



RIGHT

for better LIFE

Recombinant GlycoPEGylated EHL factors
for Higher Trough levels

ISSUE 1, 2022

What are EHL clotting factor concentrates?



Specially designed clotting factors with extended half-lives¹



Product of structural modifications and chemical alterations¹



Aimed at providing better treatment adherence¹



Improves outcomes¹

What is the need for formulating EHL clotting factors?

Mainstay of haemophilia treatment¹

Replacement of the missing factor with SHL factor concentrates¹

Challenges with SHL factors¹

Relatively short half-life¹

Need for frequent injections¹

Inadequate trough levels¹

SHL factor concentrates	Half-life	Frequency of injections
FVIII	8-12 hours ^{1,2}	≥3 times a week ^{1,2}
FIX	18-20 hours ^{1,2}	2 times a week ^{1,2}

Despite these demanding prophylactic treatment schedules, PWH still have²



Elevated risk of bleeding²



Incomplete protection from spontaneous bleeding episodes²

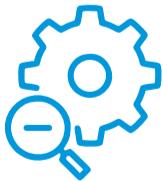
To treat PWH, there is a need for



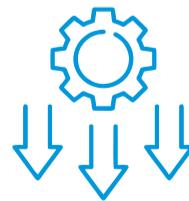
More convenient methods¹



Factor concentrates with longer half-lives¹



Less frequent dosing¹



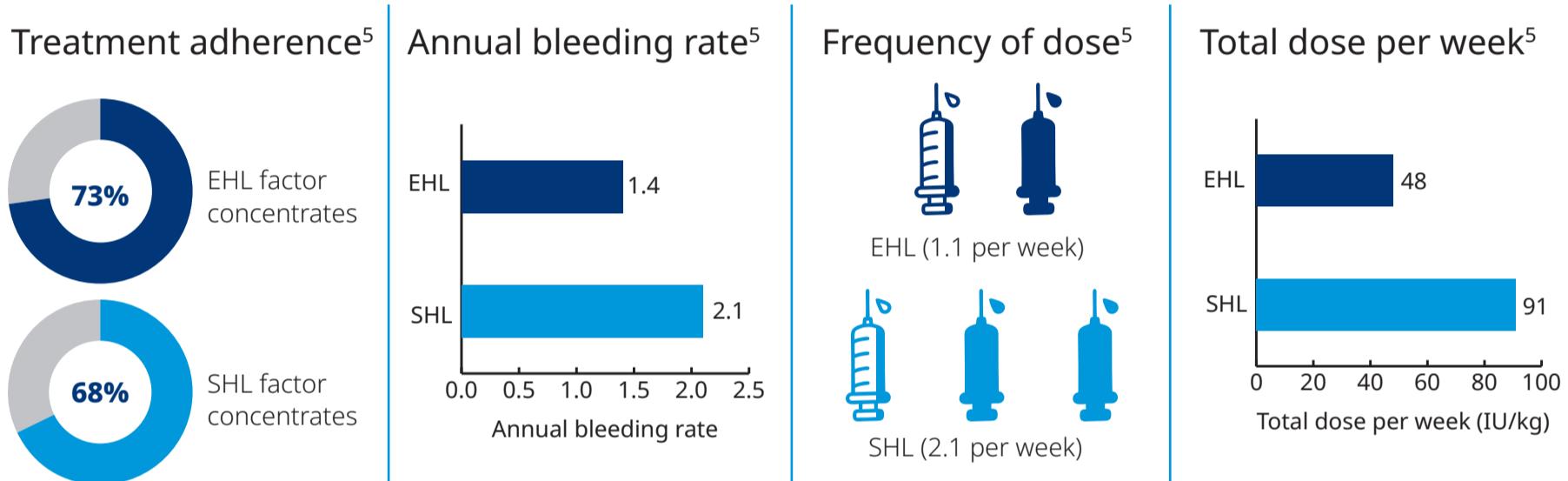
Reduced prophylactic treatment burden¹

Abbreviations: EHL: Extended half-life; SHL: Standard half-life; PWH: People with haemophilia.

