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New perspectives for hexavalent vaccines

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ABSTRACT

With the increase in the number of routine vaccinations the development of pentavalent and hexavalent combination vaccines fitting the routine vaccination schedules became a necessity. In this respect, Europe has taken the lead in comparison with other world regions, and routine vaccination with pentavalent and hexavalent combinations including DTPa, Hib, HepB and IPV has been on European vaccination programs for >15 years. Since the marketing authorization of Hexavac® and Infanrix Hexa® in 2000, immunization schedules in most European countries have included hexavalent vaccines. In the last years, two new hexavalent vaccines have been licensed and commercialized worldwide. This paper presents a review of the pharmaceutical profiles of the three hexavalent vaccines currently available. In addition, we aim to review safety, co-administration, tolerability and other practical concerns of their use.

1. Introduction

Since the beginning of the vaccination era, the number of vaccine-preventable diseases has continued to increase at a fast rate. Combination vaccines are individual preparations that include two or more antigens of different microorganisms. Combination vaccines have been used in adults and children alike for over half a century; in 1948 the combination of diphtheria, tetanus, and pertussis antigens into a single vaccine was first used to vaccinate infants and children [1–3]. Since then, many new techniques have been developed and the number of components combination into a single product has risen greatly [1–3].

Combination vaccines have not only solved the burden of multiple injections. Other challenges such as the storage and shipment of vaccines, the increasing number of visits, the injection of more adjuvants or the introduction of new vaccines into the calendar have been met owing to the availability of combination vaccines (Fig. 1).

Commonly administered combination vaccines include as base the diphtheria and tetanus toxoid, used alone (DT or Td) or with whole cell (DTwP) or acellular (DTaP) pertussis component. To this baseline product, a plethora of components can be added. Common combinations include inactivated poliovirus (IPV), *Haemophilus influenzae b* vaccine (Hib) and/or hepatitis B vaccine (HepB) [1–3].

With the new immunization recommendations made by the WHO, the number of routine vaccinations has grown from the initial 6 recommended EPI antigens – Bacillus Calmette-Guérin, diphtheria, tetanus, pertussis, poliomyelitis and measles – to the current 11 antigens, which additionally include HepB, Hib, pneumococcus, rotavirus, and rubella. This increase meant that the development of pentavalent and hexavalent combination vaccines fitting the routine vaccination schedules became a necessity [1–3]. In this respect, Europe has taken the lead in comparison with other world regions, and routine vaccination with pentavalent and hexavalent combinations including DTPa, Hib, HepB and IPV has been on European vaccination programs for >15 years [4]. Since the marketing authorization of Hexavac® and Infanrix Hexa® in 2000 (although Hexavac® was later withdrawn from the market in 2005 [5]), immunization schedules in most European countries have included hexavalent vaccines (Table 1).

In the last years, two new hexavalent vaccines have been licensed and commercialized worldwide [6,7]. This paper presents a review of the pharmaceutical profiles of the three hexavalent vaccines authorized and currently available. In addition, we aim to review safety, co-administration, tolerability and other practical concerns of their use.

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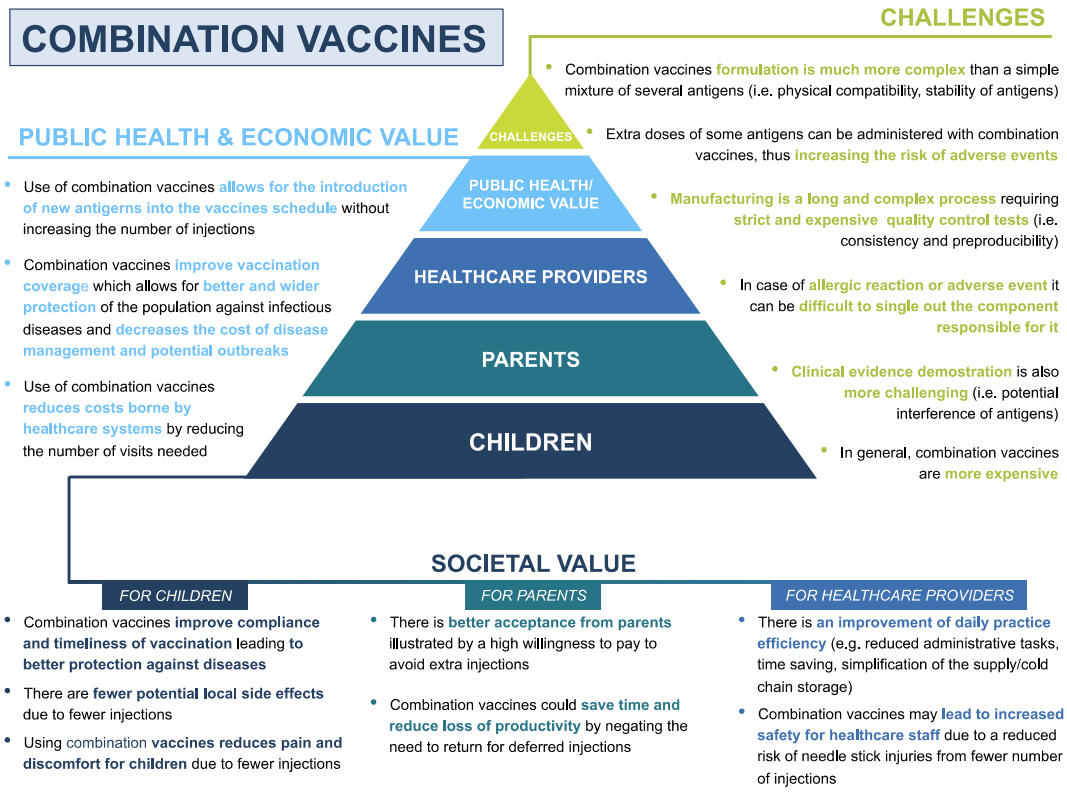

