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Gurgaon, Haryana - 122002 INDIA. Tel: +91 124 4559100 | www.shire.com

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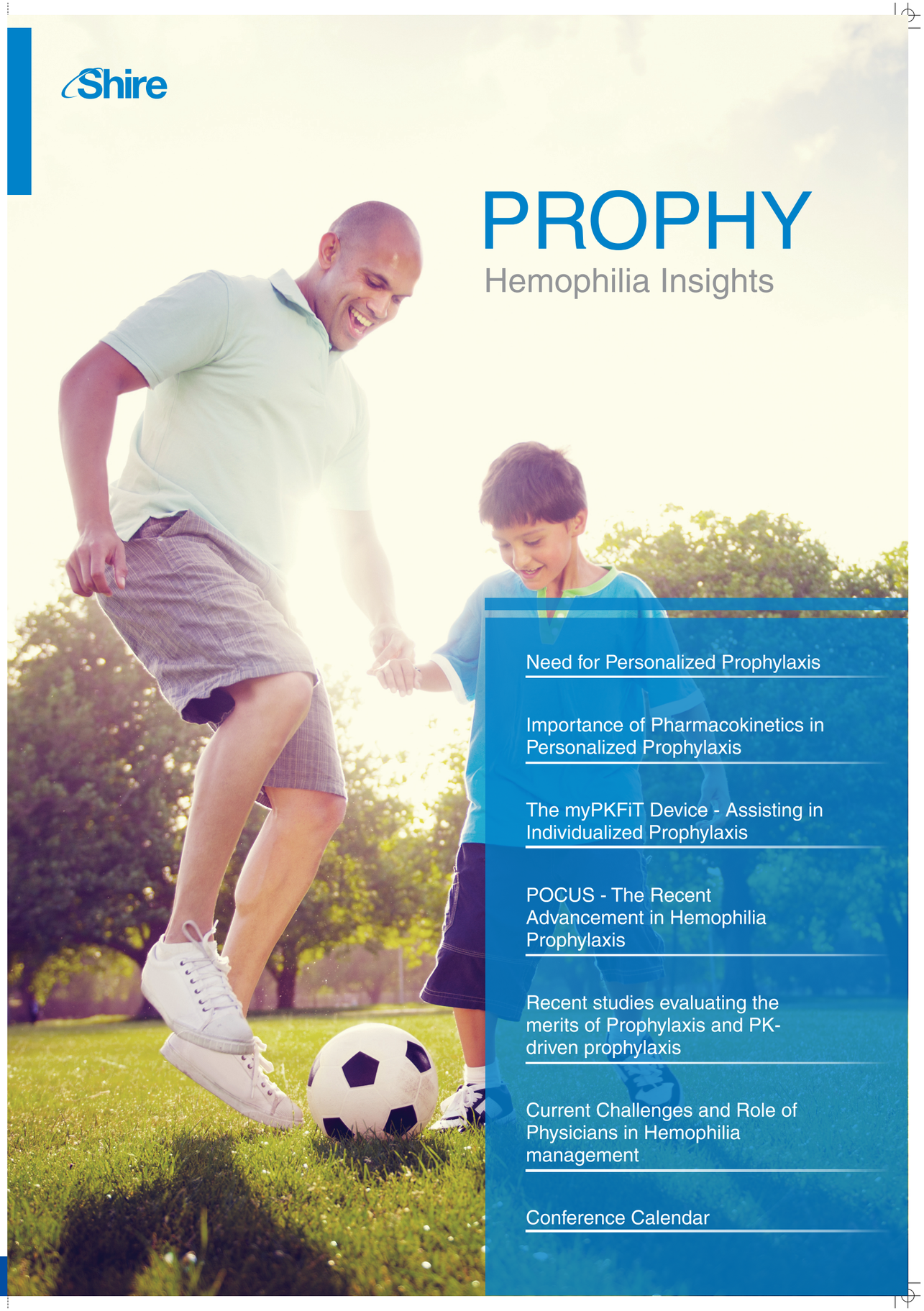
Hemophilia Insights



PHYSICIANS ROLE IN SELECTING A FACTOR REPLACEMENT THERAPY

Consider the safety and efficacy of the factor replacement therapy, especially in the vulnerable and susceptible patient population and chose a factor that is effectively screened, and inactivated with the most tested techniques.