Advantages of EHL clotting factors

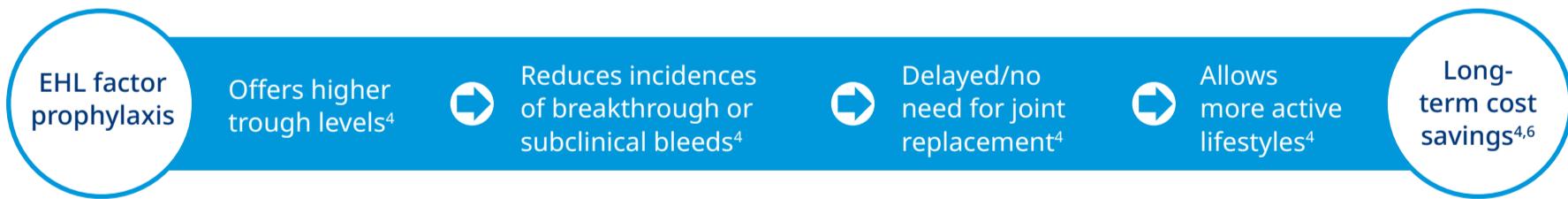


Edge of EHL FIX over SHL FIX



Cost-effective, life-long treatment

- Total IU dose administered is **numerically lower with EHL** v/s SHL factor concentrates⁵



elevated care for
EASE OF LIFE.

esperoct®
turoctocog alfa pegol

India's 1st glycopegylated EHL factor for Haemophilia A**

**EHL, Extended Half-life; **Esperoct Prescribing Information, 2021

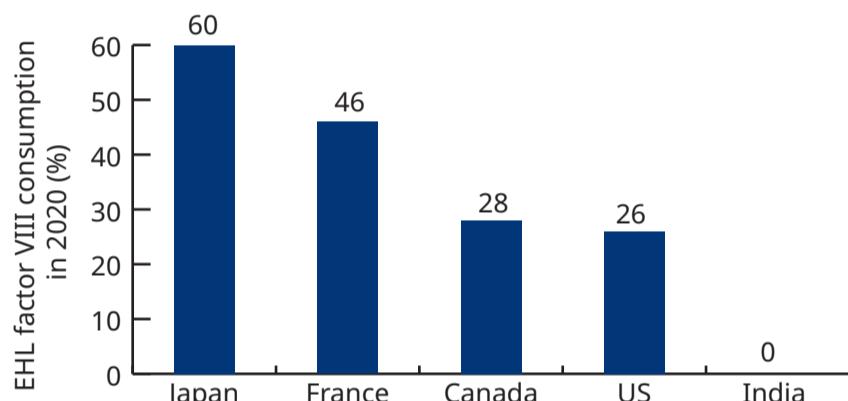


World Federation of Hemophilia (WFH) Report on the Annual Global Survey 2020

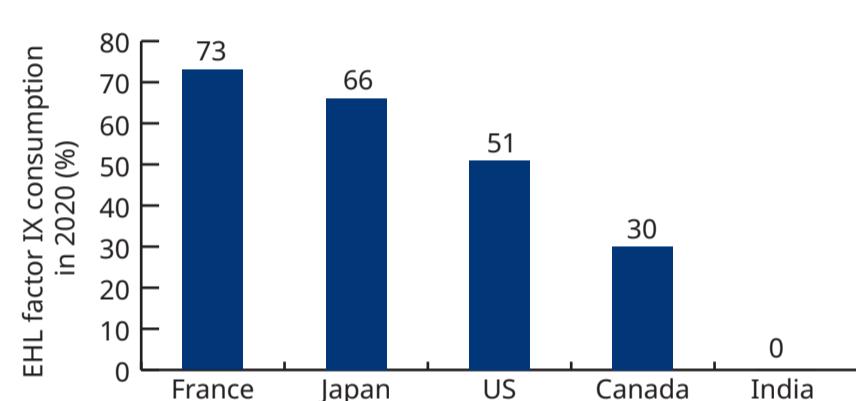
India has the highest reported cases of haemophilia globally⁷



Use of EHL factor VIII concentrates in India versus other countries (WFH 2020)⁷



Use of EHL factor IX concentrates in India versus other countries (WFH 2020)⁷



Recommendations for use of EHL factor concentrates (WFH 2020)

Recombinant clotting factor concentrates (CFCs) with EHL are formulated to provide longer-lasting therapy than SHL CFCs⁸

Recommendations

- PWH who are transitioning from SHL clotting factor concentrates to EHL clotting factor concentrates would typically require **decreased dose frequencies**, but EHL products may also be used to **maintain higher trough levels** to optimize prophylaxis⁸
- For patients with severe phenotype hemophilia A or B using EHL factor concentrates, the **WFH recommends prophylaxis with EHL CFCs at sufficient doses and dosing intervals** to prevent hemarthroses and spontaneous and breakthrough bleeding and preserve joint function.⁸

reinvent
LIFE

Refixia™
once-weekly prophylaxis gives patients the
confidence to live beyond Haemophilia B¹⁻⁵



refixia™
nonacog beta pegol
The only LONG-ACTING FIX*

How patients perceive EHL products: Notions from real-world experience

HOw Patients view Extended half-life products (HOPE) study (UK)⁹

- Patients switching to EHL treatments believe:



