GILEAD | Medical Information

Hepcludex® (bulevirtide-gmod) Use in Pediatric Patients

This document is in response to your request for information regarding the use of Hepcludex® (bulevirtide-gmod [BLV]) in pediatric patients (ie, <18 years of age) for the treatment of chronic HDV infection.

Some data may be outside of the US FDA-approved prescribing information. In providing this data, Gilead Sciences, Inc. is not making any representation as to its clinical relevance or to the use of any Gilead product(s). For information about the approved conditions of use of any Gilead drug product, please consult the FDA-approved prescribing information.

The full indication, important safety information, and boxed warnings are available at: www.gilead.com/-/media/files/pdfs/medicines/hdv/hepcludex/hepcludex_pi.

Product Labeling[1]

BLV is indicated for the treatment of chronic HDV infection in adults without cirrhosis or with compensated cirrhosis.

This indication is approved under accelerated approval based on a decrease in HDV RNA and ALT normalization. An improvement in disease-related clinical outcomes has not been established. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

The recommended dosage in adults is BLV 8.5 mg once daily administered by SUBQ injection.

The safety and effectiveness of BLV in pediatric patients <18 years of age have not been established.

The efficacy of BLV once daily in the treatment of adults with chronic HDV infection without cirrhosis or with compensated cirrhosis is based on data through Week 144 from a multicenter, randomized, open-label, parallel-arm phase 3 trial, Trial MYR301 (NCT03852719), in which 100 participants received BLV 8.5 mg once daily. The MYR301 protocol specified the BLV dose as 10 mg; however, a dose recovery study later showed that the delivered dose was 8.5 mg.

Clinical Data on BLV Use in Pediatric Patients

In a phase 3 study (MYR301) and phase 2/2b clinical studies (MYR202, MYR203, and MYR204), participants aged ≥18 years were enrolled. No clinical studies with BLV have been conducted in pediatric patients.[2-5]

PopPK Analysis: Weight-Based Dosing in Pediatric Patients[6]

Using previous data from BLV phase 1, 2, and 3 studies, a one-compartment PK model with first-order elimination was developed to simulate steady-state exposures to SUBQ BLV in a pediatric population. Dose evaluations in children included a flat-dose regimen of BLV 2 mg SUBQ once daily or a weight-based regimen of BLV SUBQ once daily, as follows: in children weighing 10 kg to <25 kg, BLV 1 mg; in children weighing 25 kg to <35 kg, BLV 1.5 mg; and in children weighing ≥35 kg, BLV 2 mg.

The flat-dose regimen resulted in high exposure levels relative to adults, and this was more prevalent among lower weight children. Weight-based BLV dosing, on the other hand, generally aligned with adult exposure (reference: 2 mg dose); the IQRs of the pediatric PK profiles for the 10 kg to <25 kg and ≥35 kg dosing groups were fully within the 5th and 95th percentile of the adult reference, and nearly all values for the 25 kg to <35 kg dosing group were within the 5th and 95th percentile of the adult reference (Table 1). Although some PK values for the 25 kg to <35 kg dosing group were above the 95th percentile range, they were below the exposure observed with 10 mg of BLV in adults.

Table 1. PopPK Analysis in Pediatric Patients: Simulated Exposures at Steady State After Weight-Based SUBQ Dosing of BLV and Reference Adult Exposures[6]

Age Group and Weight Category		AUC, ng·h/mL	C_{max}, ng/mL	C_{min}, ng/mL	Elimination $t_{1/2}$, h	T_{max}, h
Children,[a] GM (GM CV%) [5th–95th percentile]	10 to <25 kg	399 (101) [100–1570]	43.2 (101) [10.6–166]	1.79 (992) [0.0375–23]	5.71 (69.2) [2.05–16]	1.34 (99.7) [0.32–4.88]
	25 to <35 kg	459 (101) [117–1810]	48.6 (99.8) [12–184]	2.12 (929) [0.0483–27.6]	5.73 (69.6) [2.06–16.2]	1.51 (96.7) [0.374–5.32]
	≥35 kg	405 (104) [99.3–1640]	41.3 (99.5) [10.3–156]	1.99 (975) [0.0438–26.7]	5.83 (69.9) [2.08–16.6]	1.73 (95.4) [0.425–5.9]
Adults,[b] 5th–95th percentile	2 mg	85.9–763	8.22–87.8	0.494–11.8	3.73–10.2	0.753–4.18
	10 mg	556–6280	47.2–531	1.69–92.4	2.9–9.44	1.1–5.43

Abbreviations: CV=coefficient of variation; GM=geometric mean; $t_{1/2}$=half-life; T_{max}=time to maximal concentration.
[a]Weight-based BLV dosing administered once daily: in children weighing 10 kg to <25 kg, BLV 1 mg; in children weighing 25 kg to <35 kg, BLV 1.5 mg; and in children weighing ≥35 kg, BLV 2 mg.
[b]Reference data in adults represent BLV administered SUBQ once daily.

PK/PD Extrapolation to Determine Optimal Dosing in Pediatric Patients[7]

A PK/PD modeling and simulation approach was used to identify the optimal BLV dosing regimen for pediatric patients with chronic HDV infection. The analysis applied PK/PD extrapolation and exposure matching to determine the pediatric doses expected to achieve exposure levels similar to those observed in adults. Simulated pediatric PK profiles and steady-state exposures were compared with adult data from phase 2 and 3 studies (MYR202, MYR203, MYR204, and MYR301), in which patients received SUBQ BLV 2 mg or 10 mg once daily. In addition, simulated pediatric exposures were compared with the adult C_{trough} at EC_{50}. Dose evaluations in the pediatric population included the following regimens: flat SUBQ dose regimen (1 mg, 1.5 mg, or 2 mg once daily); an age-based regimen (1 mg once daily for ages 3–6 years, 1.5 mg once daily for ages 6–12 years, and 2 mg once daily for ages 12–18 years); and a weight-based regimen (1 mg once daily for 10–25 kg, 1.5 mg once daily for 25–35 kg, and 2 mg once daily for ≥35 kg).

