Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

# Report on the results of the public consultation on the Health Technology Assessment of the expansion of the childhood immunisation schedule to include varicella (chickenpox) vaccination

13 July 2023

# Contents

# Introduction

Following a request from the Department of Health, the Health Information and Quality Authority (HIQA) undertook a health technology assessment (HTA) of the expansion of the childhood immunisation schedule to include varicella (chickenpox) vaccination. The aim of the HTA was to establish the clinical effectiveness, safety, cost effectiveness and budget impact of a varicella vaccination programme for children.

The draft HTA report was published for public consultation in April 2023.[(1)] This Summary of Outcomes report summarises the feedback received during the public consultation period and outlines HIQA's responses to the issues raised, including any changes that were made to the report as a result.

# Methods

The aim of the public consultation was to seek feedback to identify any issues with the draft HTA report, to consider that feedback and to amend the report, as necessary.

## The consultation process

The draft HTA was published on the HIQA website on 20 April 2023 and was available for public consultation until 29 May 2023. The consultation webpage contained a link to the draft report, a link to the online survey (using the Crowdsignal platform) for online submission of feedback, and a consultation feedback form that could be downloaded. To ensure wide accessibility, feedback could be submitted via email or an online survey and notifications of the public consultation were posted via social media sites (Twitter, Facebook, Instagram and LinkedIn).

A press release was issued at the beginning of the consultation period, and the findings of the draft HTA were reported in the media. E-mail requests for feedback were sent to a targeted list of stakeholder organisations with relevant expertise and those who are likely to be affected by the proposed introduction of a childhood varicella vaccination programme.

### Feedback form

The template for submission comprised a general request for feedback to enable respondents to flexibly provide their submission for any aspects of the report. A copy of the submission template is provided in Appendix A.

### Synthesis

Each submission was recorded (excluding personal information), read in its entirety and, where appropriate, broken down into individual components. In cases where a question was skipped by the respondent, it was assumed that there were no issues of concern specific to that question.

The submissions were stratified according to whether they were from members of the general public or stakeholder organisations. Feedback considered broad in nature was described narratively. Feedback relating to specific content in the draft report is presented in tabular format alongside direct responses to the feedback (Table 2). To enhance readability and interpretation, specific comments pertaining to the content of the report were categorised under the following headings:

- vaccine safety
- vaccine description
- epidemiology and burden of disease
- exogenous boosting
- rapid review of economic modelling studies
- economic evaluation
- organisational issues
- vaccination catch-up programme
- chickenpox in pregnancy.

Where amendments were made to the report based on feedback, this is highlighted in the HIQA response.

# Results

Overall, 80 unique and complete submissions were received during the public consultation period. In addition, 12 incomplete and two duplicate survey responses were also received. As the incomplete responses contained no feedback they have been excluded from the summary below. Of the 80 submissions, 73 were submitted via the online survey and seven were received by email. A total of 70 submissions were received from individual members of the general public, eight were submitted on behalf of stakeholder organisations or institutions and two were submitted by healthcare professionals responding in a personal capacity.

# Summary of feedback

### Members of the general public

Seventy responses were received from members of the general public; 62 of these were from people in Ireland and eight respondents did not specify their country.

The societal impact of varicella, specifically the need for both parents caring for children with varicella and those ill with varicella to take time off work, was highlighted by nine respondents. Ten respondents noted the prohibitive cost of paying for the vaccine privately, while nine respondents stated that they had paid to vaccinate some or all of their children against varicella. Eleven respondents commented on the clarity of the report with eight respondents specifically stating that that they had no issues. One respondent noted that that the report was probably too technical for parents without medical backgrounds, one specifically highlighted issues with understanding chapter seven (economic evaluation) and one felt that more detail on the data underpinning the safety of the vaccine may be warranted in the Executive Summary given that most lay persons may not read beyond this section.

Six respondents described anecdotal experience of the impact of varicella on children within their own families. The verbatim of these responses is presented in Table 1.

