treatment. Breast-feeding should be discontinued during Zepatier therapy.

SIDE EFFECTS: Refer to Summary of Product Characteristic for complete information on side-effects.
In clinical studies, the most commonly reported adverse reactions were fatigue and headache. Less than 1 % of subjects treated with ZEPATIER with or without ribavirin had serious adverse reactions (abdominal pain, transient ischaemic attack and anaemia).
Very common (≥ 1/10): headache; fatigue
Common (≥ 1/100 to < 1/10): decreased appetite; insomnia, anxiety, depression; dizziness; nausea, diarrhoea, constipation, upper abdominal pain, abdominal pain, dry mouth, vomiting; pruritus, alopecia; arthralgia, myalgia; asthenia, irritability.
Serum Late ALT elevations: During clinical studies with ZEPATIER with or without ribavirin, < 1% of subjects experienced elevations of ALT > 5 x ULN, generally at or after treatment week 8. These were typically asymptomatic, with most late ALT elevations resolving with on-going therapy or after completion of therapy.

PACKAGE QUANTITIES AND BASIC NHS COST:
Packs of 28 tablets: £12,166.67

Marketing Authorisation number:
Great Britain: PLGB 53095/0082
UK (Northern Ireland): EU/1/16/1119/001

Marketing Authorisation Holder:
Great Britain:
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Legal Category: POM

Date of review of prescribing information: November 2021

PI.ZPT.21.GB-NI.7884.II-008.RCN09499