Fig. 1. Combination vaccines: from challenges to benefits (adapted from Maman K et al. (Ref. [2])). Several key benefits from combination vaccines can be easily identified, with societal and public health & economic categories being the most important. Also important challenges have to be considered.

Table 1
Use of pentavalent and hexavalent vaccines in immunization schemes in Europe (data compiled in Jan 2017).

	Countries	DTPa, VPI, Hib		HepB		Use of Hexavalent vaccine	Use of Pentavalent vaccine
		Priming age	Booster age	Universal	Schedule		DTPa, VPI, Hib
2 + 1	Austria	3,5 m	12 m	Yes	3, 5, 12 m	3, 5, 12 m	No
	Italy		11–13 m	Yes	3, 5–6, 11–13 m	3, 5–6, 11–13 m	3, 5–6, 11–13 m
	Iceland		12 m	No	–	No	3, 5, 12 m
	Denmark		12 m	No, RG only	–	3, 5, 12 m	3, 5, 12 m
	Finland		12 m	No, RG only	–	No	3, 5, 12 m
	Norway		12 m	No, RG only	–	No	3, 5, 12 m
	Sweden		12 m	No, RG only	–	3, 5, 12 m	3, 5, 12 m
	Slovakia	2, 4 m	10–11 m	Yes	2, 4, 10 m	2, 4, 10 m	No
	France		11 m	Yes	2, 4, 11 m	2, 4, 11 m	No
	Spain		11 m	Yes	2, 4, 11 m	2, 4, 11 m	No
3 + 1	Greece	2, 4, 6 m	15–18 m	Yes	2, 4, 6–18 m	No	No
	Ireland		13 m (Hib)	Yes	2, 4, 6 m	2, 4, 6 m	No
	Portugal		18 m (DTPa, Hib)	Yes	0, 2, 6 m	No	2, 4, 6 m
	Romania		12 m	Yes	0, 2, 6 m	2, 4, 11 m	No
	Lithuania		18 m	Yes	0, 1, 6 m	No	2, 4, 6, 18 m
	Latvia		12–15 m	Yes	2, 4, 6, 12–15 m	2, 4, 6, 12–15 m	2, 4, 6 m
	Cyprus		15–18 m	Yes	2, 4, 8–12 m	No	2, 4, 6, 15–18 m
	Croatia		12–23 m	Yes	0, 2, 6 m	2, 4, 6, 12 m	No
	Switzerland		15–24 m	No	1, 6, 15–24 m	No	2, 4, 6, 15–24 m
	Germany	2, 3, 4 m	11–14 m	Yes	2, 3, 4, 11–14 m	2, 3, 4, 11–14 m	2, 3, 4, 11–14 m
	Belgium		15 m	Yes	2, 3, 4, 15 m	2, 3, 4, 15 m	No
	Netherlands		11 m	Yes	2, 3, 4, 11 m	2, 3, 4, 11 m	No
	Luxembourg		13 m	Yes	2, 3, 13 m	2, 3, 13 m	4 m
	UK		12–13 m (Hib)	No, RG only	–	No	2, 3, 4 m
	Malta		18 m	Yes	12, 13, 18 m	No	6 w, 3, 4, 18 m
	Hungary		18 m	Yes	Over 2 years	No	2, 3, 4, 18 m
	Czech Republic		10 m	Yes	2, 3, 4, 10 m	2, 3, 4, 18 m	No
	Bulgaria		16 m	Yes	0, 1, 6 m	2, 3, 4 m	2, 3, 4, 16 m
	Estonia	3,4–5, 6 m	24 m	Yes	0, 1, 6 m	No	3,4–5, 6 m, 2 y.
	Slovenia		12–24 m	No, RG only	Over 2 years	No	3, 4–5, 6, 18 m
	Poland		16–18 m (DTPw, VPI, Hib)	Yes	0, 2, 7 m	No	No

RG: Risk groups.

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