## Table 1 Verbatim of personal experiences with varicella and commentary*

| Number | Comment |
|---|---|
| **Personal experiences** | |
| 1 | "My son had very bad eczema and when I asked at my doctor's surgery about paying to get him vaccinated against chickenpox, I was told he would be better off getting chickenpox. When he got chickenpox, he ended up in hospital on a drip for two nights as his skin got infected and I had to take two weeks off work to mind him." |
| 2 | "I vaccinated my first child and was too late vaccinating my second and she suffered so much with the illness." |
| 3 | "I am the grandfather of five boys aged from four months to 14 years, who in recent months have all had chickenpox. This has led to these boys suffering and in a lot of pain. I have seen their poor bodies in a terrible state. I have also seen the physiological effects it has on them, especially the 14 year old who has missed school, outdoor pursuits, and going out in general because he is so conscious of his appearance." |
| 4 | "My three year old had a severe case of chickenpox and required eye surgery to provide a new tear duct. I subsequently vaccinated my second child. |
| 5 | "My son recently had chickenpox and also developed invasive Strep A in his skin. Necrotising fasciitis resulted in six surgeries for him (three to deal with the infection, one to remove the drain and two skin grafts). We spent 18 nights in Cork University Hospital. He is lucky to be alive." |
| 6 | "I am a father of a son, aged three, who was hospitalised in 2011 with severe chickenpox. As I sat there watching him lying in a hospital bed, hooked up to a drip getting a cocktail of antibiotics, antivirals, pain and anti-itch medications, I thought that this could have been prevented with a simple vaccine, which I discovered was widely available and included in childhood immunisation programmes in so many countries. My son was hospitalised for four days and thankfully recovered, with no long lasting effects. However, I was horrified to find out just how lucky he was." |

*Responses have been slightly amended to correct for minor grammatical errors and or typos.
†Response has been amended to ensure anonymity.

### Stakeholder organisations or institutions

Eight responses were received on behalf of stakeholder organisations or institutions. One organisation requested anonymity and the seven remaining responses were from:

- Department of Public Health Area B (Dublin South, Kildare, West Wicklow, Laois, Offaly, Westmeath, Longford), Health Service Executive (HSE)
- Department of Public Health Area D (Cork and Kerry), HSE
- GlaxoSmithKline (GSK) (Ireland) Ltd

- Invasive Group A Streptococcus (iGAS) Incident Management Team, Health Protection Surveillance Centre, HSE
- Irish Neonatal Health Alliance
- MSD Ireland
- National Immunisation Advisory Committee (NIAC).

The Department of Public Health Area B noted the complications associated with varicella and the resulting need for hospitalisation. The increase in iGAS notifications in Ireland since October 2022, resulting morbidity and mortality, and the association between iGAS infection and previous VZV infection were also highlighted. Given the risks of serious complications from varicella and the proven efficacy, effectiveness and cost effectiveness of the vaccine, the submission was supportive of adding the varicella vaccine to the childhood immunisation schedule.

The Department of Public Health Area D advocated for the two-dose short interval strategy due its predicted significant reduction in varicella and herpes zoster cases. The submission expressed concern with the lower clinical effectiveness of a two-dose long interval strategy compared with a two-dose short interval strategy. The submission also highlighted the increase in iGAS notifications in Ireland in recent months, resulting morbidity and mortality, and the association between iGAS infection and previous VZV infection. A number of questions were raised with regard to chapter seven which are addressed in Table 2 below.

The response on behalf of GSK (Ireland) included a number of suggested changes to the content in chapter two and chapter six (see Table 2).

The submission on behalf of the iGAS Incident Management Team at the HPSC noted the evidence on the efficacy, safety and cost effectiveness of the varicella vaccine which provides a strong public health argument in favour of vaccination. It also highlighted the association between iGAS infection and preceding VZV infection. The submission advised that the monitoring of the impact of vaccination was not covered in great depth in the report (see Table 2).

The Irish Neonatal Alliance noted that vaccination against varicella would be very well received by the patient community, benefiting children and adults into the future.

MSD Ireland provided information relating to the concomitant administration of VARIVAX® and ProQuad® with other paediatric vaccines (see Table 2). While the limited data directly examining the interchangeability of VARIVAX® with other

varicella containing vaccines was noted in the submission, real world guidelines that support the interchangeability of varicella vaccines were also highlighted. Vaccine efficacy data specifically relating to MSD varicella vaccines VARIVAX® and ProQuad® were provided.