These products will result in fewer infusions⁹



Less disruption of everyday life⁹



Feeling more protected⁹



Fewer bleeds⁹



Increased activity levels⁹



Enhanced mental health⁹

EHL factor VIII **esperoct®** *turoctocog alfa pegol*



22-hour average half-life in adults¹⁰



Factor levels $\geq 3\%$ for 100% of the time in people ≥ 12 years¹⁰



As compared to SHL infusion every other day¹⁰

EHL factor IX **refixia™** *nonacog beta pegol*

- 60% reduction in overall factor consumption^{*11}
- Increase in plasma half-life \approx 5 fold^{*11}
- Successfully treated¹²



of spontaneous bleeds



of traumatic bleeds

* in comparison to SHL FIX

References

- Ar MC, Balkan C, Kavaklı K. Extended Half-Life Coagulation Factors: A New Era in the Management of Hemophilia Patients. *Turk J Haematol.* 2019;36(3):141-154.
- Graf L. Extended Half-Life Factor VIII and Factor IX Preparations. *Transfus Med Hemother.* 2018;45(2):86-91.
- Matsushita T, Manglès S. An overview of the pathfinder clinical trials program: Long-term efficacy and safety of N8-GP in patients with hemophilia A. *J Thromb Haemost.* 2020;18 Suppl 1(Suppl 1):26-33.
- Lambert T, Benson G, Dolan G, et al. Practical aspects of extended half-life products for the treatment of haemophilia. *Ther Adv Hematol.* 2018;9(9):295-308.
- Chhabra A, Spurden D, Fogarty PF, et al. Real-world outcomes associated with standard half-life and extended half-life factor replacement products for treatment of haemophilia A and B. *Blood Coagul Fibrinolysis.* 2020;31(3):186-192.
- Henry N, Jovanović J, Schlueter M, et al. Cost-utility analysis of life-long prophylaxis with recombinant factor VIIIfc vs recombinant factor VIII for the management of severe hemophilia A in Sweden. *J Med Econ.* 2018;21(4):318-325.
- Report on the Annual Global Survey 2020: World Federation of Hemophilia. Available at: <https://www1.wfh.org/publications/files/pdf-2045.pdf>. Accessed on 29/12/2021.
- Srivastava A, Santagostino E, Dougall A, et al; WFH Guidelines for the Management of Hemophilia panelists and co-authors. WFH Guidelines for the Management of Hemophilia, 3rd edition. *Haemophilia.* 2020;26 Suppl 6:1-158.
- Khair K, Pollard D, Harrison C, et al; HOw Patients view Extended half-life products: Impressions from real-world experience (The HOPE study). *Haemophilia.* 2019;25(5):814-820.
- Esperoct. Available at: <https://www.esperoct.com/>. Accessed on 09/02/2022.
- Mannucci PM. Hemophilia therapy: The future has begun. *Haemotologica.* 2020;105(3):545-553.
- Chan AK, Alamelu J, Barnes C, et al. Nonacog beta pegol (N9-GP) in hemophilia B: First report on safety and efficacy in previously untreated and minimally treated patients. *Res Pract Thromb Haemost.* 2020;4:1101-1113.



Disclaimer: The contents of this newsletter are developed by Passi HealthCom Pvt. Ltd. exclusively for Novo Nordisk India Private Limited. Although great care has been taken in compiling and checking the information, the authors, Passi HealthCom Pvt. Ltd. and its agents and sponsors shall not be responsible, or in anyway liable for any errors, omissions or inaccuracies in this publication whether arising from negligence or otherwise or for any consequences arising therefrom.

Don't let their dreams
bleed inside

In haemophilia,
internal bleeding
leads to **disability**
in 8 out of 10
youngsters¹.



Let their dreams
BECOME A REALITY

Think Prophylaxis - The proven measure to prevent disability among patients with haemophilia²

References:

- Kar A, Mirkazemi R, Singh P, et al. Disability in Indian patients with haemophilia. *Haemophilia.* 2007 Jul;13(4):398-404.
- Srivastava et al, WFH Guidelines. Guidelines for the management of hemophilia. *Haemophilia* (2013), 19, e1–e47.

For more information on haemophilia and other rare blood disorders, please visit changinghaemophilia.com