## CSL Behring

## Privigen ${ }^{\circledR}$

Name of the medicinal product
Privigen
Human noral inmunogobulin
Solution for infusion $(10 \%)$.
Human normal immunogoo
Soltion for intision 1 (10\%)
For intravenous use only
composition
a. Active substance
and
a. ACtive substance
Human inmunoloblin for intravenous use (IVg $\mathrm{g}^{*}$.
Human plasma protein containing a t least $98 \%$ imm

Distribution of the $\operatorname{lgG}$ subclasses average values): $\lg , 69 \%, \operatorname{lgG} 2.26 \%, \operatorname{lgG} 3 \%, 1 g G_{2} 2 \%$,
The maximum IgA content is 25 micrograms/ $/ \mathrm{m}$.
*Produced from the plasma of human donors.
$\underset{\substack{\text { b. Excipients } \\ \text { L-proline, wa }}}{ }$
Privigen contains trace amounts of sodium ( $\leq 1 \mathrm{mmol} / 1)$
Privigen contains no preservatives.
Privigen contains no carbohydrate stabiliser (e.g. sucrose, maltose)
Pharmacotherapeutic group


## Pharmaceutical form and active substance content per unit

Solution for intravenous infusion.
ml l of solution contains: 100 mg human plasma protein with an Ig content of at least $98 \%$
Thl of solution contains: 100 mg huma
(10\% solution).
The solution is clear to slighty opalesent and colourless to pale yellow. Privigen is isotonic, with an
osmolality of 320 mosmol $/$ kg.
The pH value of the ready-to-use solution is 4.6 to $5.0[4.8]$.

## Therapeuticindications Replacement therapy in


common variable immunodeficiency
severe combined immunodeficiency
Wiskott-A dricic syndrom
Myeloma or chronic shynrome
recurrent infections
Children with congenital AIDS and recurrent infections

- Immunomodulation - Immune thrombocytopenic purpura (ITP) in children or adults at high risk of bleeding or prior to surgicial interventions to correct the platelete count
Guilain-Bare syndrome
Guillain-Barrés syndrom
Kavasaki isease
- Chronicic inflammatory demyelinating polyneuropathy (CIDP)


## Allogeneic bone marrow transplantation

## Sosage / Administration Dosage

Dosage
The cosage and dosage regimen is dependent on the indication. In replacement therapy the dosage
may need to beindividualsed for each patient deend
dosong on the clinical response. The following dosage regimens are given as a guideline.
$\frac{\text { Replacement therapy in primary immunodeficiency syndromes }}{\text { The dosage regimen should achieve a trough lig level Imea }}$
The dosage regimen should achieve a trough log level (measured before the next infusion) of at
least 5 to 6 gll. Three to 6 months are required after the intitition of therapy for equilibration to ccur. The recommended starting dose is is 0.44 to $0.8 \mathrm{~g} / \mathrm{kg}$ body weight (bw) forlowed by bat leas 0.2 g kg g wevery 3 to 0 weeks.
The dose required to achieve t tro

$\frac{\text { Replacement therapy in myelomas or chronit lymohocyic leukemia with severe secondary }}{\text { hhoogammaglobuliñemia and receurrent infectionss replaceement therapy in chiddren with congenita }}$


$\frac{\text { Guillian-Baré syndrome }}{0.4 \mathrm{~g} / \mathrm{kg} \text { bw } / \text { day over } 5 \text { days. Experience in children is imited. }}$

Kawasaki disease
1.6 to 0.0 g 隹 b should be administered in divided doses over 2 to 5 days or $2.0 \mathrm{~g} / \mathrm{kg}$ bw as a
single dose. Patients should receive concomitant treatment with ceetylsalicylic caid. single dose. Patients should receive concomitant treatment with acetylsalicylic acid. $\frac{\text { Chroni i inflammatory demyelinating polyneuropathy (CIDP) }}{\text { The ereommended starting dose is }} 2 \mathrm{~g} / \mathrm{kg}$ bw divided over
he recommended starting dose givg on bw divided over 2 to 5 consecutive days followed by
maintenance doses of 19 gkw bw iven one day or divided over 2 consecutive day severy 3 weeks
 therapy. The lowest ffective mainten
the individual course of the disease.