Take into account patient convenience.

Regard issues related to the consistency and reliability of supply for the chosen therapy.

Pay heed to take patient preference, and brand loyalty as some patients may be resistant in changing to new products.

Be proactive in engaging patients in a conversation about emerging pathogens and the relative risks that are associated via factor therapies.

Enhance patient's trust in the physicians treating them and the therapy by addressing patient's individual needs and concerns regarding the treatments with up to date available information.

Be informed with recent guidelines, research and recommendations in the field of hemophilia about the issues of safety, efficacy and emerging trends and challenges and act respond appropriately.

Do not completely depend on the current available scientific evidence while choosing the therapy, instead be proactive in your choices and employ current knowledge of associated risks and knowledge of pathogens to deliver safe and effective treatment.[11,12]

CONFERENCE CALENDAR

Sl. No	Conference	Date	Venue
1.	NEW FRONTIERS IN COAGULATION MEDICINE AND TRAINEES MEETING 2018	JANUARY 10 - 11	OLD WINDSOR , UNITED KINGDOM
2.	11TH ANNUAL CONGRESS OF EAHAD	FEBRUARY 7 -9	MADRID, SPAIN
3.	MAYO CLINIC CLINICAL AND MULTIDISCIPLINARY HEMATOLOGY AND ONCOLOGY 2018: THE 15TH ANNUAL REVIEW 2018	FEBRUARY 16 -18	SCOTTSDALE , ARIZONA , UNITED STATES
4.	SCRIPPS' 38TH ANNUAL CONFERENCE: CLINICAL HEMATOLOGY & ONCOLOGY 2018	FEBRUARY 17 -20	SAN DIEGO , UNITED STATES
5.	12TH WORLD HEMATOLOGISTS CONGRESS	MARCH 15-16	LONDON, UK

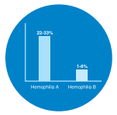
Study Population: Total 6 pediatric patients below 12 years with severe hemophilia A, who were on prophylaxis with Advate® with no presence of FVIII inhibitors.

Results: The study reported reduced weekly frequency of infusions in one patient, and a slight increase in three children. the dosage was changed in the remaining two children. Scheduled follow-up after 6 months identified a complete adherence to treatment, a reduction of bleeds and a general improvement in the quality of life with PK-driven prophylaxis was assessed as cost-saving in 5/6 cases (83.4%) and a total saving of € 54,797.40 (–10.67%) was noted in case of tailored prophylaxis.

Summary: Tailored prophylaxis based on PK and clinical characteristics of every patient could be an effective option for children with HA than standard prophylaxis, thus reducing costs. The different PK among patients can help clinicians tailor the prophylaxis and therefore improve the QoL, reducing infusions and bleeding. In general cost of therapeutic management of hemophilia is costly and a PK-driven prophylaxis can decrease the direct and indirect costs of therapies.

New Finding: Tailored treatment with PK-driven prophylaxis is possible in clinical set-ups and is also cost saving in the long-term management of hemophilia A in children.

CURRENT CHALLENGES IN HEMOPHILIA MANAGEMENT



Development of Inhibitors - Development of inhibitory alloantibodies against FVIII or FIX is seen in 22-33% of severe hemophilia A and 1-6% of hemophilia B patients that renders replacement therapies ineffective. Can be successfully managed with screening of inhibitors and by employing bypassing agents.[8,9]

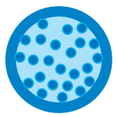
Venous Access - Managing venous access in very young children raises complications, such as infections and thrombosis and can be addressed with by using implantable catheters (ports).[8]

Multidisciplinary Approach – Over the lifetime hemophilia patients require access to other specialists, like rheumatologists, pain specialists, infectious disease specialists, surgeons, hepatologists, nutritionists, and dentists for their needs.