Age- and weight-based dosing regimens resulted in consistent BLV exposures across all pediatric age groups. Simulated steady-state PK parameters (AUC_T, C_{max}, C_{min}, C_{av}) in pediatric patients generally fell within the 5th to 95th percentile range of adult exposures (2 mg once daily dose), except that median C_{min} values in younger and lower-weight pediatric patients were below the 5th percentile of adult values. Bile salt exposures (IQR) across all pediatric age- and weight-based dosing regimens fell within the 5th to 95th percentile range for adults at 2 mg once daily and remained below the median exposure observed in adults at 10 mg once daily. In patients aged 12 to 18 years, a 1 mg flat dose resulted in BLV exposures (IQR) below the 5th percentile of adult exposures at 2 mg once daily. In patients aged 3 to 6 years and 6 to 12 years, flat doses of 1.5 mg and 2 mg, respectively, produced exposures that exceeded the 95th percentile of adult values at 2 mg once daily but remained within the adult 5th to 95th percentile range at 10 mg once daily. Across all dosing regimens, the median C_{trough} at the end of the dosing interval exceeded the adult C_{trough} at EC_{50} in >70% of pediatric patients in each age group.

References

1. Enclosed. Gilead Sciences Inc. HEPCLUDEX® (bulevirtide) injection, for subcutaneous use. US Prescribing Information. Foster City, CA.
2. Wedemeyer H, Schoneweis K, Bogomolov P, et al. Safety and efficacy of bulevirtide in combination with tenofovir disoproxil fumarate in patients with hepatitis B virus and hepatitis D virus coinfection (MYR202): a multicentre, randomised, parallel-group, open-label, phase 2 trial. *Lancet Infect Dis.* 2022.
3. Wedemeyer H, Aleman S, Brunetto MR, et al. A Phase 3, Randomized Trial of Bulevirtide in Chronic Hepatitis D. *N Engl J Med.* 2023;389(1):22-32.
4. Asselah T, Chulanov V, Lampertico P, et al. Bulevirtide Combined with Pegylated Interferon for Chronic Hepatitis D. *N Engl J Med.* 2024;391(2):133-143.
5. Lampertico P, Bogomolov PO, Chulanov V, et al. Phase 2 Randomised Study of Bulevirtide as Monotherapy or Combined With Peg-IFNalpha-2a as Treatment for Chronic Hepatitis Delta. *Liver Int.* 2025;45(2):e70008.
6. European Medicines Agency (EMA), Committee for Medicinal Products for Human Use (CHMP). *CHMP extension of indication variation assessment report. Hepcludex. EMA/542920/2024. The Netherlands.* October 2024.
7. Kumar P, Mc Laughlin AM, de Mendizabal NV, et al. Paediatric Pharmacokinetic-Pharmacodynamic Extrapolation to Identify Suitable Bulevirtide Doses for Children and Adolescents With Chronic Hepatitis Delta. [Poster #WED-311]. Paper presented at: European Association for the Study of the Liver; May 7–10, 2025; Amsterdam, the Netherlands.

Abbreviations

AUC=area under the concentration-time curve
AUC_T=area under the concentration-time curve over the dosing interval
BLV=bulevirtide-gmod
C_{av}=average plasma concentration
C_{max}=maximum plasma concentration
C_{min}=minimum plasma concentration
C_{trough}=trough plasma concentration
EC_{50}=half maximal effective concentration
PD=pharmacodynamic(s)
PK=pharmacokinetic(s)
PopPK=population pharmacokinetics
SUBQ=subcutaneous(ly)

Product Label

For the full indication, important safety information, and boxed warning(s), please refer to the Hepcludex US Prescribing Information available at: www.gilead.com/-/media/files/pdfs/medicines/hdv/hepcludex/hepcludex_pi .

Follow-Up

For any additional questions, please contact Gilead Medical Information at:

☎1-866-MEDI-GSI (1-866-633-4474) or www.askgileadmedical.com

Adverse Event Reporting

Please report all adverse events to:

Gilead Global Patient Safety ☎ 1-800-445-3235, option 3 or www.gilead.com/utility/contact/report-an-adverse-event

FDA MedWatch Program by ☎ 1-800-FDA-1088 or ✉MedWatch, FDA, 5600 Fishers Ln, Rockville, MD 20852 or www.accessdata.fda.gov/scripts/medwatch

Data Privacy

The Medical Information service at Gilead Sciences may collect, store, and use your personal information to provide a response to your medical request. We may share your information with other Gilead Sciences colleagues to ensure that your request is addressed appropriately. If you report an adverse event or concern about the quality of a Gilead or Kite product, we will need to use the information you have given us in order to meet our regulatory requirements in relation to the safety of our medicines.

It may be necessary for us to share your information with Gilead's affiliates, business partners, service providers, and regulatory authorities located in countries besides your own. Gilead Sciences has implemented measures to protect the personal information you provide. Please see the Gilead Privacy Statement (www.gilead.com/privacy-statements) for more information about how Gilead handles your personal information and your rights. If you have any further questions about the use of your personal information, please contact gilead.privacy@gilead.com.