In its submission, NIAC expressed support for universal varicella vaccination, with a recommendation for the two-dose long interval strategy. It expressed concern that a two-dose short interval strategy, which would require an additional GP immunisation visit, could impact uptake of the varicella vaccine and potentially undermine the existing immunisation programme. The Committee acknowledged the concerns raised in the draft HTA report regarding the potential for breakthrough infections between 12 months and five years, but also noted the effectiveness of one dose against severe disease and that varicella infection between these ages tends to be less severe than infection which occurs later in childhood. The submission also highlighted that the current situation in Ireland, where parents can choose to vaccinate their children against varicella at substantial personal cost, contributes to healthcare inequity.

The organisation that requested anonymity provided feedback on specific wording in chapter two (see Table 2).

### Others

Two submissions were received from groups or individuals who clearly identified as healthcare professionals and responded in a personal capacity.

One of the two submissions was received from a group of nine medical consultants working in Children's Health Ireland. The submission noted the complications that can arise from varicella, the association between iGAS and previous VZV infection as well as the individual, healthcare and societal burden associated with the illness. The respondents believe that adding the varicella vaccine to the childhood immunisation schedule will save lives, prevent avoidable suffering and serious illness, and conserve limited healthcare resources. The submission also highlighted the current inequitable situation in Ireland where parents can personally pay to vaccinate their children against varicella, but that this may not be an affordable option for all. The respondents advised that they had paid to vaccinate their children.

The second submission was received from an individual healthcare professional. The submission noted the strong evidence supporting the benefits of varicella vaccination for both those vaccinated against the disease and susceptible others. The respondent highlighted the complications associated with varicella and the potential increase in the numbers of susceptible adults due to inward migration from countries

where varicella seroprevalence may not be as high as in Ireland, the effect of which is evident from notable varicella outbreaks in accommodation and residential centres. The submission also emphasised the importance of vaccine uptake to the success of a vaccination programme and the need to ensure that it is a key consideration in the selection of the dosage schedule. The risks to vaccine uptake associated with introducing an additional vaccination visit specifically for the second dose in the two-dose short interval strategy were highlighted. The respondent expressed their belief that the introduction of a two-dose varicella vaccination programme will confer significant benefits to the population, where cases of varicella in children are rare. Two points were raised with regard to the economic evaluation, both of which are addressed in Table 2.

Specific feedback relating to the content of the report received during the public consultation is presented in Table 2.

# Specific comments on report content

## Table 2 Comments received on report content and responses

| Comment | Response |
|---|---|
| **Vaccine safety** | |
| Would need to consider whether it is safe to give the varicella vaccine at the same time as the MMR vaccine at 12 months (also a live vaccine). | An overview of reviews of the safety of varicella vaccination, comprising evidence from 34 randomised controlled trials and 62 other primary studies/reviews, was conducted for this HTA (see chapter 5). Co-administration of the varicella vaccine with other vaccines (including MMR) was specified as a relevant comparator. The review concluded that the limited evidence on the co-administration of the varicella vaccine with other vaccines suggests that co-administration does not compromise the safety of the vaccines.<br><br>There are currently two licensed monovalent varicella-only vaccines in Europe. The Summary of Product Characteristics for both licensed monovalent vaccines published on the Health Products Regulatory Authority (HPRA) and the European Medicines Agency (EMA) websites state that the vaccines may be given at the same time as the measles, mumps and rubella (MMR) vaccine. |
| **Description of the technology** | |
| Section 2 Description of technology, second sentence: Suggest for clarity "Approximately 96% of those exposed to VZV and who are not immune, through prior infection or vaccination, will develop the disease." | Wording of the sentence in Chapter 2 and other relevant sections has been updated. |
| Section 2.5.1 vaccine description page 27: "Currently there are four varicella vaccines authorised for vaccination against varicella by either the Health Products Regulatory Authority (HPRA) in Ireland or the European Medicines Agency (EMA)." This statement is inaccurate. ProQuad® is authorised centrally by the EMA. VARIVAX® and Priorix-Tetra® are authorised nationally by the HPRA through decentralised procedures. Varilrix® is not authorised in Ireland by HPRA nor centrally by the EMA. It is authorised in a number of EU countries via national procedures. | Wording of the relevant sentence in Section 2.5.1 has been updated and reflected in the other relevant sections of the report. |