Alogeneic bone marrow transplantation Hea as part of the conditioning regimen and afte transplantation. To treat infections and prevent gratt-versus-host disease, the dosage should be
individually adjusted. The statring dossogei i $\mathbf{s}$ usuall $0.5 \mathrm{~g} \mathrm{~g} / \mathrm{kg}$ bw/week, commencing seven days before the transplant. The
treatment is continued for up to 3 monthts after the transplant. If the lack of antiody production

The dosages recommendations are summarised in the following table:

| Indications | Dose | Intervals between injections |
| :---: | :---: | :---: |
| Replacement therapy in primary immunodeficiency syndromes | $\begin{gathered} \text { starting dose: } \\ 0.4-0.8 \mathrm{~g} \mathrm{~kg} \text { bw } \\ \text { tereafter: } \\ 0.2-0.8 \mathrm{~g} / \mathrm{kg} \mathrm{bw} \end{gathered}$ | every 3-4 weeks to obtain lgG trough levels of at least $5-6 \mathrm{~g} / /$ |
| secondary immunodeficiency syndromes | $0.2-0.4 \mathrm{~g} / \mathrm{kg} \mathrm{bw}$ | every $3-4$ weeks to obtain $\lg G$ trough levels of at least $5-6 \mathrm{~g} / \mathrm{l}$ |
| children with congenital HIV infection and recurrent infections | $0.2-0.4 \mathrm{~g} / \mathrm{kg} \mathrm{bw}$ | every $3-4$ weeks |
| Immunomodulation Immune thrombocytopenic purpura | $0.8-1 \mathrm{~g} / \mathrm{kg} \mathrm{bw}$ | on the first day; the therapy may be repeated once within 3 days |
|  | $\begin{gathered} \text { or } \\ 0.4 \mathrm{~g} / \mathrm{kb} \text { bway } \end{gathered}$ | over $2-5$ day |
| Kawasaki disease | $0.4 \mathrm{~g} / \mathrm{kg} \mathrm{bw} / \mathrm{day}$ | over 5 days |
|  | $1.6-2 \mathrm{~g} / \mathrm{kg}$ bw | divided into several doses given over $2-5$ days in conjunction with acetylsalicylic acid |
|  | $\stackrel{o r}{2 \mathrm{~g} / \mathrm{kg} \mathrm{bw}}$ | as a single dose in conjunction with acetylsalicylic acid |
| Chronic inflammatory demyelinating polyneuropathy (CIDP) | $\begin{aligned} & \text { starting dose: } \\ & 2 \mathrm{~g} / \mathrm{kg} \mathrm{bw} \end{aligned}$ | in divided doses over $2-5$ days |
|  | maintenance dose $1 \mathrm{~g} / \mathrm{kg}$ bw | every 3 weeks over $1-2$ days |
| Allogeneic bone marrow transplantation |  |  |
| - treatment of infections and prevention of graft versus-host disease | $0.5 \mathrm{~g} / \mathrm{kg} \mathrm{bw}$ | weekly, from day 7 before up to 3 months after the transplant |
| - persistent lack of antibody production | 0.5 g kg bw | monthly, until antibody levels return to norma |

Use of the product in paediatic population
In the ehase III pivatal study on patients with primany immunodeficiency diseases $(n=80)$,
19 patients between 3 and 11 years of age and 15 patients from 12 upto and indududing 18 years of age were treated. In an extension study of patients with primany immunodeficiency diseases (n $n=55)$,
11 p patient between 3 and 111 years of age and 11 between 12 and indluding 18 years of age were
treated treated.
In the linical study on 57 patients with chronic immune thrombocytopenic purpura 2 paediatic
patients (15 and 16 years of age) were treated. No dose adjustment tor chidren was required in patients (15 and 16 years of age) were treated. No dose adiustment for children was required in
these three studies
Literature reports indicate that intravenous inmunoglobulins are effective in children with cIDP. Herature reports indicate that intravenous immunoglob

## Method of administration




Hypersensitivivity to the active substance or the excipient (see section "composition"
typersensitivity to human immunoolobutins, especially in patients with got deficiency where the patient has anti-IgA antibodies.
Warrings and precautions for use
Privigen ontanins the excipient L-proline. Physicians should weigh the isk/ benefit of Privigen
in patients with hyperpolinaemia type land type II on an individual basis.

Certan severe adverse reactions may be related to the rate of intusion. The recomme ded infusion rate given under section "Dosage/ Administration: Method of administration" must be closely
followed. Patients must be cosely monitored and carefully observed for any symptoms throughout the infusion period and thereaterter
Certain adverse reactions may
in case of high rate of mintusion
in patients with hypogammaglobulinaemia or agammaglobulinaemia, with or without IgA
deficiency.
in patients who receive human normal immunoglobulin for the first time or, in rare cases, when
the human normal immunoglobulin product is swithed or when there has been a long intenal the human normadimmunog
since the previous intusion.
Potential compications can often be avoided by ensuring that patients.

- are not sensitive to human normal im munoglobulin by initially
are not sensitive to human normal immunoglow in by initially infusing the product slowly
$(0.3 \mathrm{~m} / \mathrm{kg}$ bw/hr);
are carefully monitored for any symptoms throughout the infusion period. II particular, patients,
naive to lo mman normal immunoglobuli, swithed trom an altenative IVlo productur or when there tas been a long interal since the previous intusion, should be monitored during the first
infusion and for the first All other patients should be obsened for a t least 20 minutes after administration.
In case of adverse reaction, either the rate of administration must be reduced or the iffusion
stopped. The treatment required depends on the nature and severity of the adverse reaction. stopped. The treatment required depends on the nature and severity of the adve
In case of shock, standard medical treatment for shock should be implemented.
Higher doses may be associated with increased rates of adverse e effects. Therefore, the lowest
effective dose should be sought in individual patients and careful monitoring routine is to establish. In all patients, IVIg administration requires adequate hydration prior to the intiation of the infusion. $\frac{\text { Hypersensitivity }}{\text { True hypersensitiv }}$
True hypersensitivity reactions are are. They can occur in patients with anti-IGA antibodies.
IVIg is not indicated in patients with selective IgA deficiency where the IGA deficiency is the only abnormality of concern.
Rarely, human normal immunoglobulin can induce a fall in blood pressure with anaphylactoid
reaction, even in patients who had tolerated previoustreatmentwith human normal immunoglobulin. Haemolytic anzemia
INg promudtse can contain blood group antibodies (e.g. anti-A and anti-B) which may act as
haemolysins and induce in vivo coating of red blood celis (RBC) with immonoglobulin, causing a positive direct antitglobulin reaction (Coombs' test) and, rarely, haeemolysis. Heemolytic anneemia can develop subsequentto NI therapy due to enhanced RBC sequestration. The Privigen manufacturing
process indudes an immunoaftinity chromatography
(AC) step that specfifally reduces
blood group

Isolated cases of haemolysis-related renal dysfunction/renal failure or disseminated intravascular

 vigilance is recommended.
Hzaemolysis har sarly been reorted in patients given replacement therapy for PDD
HVg Haemolysis has rarely been reported in patients siven replacement therapy for PID.
WIg recientens should de montiored for clinical signs and symptoms of haemolysis. If signs and/or

$\frac{\text { Asseptic meningitis syndrome (AMS) }}{\text { Aseptic meningolits syndrom e has bee }}$

 Cerebrossinal fliud studies are frequently positive with pleocytosis up to several thousand cells per
$\mathrm{m}^{m}$ ( predominanty


Thromboembolism
There is cinical evid
vidence of an association between IVIg administration and thromboembolic events
 deep vein thromboses which is assumed to be related to a relative increase in blood visisosity
through the high infux of fimmonoglobulins in at-isk patients. Theerefere caution should be exerised



In patients at rist for thromboembolic reactions, IIlg products should be administered at the
minimum rate of intusion and minimum dose practicable.

## Acute renal failure

Cases of acute renal failure have been reported in patients receiving IVG therapy. In most cases r isk
factors have been identified e .g. pre-existing renal insufficiency, diabetes mellitus, hypovolaemia, thedexic medicina produts or age over 65

In case of renal impairment. IIII discontinuation should be considered.
While these reports of renal dy ysunction and a cute renal failur
While these reports of renal dysfunction and acute renal failune have been associated with the use
 number. II patients at isk, the use of VIIg products that don not contain sucrose should therefore be crose, maltose or olucose.

In patients at risk of a aute renal failure, Vll produtts should be administered at the minimum rate
of infusion and minimum dose practicable.

Transtusion-reated acute lung iniury (TRA)
Noncardiogenic pulmonary edema may very rarely occur following treatment with IVI product
TRAL is characterized by severe respirator distress, pulmonay edema, hypoxemia, normal let
 ventriciular function, and fever. Symptoms typically appear within 1 to 6 hours following treatment.
Monitor patients for pulmonary daverse reactions. TRALI may me managed using oxygen therapy
with adeuate ventil aton support. with adequate ventilatory support,
$\frac{\text { Pathogen safety }}{\text { Privige is made }}$
Privigen is made from human plasma. Standard measures to prevent infections resulting from the
use of medicinal produtsts prepared from human blood or plasma include selection of donors screening of individual donations and plasma pools for specific markers of infection and the inclusion of effetetive manufacturing steps for the inativation/removal of viruses (see also section "Properties Effects"). Despite this, when medicinal products preared from human blood or plasma are
administered the possibility of transmiting infective agents cannot be totally excluded. This also adm inistered, the possibility of transmititing infective agents
applies to unknown or emerging viuses and other pathogens.

There is reassuring clinical experience reagrding the lack of hepatitis A or pavovirus B19
transmssion with imunoog obuins, and it ats also assumed that the antibody content makes an
imporant contribution to the veviral sadety Itis recommended that every time Privigen is administered to a patient, the name and batch numb
of the product are recorded in order to maintain a link between the patient and the batch of the of the prod
product.
$\frac{\text { Sodium content }}{\text { Privigen is essentilly sodium-free (Privigen has a low sodium content of } \leq 1 \mathrm{mmol} / \mathrm{l}) \text {. } \mathrm{m}}$
Paediatric population
Athough limited data is avilable, it is expected that the same warrings, precautions and riskfacto A Athough limited data is available
apply to the paediatric copulatio
Interactions
Live attenuated virus vaccines
treatment with immunoglobulins, the efficacy of live attenuated vacines, such as measles, mumps, rubela and chickenpox vaccines, may be impaired for a period of at least 6 weeks and up
to 3 months. An interval of 3 month should elapse before vacination with live attenuated vacines In the case of measies vaccinations, the decrease in efficacy may persist for up to a y year. Patient

Paediatric population
Athough
paediatictic populdation. dit avaiable, it is expected that the same interactions may occur in the
Pregnancy
Pregnancy
Contronled dinical data on the use of Privigen in pregnant women are not available. Caution should therefore be exercised with reage off trivigun in in rregnant women are not avala abie. Caution sho Extensive clinical experience of immunoglobulins suggests that no harmful effects on the course of
the pregnancy or on the feetus and the newlom chid are to be expected Experimental studies of the excipient t-proline carried out in animals found no direct or indirect
toxicity Experimentala studies of the excipient L-proiline carred out
toxicity aftecting pregnanyy, embryonal or or oeetal develoloment.
Breast-feeding
immunooloblins are excreted into the milk and may contribute to protecting the neonate from
pathogens ,
Fertility
Clinial ex
expected

## Effect on driving and the operation of machine

The ability to drive and operate machines may be impaired by some adverse reactions asociated
with Privigen Pationts who eveivine adverse reaction resolve before driving or operating machines. Adverse reactions such as chills, headache, dizziness, fever, vomiting, allergic reactions, nausea
arthralgia, low blood peressure, and moderate back pain may occur occasionally in connection witt - minstration of human immunoglobulin

Rarely human immunoglobulin may cause hypersensitivity reactions with a sudden fall in blood
pressure and, in in isolated cases.
anaphylactic shock, elen when the patient has shem pressure and in isolated cases, anaphylactic shock, even when tatient has shown
hypersensitivity to previous administration. Cases of reversible aseptic meningitis and rare cases of transient cutaneous reactions have been
observed with human normal immunoglobulin. Reversible haemolytic reactions have been observed in patients, especially those with blood grouss $A, B$, and $A B$ (non---blood groups) in inmunomodulatory treatment. Rarely, haemolytic anaemia
requiring $t$ transtusion may develop after high dose VIV treatment (see section "Warnings and precautions")

Increase in serum creatinine levels and/or acute renal failure have been observed.
Very rarely: transtusion related acute lung iniury and thromboembolic reactions such as myocardia
infartion.st

## abulated list of adverse reaction

The following table shows an oveniew of the ADR in the six studies, categorized according to
MedDRA System Organ Class SOC and Prefereed Tem Level ( (TT) and frequency. Frequencies pe nftusion were evaluated according to the following conventions: Very common ( $(1) 1 / 10$ ), Commo
$21 / 1000$ to $<1 / 10)$, Uncommon $(\geq 111,000$ to $<1 / 100)$. For spontaneous post-marketing ADS, the eporting frequency is iscategorized as unknown. Within each frequency grouping, undesirable effects are presented in order of decreasing frequency.

| MedDRA System Organ Class | Adverse Reaction MedDRA Preferred Term | ADR frequency category category |
| :---: | :---: | :---: |
| Infections and infestations | Aseptic meningtits | Uncommon |
| Blood and lymphatic system disorders | Anaemia, haemolysis (including haemolytic anaemia), leukopenia | Common |
|  | Anisocytosis (including microcytosis), thrombocytosis | Uncommon |
|  | Decreased neutrophil count | Unknown |
| Immune system disorders | Hypersensitivity | Common |
|  | Anaphylatic shock | Unknown |
| Nerous system disorders | Headaches (including sinus headache, migraine, head discomfort, tension headache) | Very Common |
|  | Dizziness (incuding veritio) | Common |
|  | Somnolence, tremor | Uncommon |
| Cardia disorders | Palpitations, tachycardia | Uncommon |
| Vascular disorders | Hypertension, flushing (including hot flush, hyperaemia), hypotension | Common |
|  | Thromboembolic events, vasculitis (including peripheral vascular disorder) | Uncommon |
|  | Transusion related acute lung injury | Unknown |
| Respiratory, thoracic and mediastinal disorders | Dyspnoea (including chest pain, chest discomfort, painful respiration) | Common |
| Gastrointestinal disorders | Nausea | Very Common |
|  | Vomiting, diarrhoea, abdominal pain | Common |
| Hepatobiliary disorders | Hyperbilirubinaemia | Common |
| Skin and subcutaneous tissue disorders | Skin disorder (including rash, pruritus, urticaria, maculo-papular rash, erythema, skin exfoliation) | Common |
| Musculoskeletal and Connective tissue disorders | Myalgia (including muscle spasms, musculoskeletal stiffness, muscuskeletal pain) | Common |
| Renal and urinary disorders | Proteinuria, increased blood creatinine | Uncommon |
|  | Actute renal failure | Unknown |
| General disorders and administration site conditions | Pain (including back pain, pain in extremity, (including chills), influenza like il'ness (including oropharyngeal blistering, throat tightness) | Very Common |
|  | Fatigue, asthenia (including muscular weakness) | Common |
|  | Injection site pain | Uncommon |
| Investigations | Decreased haemoglobin (including decreased red blood cell count, decreased haematocrit), Coombs' (direct) test positive, increased alanine aminotransferase, increased aspartate minotransterase, increased blood lactate dehydrogenase | Common |

For safety with respect to traz
$\frac{\text { Paediatric Population }}{\text { In Privigen Clinical stur }}$
eactions didid not difter between with paedidiatric and patients, the frequency, nature and severity of adverse proportion of haemolysisis cases to to all case reports occurring in chidrden is slightyby higher that th proportion of haemolysis cases to all case reports occurring in thildren is slighty higher than in
adults. Please ereferto section "Warnings and precautions tor details on risk factors and monitoring

## Reporting of suspected adverse reactions

Reporting sussepected dadervere reare reactions after authorisation of the medicinal product is important.


Overdose
overdose can lead to fluid volume overload and hyperiscosity, particularly in patients at risk,
ncluding elderly patients or patients with cardiac or renal impaiment.

## roperties / Effects

Privigen is prepared from plasmacorymamics 1000 or more human donorss. The manufacturing process for Hivigen incudes the following steps: ethanol precipitation of the lgG plasma fraction, followed by Altration, chrom atography, immunoaf inity chromatography to specifically reduce blood group $A$ and $B$ antibodies (isoagglutinins $A$ and $B$ ) and a filtitaion step that (an remove partices to a size of
20 nm. Privigen contains mainly llg that are present in the normal human population and that show at
broad spectrum of functionaly intact antitodies agains infectios agents in the replaeement
 thus help against sinections.




The mechanism of action in indications other than replacement therapy is not fully elucidated, bui
Clinical Efficacy
The safety and effic
The safety and efficary of Privigen was investigated in 6 prospective open, single-rm, multicentre adery and eficicay were collected in a prospective, open, single-arm, multicentre extension study with PID patients performed in the USA.

PID
In th
intusi
 treatment, constant $19 G G$ truyh levels were achieved over the whole of the treatment period, the
mean concentrations being $8.84 \mathrm{~g} / \mathrm{I}$ to 10.27 g gl. The incidence of acute, severe bacterial infections

 5patients Of which 45 had already been treated in the pivotalstudy and 10 were newly recruited $011.15 \mathrm{~g} / \mathrm{I})$ and the rate of asBl ( 0.018 per patient per year with an upper $97.5 \%$ confidence to $11.15 \mathrm{~g} /(1)$ and
interval of 0.098$)$.

57 patients aged between 15 and 69 years with chronic ITP took part in the ITP study. Their platelet

 second infusion. The mean time until this platelete count was reached was 2.5 days In patients who
responded to the treatment, the platelet count remained $\geq 50 \times 10^{\circ} / /$ I for a mean period of 15.4 days.
the second ITP study on patients aged between 18 and 65 years in 42 subjects (74\%) the platele within the expected range and similar to response rates were reported for other IVIGs in this
 provided $a$ relevant additional benefitit in terms of higher and longer-lasting increases in platelet
counts compares toa s single doses. In subjeets w with platelet counts $050 \times 10$ mandatory second intusion, the lowest median platetet count $\left(8.0 \times 10^{\circ} / 1\right)$ ) was observed already at te adseline. In this group, only $30 \%$ of subjects were obseved with platelet response atter the mandatorn second dose,
hnusion in these subjects.

IID the first CIDP study, a prospective multicenter open Iabel trial PRIMA (Privigen impact on mobility and autonomy study) 28 patients with cIIP $(13$ subjects with and 15 without IIIG pre-treatment) were
treated with a loading dose of $2 \mathrm{~g} / \mathrm{kg}$ bw given verer $2-5$ days 5 ollowed by 6 maintenance doses of $1 \mathrm{~g} / \mathrm{kg}$ bw given over $1-2$ days evern 3 weeks. Previously treated patients were withdrawn from Vlg Sefore treatment with Privigen until the deteriorotion of clinical symptoms was confirmed on the basis


In a second clinical study, a prospective, multicenter randomized, placebo-controlled PATH
lPolvneuropathy and Tremment with Hizentral study 207 subjects with ciDP were treated with
Priviven in the


 oollowing linical deterioration during IVIG withdrawal, clinical impovement of of cIP was primarily
defined by a decrease of $\geq 1$ point at the adiusted INCAT score. Additional measurus of cipp
 MRC sum score increase of $\geq 3$ points Overall, , 11\%, of subjects $(188$ patients) showed improvement


 The comparability of the response rates and mean adiusted INCAT sco
subjects in both PRIMA and PATH study are shown in the figure 1 below


The mean improvement at the end of the treatment period compared to reference v
in the PRIM 1.8 point in IVIg pretreated subjects) and 1.2 points in PATH study.
In PRIMA, the percentage of responders in the overall Medical Research Council (MRC) score (defined

 score in PRIMA improved by 6.9 points ( 7.7 points for VIG -untreated and 6.1 points for VIV -
reetereated) and by 36 points in PATH. The gip strength of the dominant hand improved by $14.1 \mathrm{KPa}(17.0 \mathrm{kPa}$ in IVg-untreated and
10.8 KPa in $\mathbf{V} \mathrm{VIg}$ pretreated subjects) in the PRIMA study, while in PATH the grip strength of the


The efficary and safety profile in the PRIMA and the PATH study in cIIP patients were overall
comparable.

## Paediatric population

No differences were seen in the pharmacodynamic properties between adult and paediatric study

## Pharmacokinetics

Privigen is inmediately and completely bioavalable in the recipient's circulation after intravenous administration. It is distributed relatively quickly between plasma and extravascular fluid
Equilibrium between the intravascuar and extravascular compartments is reached atter Equilibrium between the
approximately 3 to 5 days.
$I g G$ and $1 g G$ complexes are broken down in the cells of the reticuloendothelial system. The hall-life
may vary from patient to atient
The pharmacokinetic parameters for Privigen were determined in both hlinical studies in patie
 69 years) in the piotatalstudy nad 13 patients (aged 9 to 59 years) in
participated in the pham tuackinetic (Fk) assessment (see table below).