Access to Specialized Centers - Require lifelong access to specialized centers and comprehensive care.

Shortage of Specialists – Availability of fewer physicians sufficiently trained to treat inherited bleeding disorders and improper or inadequate training puts the patient at risk. They not only require experienced hematologic care but also care from other specialists experienced in treating patients for hemophilia.

Cost of Therapy – Factor replacement is an expensive and necessary treatment. The severity of disease and presence of inhibitors dictate the use or choice of therapy and ultimately the cost.



Frequent Injections - Inhibitors with relatively short half-life of molecules require frequent injection to maintain effective concentration.[9,10]

Prophylaxis intends to convert patients with hemophilia from a severe to a moderate clinical phenotype with the regular infusion of FVIII. In patients receiving prophylaxis, half-lives and infusion regimens have a large influence on predicted FVIII levels. The longer the patient is with a low FVIII the higher will be the risk of bleeding.

The natural history of severe haemophilia is characterized by recurrent joint and muscle bleeds resulting in severe and gradual musculoskeletal damage and ultimately compromised mobility. It is well established that early prophylaxis helps reducing or preventing musculoskeletal problems. Hence prophylaxis should be started as a minimum after the first joint bleed to increase the trough level of factor VIII or IX above 1 IU dL–1.[1]

NEED FOR PERSONALIZED PROPHYLAXIS

Standard prophylaxis prescribed based on weight may not be the most scientific approach for all as neither the in vivo recovery nor the half-life of FVIII is directly proportionate to weight and both vary from patient to patient. This results in a broad variation in the trough level achieved. Hence each individual should have a personalized regimen taking into account the following determinants:[1]

DETERMINANTS OF PERSONALIZED PROPHYLAXIS

Bleeding pattern & Hemophilia severity

PK profile

Adherence to treatment

Personal and treatment goals

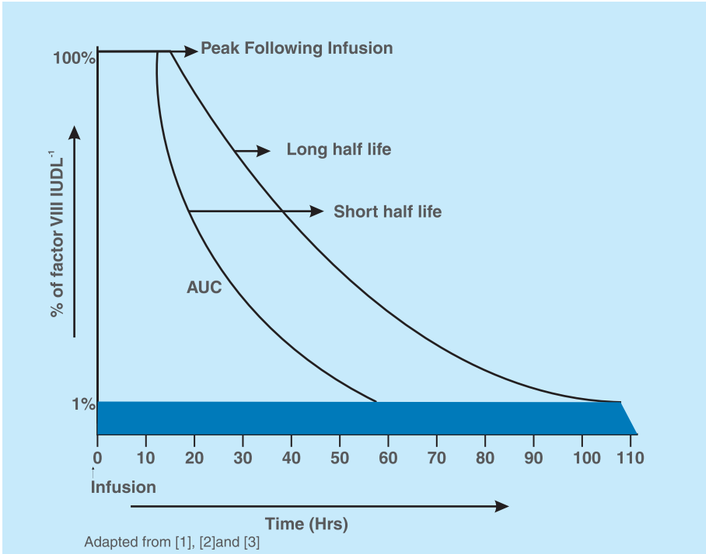
Level and schedule of physical activities

Joint status

IMPORTANCE OF PHARMACOKINETICS (PK) IN TAILORING PROPHYLAXIS PK

PK varies for each patient as it is influenced by the patient's age, weight and metabolic characteristics making it variable in each patient. The important PK data that need to be evaluated are the area under the curve (AUC), the maintenance of an appropriate trough level of 1%, the maximum peak of the FVIII level obtained after infusions, the clearance and the half-life of FVIII.[3]

The knowledge of individual patient PK profiles will possibly have significant implications for treatment regimens, as there is a wide inter-patient variation in FVIII requirement. Individual PK profiles will also permit better-tailored regimens and at times are more cost-effective.[2]