| Comment | Response |
|---|---|
| Suggest rewording to: "Currently there are four varicella vaccines authorised for vaccination against varicella in Europe." | |
| Section 2.5.1 Vaccine description page 27: "Following an EMA review of Varilrix®, published in February 2021, that recommended changes to the prescribing information in order to harmonise the way the medicine is used in the EU, an authorisation update for Varilrix® was issued in April 2021.(13)" This statement is inaccurate. The EMA review consisted of an article 30 referral, i.e. a review of Varilrix® and recommended changes to the prescribing information in order to harmonise the way the medicine is used in the EU. There was not a change of the authorisation model to centralised as suggested in this sentence. The product remains nationally authorised. The European Commission implements the article 30 referral outcome. A European Commission implementing decision valid throughout the EU was issued on 21 April 2021. Suggest rewording to: "Following an EMA review of Varilrix®, published in February 2021, that recommended changes to the prescribing information in order to harmonise the way the medicine is used in the EU, a European Commission decision valid throughout the EU was issued in April 2021." | Wording of the relevant sentence in Section 2.5.1 has been updated. |
| Table 2.1 Varilrix® license issued: "EU authorisation update issued on 21 April 2021 following a request from GSK to EMA to harmonise the marketing authorisations for Varilrix® in the EU". The EMA review consisted of an article 30 referral, i.e. a review of Varilrix® and recommended changes to the prescribing information in order to harmonise the way the medicine is used in the EU. There was not a change of authorisation status as suggested by this sentence. The product remains nationally authorised. The European Commission implements the EMA outcome. A European Commission implementing decision valid throughout the EU was issued on 21 April 2021. | Wording of the relevant sentence in Table 2.1 has been updated. |

| Comment | Response |
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| Suggest rewording to: "European Commission decision valid throughout the EU issued on 21 April 2021 following a request from GSK to EMA to harmonise the way Varilrix® is used in the EU." | |
| Table 2.1<br><br>Formulation for Varilrix® should read: varicella-zoster virus Oka strain rather than just varicella virus Oka strain. | Table 2.1 has been updated. |
| Table 2.2<br><br>Recommended that dosing schedule column for Varilrix® is updated as follows: 2 doses ≥6 weeks apart (and not less than 4 weeks) | Table 2.2 has been updated. |
| Table 2.4<br><br>Vaccine manufacturer for Menjugate® should be amended to GSK only.<br><br>Vaccine product and vaccine manufacturer for MMR vaccine should be updated to include Priorix® and GSK.<br><br>Sources for table content requires updating. | Table 2.4 has been updated. |
| Section 2.5.2<br><br>MenB can be administered concomitantly with VARIVAX® (or conjugate, measles, mumps, rubella, varicella (MMRV) vaccines) but these must be given at separate injection sites. | The following bullet point has been removed from section 2.5.2:<br><br>▪ Meningococcal serogroup B (MenB) vaccine is not listed as one of the vaccines that may be co-administered with VARIVAX® and ProQuad®. |
| **Epidemiology and burden of disease** | |

| Comment | Response |
|---|---|
| No reference to long term impact from serious illness, from physical scarring from varicella or herpes zoster. | Sections 2.3 and 3.3 have been updated to include skin scarring as a potential complication. It has also been added to the key points in Chapter 3. |
| Due to the incubation period of this virus usually siblings don't contract varicella at the same time, thereby extending the time parents have to be away from work (Section 9.2.5.4). | While Section 9.2.5.4 notes that there may be some overlap in the timing of varicella disease among individuals in the same household, the base case economic analysis assumed that there was no overlap in the calculation of productivity losses in the economic evaluation (chapter 7). As such, it was assumed that absence of work would last for one week for each child, irrespective of whether they were siblings. |
| We would like to emphasise the potential of varicella vaccination in reducing invasive Group A Streptococcus (iGAS) infections. While the HTA acknowledges this relationship, we believe it is essential to highlight the importance of varicella vaccination as a strategy to prevent potentially fatal secondary infections more prominently. There has been a very significant and sustained upsurge in iGAS notifications in Ireland in recent months, many of which have occurred secondary to varicella zoster virus infection, and some of which have resulted in severe morbidity and mortality among otherwise healthy individuals, including children. We understand that further submissions to the HTA consultation process will be highlighting this risk, and we endorse any efforts to highlight this very important risk within the HTA. | The addition of varicella vaccination to the childhood immunisation schedule is intended to reduce severe disease including complications. As noted and described in the HTA (section 3.3.2), iGAS is a serious complication that can arise after initial VZV infection. The low numbers of cases make it challenging to assess trends in the epidemiology of chickenpox-related iGAS.<br>The key points in Chapter 3 have been expanded to highlight that varicella is considered a significant risk factor for iGAS disease. This issue is also noted in the advice document. |
| **Exogenous boosting** | |
| Has the exogenous boosting hypothesis been given appropriate weight in this review? Looking at the conclusions, it seems to have almost been discounted by the experts who wrote this report. | The exogenous boosting theory was identified as a consideration in the economic modelling of varicella vaccination (chapter 6.4.6). However, the pathophysiology of exogenous boosting is poorly understood, much debated and the magnitude of the effect, if it exists, is unknown (section 7.5.2). The long-term data on routine varicella vaccination from the US show that the predicted increase in herpes zoster among adults based on the exogenous boosting theory was not observed (section 9.2.5.2). In the absence of conclusive evidence, the base case economic model assumed no exogenous boosting. The potential impact of exogenous boosting was examined in a scenario analysis (section 7.4.2.3) where the estimated change in herpes zoster cases by year and vaccination strategy and the impact of full temporary exogenous on the cost effectiveness of varicella vaccination were reported. Given the lack of conclusive evidence supporting or disputing the exogenous boosting theory, its consideration in the economic model has been acknowledged as a potential limitation (section 7.5.2). |

