Report ZEPATIER® elbasvir/grazoprevir

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: elbasvir / grazoprevir **Brand Name:** Zepatier **Originator/licensee:** Merck Sharp & Dohme B.V. **Classification:** NI **ATC code:** J05AP54 **Orphan Status:** **Eu:** No **Mechanism of action:** Grazoprevir, is an inhibitor of the NS3/4A protease. NS3/4A-mediatedcleavage of the polyprotein formed by translation of the HCV RNA genome is essential for replication.Elbasvir is an inhibitor NS5A, which is a pleiotropic protein with important roles in HCV viral replication and modulation of the physiology of the host cell[1].	**Authorized Indication:** **EMA:** the combination elbasvir/grazoprevir is indicated for the treatment of CHC in adults and paediatric pts ≥12 years of age, who weigh at least 30 kg [2] **Route of administration:**OS **Licensing status** **EU CHMP P.O. date:** 16/09/2021 **FDA M.A. date:** - **EU Speed Approval Pathway:** - --- **ABBREVIATIONS:** **AE:** Adverse Events **CHC:** chronic hepatitis C **CHMP:** Committee for Medicinal Products for Human Use **FDC:** fixed dose combination **HCV**: Hepatitis C virus **M.A.:** Marketing Authorization **NS5A:** non-structural protein 5A **P.O.:** Positive Opinion **pts:** patients **RNA:** Ribonucleic acid **SAE:** Serious Adverse Events	**Summary of clinical EFFICACY:** **NCT03379506** is a phase IIb, open-label, multi-cohort study (Cohort 1: n=22, pts aged 12 to <18 years of age; Cohort 2: n=17, pts aged 7 to <12 years of age; and Cohort 3: n=11, pts aged 3 to <7 years of age) investigating the pharmacokinetics, safety and efficacy of elbasvir/grazoprevir FDC in pediatric pts with chronic HCV. Cohort 1 received elbasvir/grazoprevir 50 mg/100 mg FDC tablets once daily for 12 weeks. Cohort 2 received elbasvir/grazoprevir 30 mg/60 mg pediatric granules once daily for 12 weeks. Cohort 3 received elbasvir/grazoprevir 25 mg/50 mg once daily for 12 weeks. The efficacy endpoint was the percentage of pts with SVR12 after discontinuation of therapy. SVR was defined as HCV-RNA <LLOQ 12 weeks after completing study therapy. In Cohort 1: all (100%) pts achieved SVR12 (95% CI: 84.6 to 100.0). In Cohort 2: all (100%) pts achieved SVR12 (95% CI: 80.5 to 100.0). In Cohort 3: all (100%) pts achieved SVR12 (95% CI: 71.5 to 100.0) [3,4]. **Summary of clinical SAFETY:** **NCT03379506** reported SAE in 1/22 (4.55%)ptsin Cohort 1 (one hand fracture), no SAE occurred in Cohort 2 and 1/11 (9.09%) of the pts in Cohort 3 (dyspepsia). Non-serious AEoccurred in 17/22 (77.27%) pts in Cohort 1, 13/17 (76.47%) subjects in Cohort 2 and 9/11 (81.82%) pts in Cohort 3. The most common AEs were (in Cohort 1, in Cohort 2, in Cohort 3, respectively):headache (36.36%, 11.76%, 18.18%,), nausea (18.18% , 0%, 0%), nasopharyngitis (18.18%, 5.88%, 9.09%), vomiting (13.64%, 5.88%, 27.27%), abdominal upper pain (13.64%, 5.88%, 0%), pyrexia (13.64%, 0%, 0%), dizziness (13.64%, 0%, 0%),respiratory tract infection (0%, 11.76%, 27.27%), bronchitis (0%, 0%, 18.18%)[3,4] **Ongoing studies:** ● ***For the same indication:***Yes ● ***For other indications:***No **Discontinued studies (for the same indication):**No --- **References:** 1. https://www.ema.europa.eu/en/documents/assessment-report/zepatier-epar-public-assessment-report_en.pdf 2. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/zepatier 3. https://clinicaltrials.gov/ct2/show/NCT03379506?term=NCT03379506&draw=2&rank=1 4. https://www.clinicaltrialsregister.eu/ctr-search/trial/2015-003006-16/results 5. https://gallery.farmadati.it/Home.aspx 6. https://www.epicentro.iss.it/epatite/dati-seieva#c 7. Guidelines for the care and treatment of persons diagnosed with hepatitis C infection, updated July 2017. Geneva: WHO; 2018(https://www.who.int/publications/i/item/9789241550345, accessed 26 February 2021) 8. https://clinicaltrials.gov/ct2/results?cond=HCV&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&age=0&gndr=&intr=&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort=	**Cost of therapy:** In Italy, the price of 28 tablets/pack of elbasvir/grazoprevir 50mg/100mgis 22.342,29€ (*retail price*) [5].12 week-treatment costs67.026,87 € **Epidemiology:** In Italy, the incidence of CHC at December 2020 was: - 0/100.000 among children aged 0-14 years old; - 0,04/100.000 among people aged 15-24 years old [6] --- **POSSIBLE PLACE IN THERAPY** In adolescents aged 12–17 years or weighing at least 35 kg with chronic HCV, WHO recommends: • sofosbuvir/ledipasvir for 12 weeks (or 24 weeks in pts who are treatment experienced and with compensated cirrhosis) in genotypes 1, 4, 5 and 6; • sofosbuvir/ribavirin for 12 weeks in genotype 2; • sofosbuvir/ribavirin for 24 weeks in genotype 3 [7]. **OTHER INDICATIONS IN DEVELOPMENT:** - **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**- **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION :** Glecaprevir/pibrentasvir [8] *Service reorganization: No *Possible off label use: Yes, for pts aged < 12 years

Issued on: