QUINVAXEM® inj.
DTwP – HepB – Hib fully liquid combination vaccine

DESCRIPTION
The vaccine is a homogenous liquid containing purified diphtheria and tetanus toxoids, inactivat-
ed whooping cough (pertussis) organisms, highly purified, non-infectious particles of hepatitis B surface antigen (HBsAg) and Hib components as a bacterial subunit vaccine containing highly purified, non-infectious Haemophilus influenzae type b (Hib) capsular polysaccharide chemically conjugated to a protein CRM197 (Cross reacting material derived from Corynebacterium diph-
erus serotype C7/C8197/MB). The HBsAg is produced by DNA recombinant technology in H. poly-
morphus yeast cells. The vaccine is adjuvanted on aluminium phosphate gel. The polysaccharide is
derived from Hib bacteria grown in chemically defined media, and subsequently purified through a
series of ultrafiltration steps. The quantity of the vaccine per single human paediatric dose is
at least 4.0 IU for whole cell pertussis (wp), 30 IU for diphtheria, 60 IU for tetanus (determined in
mice), 10 µg HBsAg and 10 µg Hib oligosaccharide conjugated to 25 µg CRM197 protein.

COMPOSITION OF VACCINE per 1 ml:

Diphtheria toxoid
Tetanus toxoid
Pertussis antigen
Hepatitis B surface antigen
Hib conjugate
Aluminium phosphate
Sodium chloride

not less than 15 IU/ml (not less than 60 IU/mg)
not less than 6.5 IU/ml (not less than 120 IU/mg)
not less than 30 CUP/ml (not less than 8.0 IU/ml)
20 µg/ml
70 µg/ml
(20 µg µl Hib oligosaccharide conjugated to 55 µg
CRM197 protein)
0.6 mg/ml AL3
9 mg/ml

Thiomersal is present in traces as residue from the manufacturing process of wp-vaccine.

ADMINISTRATION
Before the use, the vial with a vaccine should be shaken in order to homogenize the liquid
 suspension. The vaccine should be injected intramuscularly. The anterolateral part of the upper
 thigh is the preferred site of injection. An injection into a child's buttocks may cause injury to the
 sciatic nerve and is not recommended. The vaccine must not be injected into the skin as this may
give rise to local reactions. A sterile syringe and sterile needle must be used for each injection.

IMMUNIZATION SCHEDULE
Quinvaxem should NOT be used for the birth dose of hepatitis B vaccination.

In countries where pertussis is of particular danger to young infants, primary vaccination with the
combined vaccine should be started as soon as possible with the first dose given as early as
6 weeks, and two subsequent doses given in intervals of at least 4-6 weeks after the first dose.
Quin-
vaxem can be given to children who have received hepatitis B vaccine at birth. There is no evidence
suggesting that the vaccine is not interchangeable with other DTwP, HepB, Hib combined vaccines.
Reinforcing vaccination of toddlers (13-24 months after birth): one booster dose of 0.5 ml.
Quinvaxem booster dose can be given to toddlers initially vaccinated with DTwP – HepB – Hib.
The DTwP – HepB – Hib vaccine can be given safely and effectively at the same time as BCG, mor-
tella BCG (OPV or IPV) and yellow fever vaccines, and vitamin A supplementation. If DTwP –
HepB – Hib vaccine is given at the same time as other vaccines, it should be administered at
a separate site. It should not be mixed in the vial or syringe with any other vaccine unless it is
licensed for use as a combined product.

SIDE EFFECTS
The type and rate of adverse reactions of the DTwP – HepB – Hib fully liquid combination vaccine
do not differ significantly from the DTwP, HepB and Hib vaccine reactions described separately.
For DTwP, mild local or systemic reactions are common. Some temporary swelling, tenderness
and redness at the site of injection together with fever occurs in a large proportion of cases. Oc-
casionally severe reactions of high fever, irritability and screaming develop within 24 hours of
administration. Haemolytic-antibody sensitive infants may have reports of a yellowish discolouration
and fever up to 24 hours after injection. DTwP, hepatitis B and Hib booster vaccines. More serious
reactions are very rare; a causal relationship ...

Data from clinical studies:
In the four clinical trials performed 2115 doses of Quinvaxem inj. (DTwP – HepB – Hib fully liquid
combination vaccine) have been administered as a primary vaccination in 730 healthy infants
from six weeks of age. In these clinical studies, signs and symptoms were actively monitored in
all subjects for five to seven days following the administration of the vaccine. No serious adverse
reactions attributable to the vaccine have been reported during the course of clinical trials.
Solicited reported reactions are listed below. Frequencies, based on number of doses, are re-
ported as: Very common (>1/10), Common (›1/100, <1/10), Uncommon (>1/1000, <1/100), Rare
(›1/10 000, <1/10000), Very rare (<1/10 000, incl. isolated reports).

GASTROINTESTINAL DISORDERS:
Common: Diarrhoea; Vomiting

GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS:
Very common: Injection site pain; Injection site swelling; fever
Common: Injection site redness
Uncommon: fever ≥39.5 °C
Uncommon: Influenza-like illness

METABOLISM AND NUTRITION DISORDERS:
Very common: Feeding disorders

PSYCHIATRIC DISORDERS:
Very common: Irritability
Common: Crying
Uncommon: Persistent crying

NERVOUS SYSTEM DISORDERS:
Very common: Sleepiness
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS:
Rare: Coughing

SKIN AND SUBCUTANEOUS TISSUE DISORDERS:
Common: Rash

Most solicited reactions showed similar frequencies after primary vaccination and after the booster dose. Higher incidence rates after the booster dose (difference vs. primary vaccination approximately more than 10%) were observed for change in eating habits and unusual crying. The solicited systemic adverse reactions usually appeared within 48 hours after vaccination and in most cases disappeared spontaneously. All local and systemic reactions resolved without sequelae.

Data from post-marketing experience
As with any vaccine, there is the possibility that broad use of the vaccine in post-authorisation could reveal adverse reactions not observed in clinical trials. DTwP – HepB – Hib fully liquid combination vaccine is based on the combination of known and registered vaccine components. Safety and efficacy of these vaccines has been demonstrated for many years, and the differences in safety and tolerability of the DTwP – HepB – Hib fully liquid combination vaccine compared to the formulation for the established vaccines are not considered to be clinically significant. In the post-authorisation period rare cases of hypotonic-hyporesponsive episodes have been reported with DTwP – HepB – Hib. In all cases the symptoms disappeared spontaneously with no sequelae.

Allergic reactions, including anaphylactic reactions and urticaria, have been reported very rarely following vaccination with DTP, hepatitis B and containing vaccines.

CONTRAINDICATIONS
Known hypersensitivity to any component of the vaccine, or a serious reaction to a previous dose of the combination vaccine or any of its constituents is an absolute contraindication to subsequent doses of the combination vaccine or the specific vaccine known to have provoked an adverse reaction. There are few contraindications to the first dose of DTwP – fits or abnormal cerebral signs in the newborn period or other serious neurological abnormality are contraindications to the pertussis component. In this case, the vaccine should not be given as a combination vaccine but DT should be given instead of DTwP and HepB and Hib vaccines given separately. The vaccine will not harm individuals currently or previously infected with the hepatitis B virus.

As with other vaccines, vaccination should be postponed in children suffering from acute febrile illness. Minor illnesses such as common cold or other infections of the upper respiratory tract are not considered contraindications to the vaccination.

Equally, it is not necessary to postpone vaccination in the case of treatment with topical corticosteroids or systemic use at low dosage (i.e. <0.5 mg/kg prednisone or equivalent), or in case of skin diseases like dermatitis, eczema, or other localised skin disorders.

Special Warnings and Precautions for Use
As with any injectable vaccine, appropriate medical supervision and treatment should always be readily available in case of immediate allergic reactions, such as anaphylactic shock or anaphylactic reaction, following administration of the vaccine.

Before administering the vaccine, precautions should be taken to avoid undesirable reactions. These precautions include: review of the individual's medical history, particularly regarding hypersensitivity reactions to previous administration of any type of vaccine, as well as the individual's history of recent health disorders and any previous vaccinations.

The administration of any subsequent dose of a vaccine containing the whole-cell pertussis component should be carefully considered if, in connection with the administration of DTP vaccine, one or more of the following effects have been observed:

- 40 °C temperature within 48 hours following vaccination (not due to other identifiable cause);
- collapse or shock (hypotonic-hyporesponsive episode) within 48 hours following vaccination;
- persistent crying lasting more than 3 hours during the 48 hours following vaccination;
- convulsions, with or without fever, within 3 days following vaccination.

There may be circumstances, such as high incidence of pertussis, when potential benefits outweigh possible risks.

HR seroconversion does not represent a contraindication to vaccination. Patients with an immunodeficiency disorder or receiving immunosuppressive therapy may have a reduced immunological response. Individuals infected with the human immuno-deficiency virus (HIV), both asymptomatic and symptomatic, should be immunized with combined vaccine according to standard vaccines.

The vaccine must not be injected into a blood vessel. Quinvaxem inj. (DTP – HepB – Hib fully liquid combination vaccine) should be administered with caution to subjects with thrombocytopenia or a bleeding disorder since bleeding may occur following an intramuscular administration to these subjects. A fine needle should be used for the vaccination and firm pressure applied to the site (without rubbing) for at least two minutes following administration.

STORAGE
The combination vaccine must be stored and transported between +2 °C and +8 °C.

PRESENTATION
The vaccine is supplied in single dose vials.

The vaccine vial monitor

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\begin{array}{c}
\text{Inner square lighter than outer circle.}\\
\text{If the expiry date has not been passed, USE the vaccine.}
\end{array}
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\begin{array}{c}
\text{At a later time, inner square still lighter than outer circle.}\\
\text{If the expiry date has not been passed, USE the vaccine.}
\end{array}
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\begin{array}{c}
\text{Discard point:}\\
\text{Inner square matches colour of outer circle.}\\
\text{DO NOT use the vaccine.}
\end{array}
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\begin{array}{c}
\text{Beyond the discard point:}\\
\text{Inner square darker than outer circle.}\\
\text{DO NOT use the vaccine.}
\end{array}
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Vaccine Vial Monitors (VVM) are part of the label on Quinvaxem® inj. supplied through Berna Biotech Korea Corporation; (Gongdo-dong) 23, Harmony-ro 303 beon-gil, Yeonju-gu, Incheon 406-840, Korea. The colour dot which appears on the label of the vial is a VVM. This is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level. The interpretation of the VVM is simple. Focus on the central square. Its colour will change progressively. As long as the colour of this square is lighter than the colour of the ring, then the vaccine can be used. As soon as the colour of the central square is the same colour as the ring or of a darker colour than the ring, the vial should be discarded.

* In Weekly Epidemiological Record, No. 11, 7 May 1999, Page 139