Adapted from [1], [2]and [3]

ASSISTING THE INDIVIDUALIZATION PROCESS

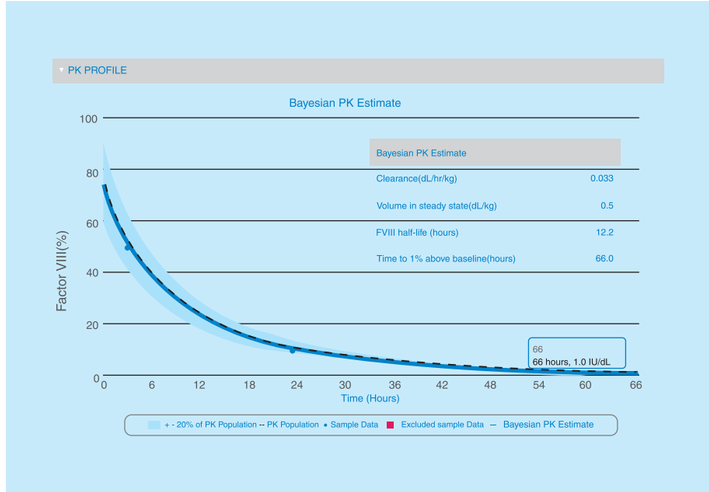
- Pharmacokinetic (PK) measurement tools like web-based user-friendly instruments
- Assessment tools such as joint status imaging and function studies/scores, QoL scoring help in determining and monitoring risk factors and outcome

THE MYPKFIT DEVICE TO ASSIST IN IN INDIVIDUALIZED PROPHYLAXIS

MyPKFiT is a web-based application that allows authorized users to simulate dosing regimens using individualized patient Pharmacokinetic (PK) profiles using only 2 blood samples, that are to be taken approximately 3 hours apart and between 24 and 32 hours post factor VIII infusion respectively.[5]

KEY FEATURES

- Trustworthy estimation of individual PK curves
- Requires only 2 samples when compared to traditional testing methods requiring 11
- Allows personalized prophylactic regimens with Octogog alpha (ADVATE). Educates the patients on their PK curves and thus engages them in the treatment regimens
- Supported by 2000 data points from Octogog alpha patient studies[5]
- The PK curves help in understanding how the patient is processing the administered factor VIII and the rate of depletion of the factor VIII



ADVANCES IN HEMOPHILIA PROPHYLAXIS

Point-of-care ultrasonography (POCUS) in hemophilia A

Early detection of joint bleeds in PWH is critical in the effort to preserve joint function. By detecting joint bleeds early in life using imaging technology, a patient may become more motivated and willing to initiate or continue prophylaxis. Magnetic resonance imaging (MRI) is currently the gold standard for detecting joint damage in hemophilia patients. Although MRI scans have been shown to have increased sensitivity in identifying hemophilic arthropathy compared with other types of radiography, the technique is very expensive and may require sedation in certain patient populations.

- Less expensive
- Requires no sedation in pediatric population
- Quick and reproducible
- High-quality images of multiple joints
- Time efficient and user friendly
- Engage and encourage patients for adherence to treatment

Challenges in the use of point-of-care ultrasonography (POCUS) are its diagnostic accuracy in hemophilia, the required of operator training, agreement on scoring systems, and agreement on the value of POCUS in routine hemophilia patient management.[4]

RECENT STUDIES

PK-driven prophylaxis versus standard prophylaxis: Observations of a retrospective study in children with severe hemophilia A and their implications on treatment costs [7]

Study Objective: To evaluate in a group of children with severe HA whether a tailored PK-driven approach may be employed to replace the standard therapy thus reducing costs.

Study Design: An observational retrospective study involving children with severe hemophilia A (HA), who were already on prophylaxis with rFVIII (Advate® – Baxalta Shire). The study was split into two different phases a PK-driven phase, and standard prophylaxis phase. The data was evaluated by comparing the costs associated prophylaxis with PK-assessment and without PK-assessment.