## Pharmacokinetic parameters of Privigen in patients with primary immunodeficiency syndrome

 syndrome| Parameter | Pivotal study ( $\mathrm{N}=25$ ) <br> Median (range) | Extension study ( $\mathrm{N}=13$ ) Median (range) |
| :---: | :---: | :---: |
| $\mathrm{C}_{\text {max }}$ (peak level) $\mathrm{ing/l}$ | 23.4 (10.4-34.6) | 26.3 (20.9-32.9) |
| C min $^{\text {(trough level) }}$ ) ig/l | 10.2 (5.8-14.7) | 9.75 (5.72-18.01) |
| tta (halfl-ife) in days | 36.6 (20.6-96.6) | $31.1(14.6-43.6)$ |

In the pivatal study the median hall-life of Privigen in primary immunodeficiency patients was
36.6 dayys and 31.1 dayys in the extension of this sudy.
Paediatric population
No differences were seen in the pharmacokinetic parameters between adult and paediatic study
patients with PID. There are no data on pharmacokinetic properties in paediatric patients with cilp. Preclinical data

 daly L-proine doses of 1450 mg kg bw did not show any evidence of teratoge
embyyotoxicity. Genotoxicity suduies of L-proline did not show any pathological lindings.
Some published studies pertaining to hyperprol inaemia have shown that long-term, high doses of
L-proline have effects on brain develoment
 observed. Further safet
behavioural disorders.

 to heterologous proteins. In local tooleability studies in rabits in which Privigen was administered
intravenously, paravenously, intra-atrerially, and subutuaneously, the product was well tolerated.

Other information
Incompatibilities
This medicine must not be mixed with other medicinal products nor with physiological saline.
However dilution with 5 \%

## Influence on diagnostic tests Atter intuion of immunolo




For interactions with attenuated live vaccines, see section "Interations:

## Shelf life and special preceutions for storage Privigen is stable unti the expiny date stated on

the impinited expiry date (EXP) the medicine
Do no store above $25^{\circ} \mathrm{C}$. Do not treeze. Do not use if frivigen has been frozen. Do not shake.
Keep out of the sight and reach of children.
Shefl lifi o f the product atter opening
Privigen is itended for single use. Because the solution contains no preservative, Privigen should be used / intused immediately once opened.

## Instructions for use and handling Privigen is ready-to ese sulution

 pierce the stopper at it ts entre, within the marked area.
If dilution is desired, $5 \%$ g lucose solution should be used. For obtaining an immunoglobulin solution of $50 \mathrm{mg} / \mathrm{ml}(5 \%)$, Privigen $100 \mathrm{mg} / \mathrm{ml}(10 \%)$ should be diluted with an equal volume of the
glucose solution. Assepic tecchnioue must be stricty obsenved during the diltion of Privi Privigen must not be mixed with physiological saline. However, atter-rinsing of the intusion tubes with physiological saline is permitted.
The solution must be clear or slighty
particuate mater.j.
Any unused product and waste material should be disposed of in accordance with loca
reauirements.
Packs
Solution

$5 \mathrm{~g} / 5 \mathrm{ml}$
$\bullet$
$-10 \mathrm{~g} / 100 \mathrm{ml}$
$20 \mathrm{~g} / 200 \mathrm{ml}$

## Packed by Benta SAL


Under license from
CSL Behring AG, Bern, Switzerlan
Date of $r$
12.2018
Note: Privigen® is a registered trademark of CSL Behring AG in many countries

## Medicament is a product which affects your health and its consumption contrary to

 Meirament is a product whiinstrutions s sadanerous for yo.
Follow stritly y he doctor's pres csipition, the method of use and the instructions of the pharmacist who sold the medicament.
The doctor and the pharmacist are the experts in medicines, their benefits and risks. Do not by yoursel interrupt the period of treatment prescribed for you
Keep all medicaments out of reach of hhidren
Council of Arab Health Ministers
Union of Arab Pharmacists