| Comment | Response |
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| The NHS do not recommend routine childhood vaccination against the chickenpox as they report it would lead to an increase in shingles in adults. "When people get chickenpox, the virus remains in the body. This can then reactivate at a later date and cause shingles. Being exposed to chickenpox as an adult (for example, through contact with infected children) boosts your immunity to shingles. If you vaccinate children against chickenpox, you lose this natural boosting and immunity in adults will d*<br><br>*This response was not complete. HIQA's response is based on an assumption that the missing word is 'decline'. | The 2016 decision of the UK's Joint Committee on Vaccination and Immunisation (JCVI) to not recommend universal childhood varicella vaccination is included in the report (section 9.2.5.2). This decision by JCVI was based on a finding that economic modelling showed that varicella vaccination was not cost effective, largely because of a predicted increase in herpes zoster incidence due to a reduction in immunological "boosting" from circulating varicella virus. Additionally, the report outlines that in September 2022, the JCVI reported that varicella vaccine modelling work is being updated to include new research on both the quality of life impact of varicella on children and families and IgG seroprevalence and to incorporate experience data from 25 years of universal childhood varicella vaccination in the US, including the dynamics of exogenous boosting (section 9.2.5.2). |
| **Rapid review of economic modelling studies** | |
| Page 132, section 6.4.7 - please update paragraph "From the payer's perspective in the UK model, a two-dose quadrivalent strategy (with both GSK and MSD vaccines) was not cost effective over the short-term (20 years) time horizon, with the cost per QALY gained >£20,000. Additionally, the two-dose quadrivalent strategy was not cost effective over the medium-term (40 years) with the MSD vaccine with the following statement. "The two-dose quadrivalent strategy was cost-effective in the medium (GSK only) and long-term only with ICURs <£20,000/QALY gained."<br><br>Please further update the same paragraph to include detail for the reader on the societal perspective economic results - "The mono+quad strategy (for both vaccines) was cost-effective across all time horizons with ICURs <£20,000/QALY gained (GSK vaccine was dominant in the long-term). The two-dose quadrivalent strategy was cost-effective across all time horizons with ICURs <£20,000/QALY gained". | Section 6.4.7 reports that all strategies assessed were cost effective, with a limited number of exceptions for each study. Only the exceptions are listed in the report and therefore no changes have been made to this section. |
| **Economic evaluation** | |

| Comment | Response |
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| The economic evaluation (section 7) states the annual cost would be €28 million for a 2 dose short interval strategy, suggesting the annual cost would be well over €400 per vaccine recipient - this is completely ridiculous considering our daughter got both doses for less than €200 at our GP. The report should clearly state the average cost and the average benefit. | The estimated budget impact of all three varicella vaccination strategies was calculated over a five year time period (see chapter 7.4.3.1). This approach is in line with national guidelines for conducting a budget impact analysis (see chapter 7.3.1.7). Based on the estimated five year budget impact of the two-dose short interval strategy of €28.1 million, the estimated annual budget impact would therefore be €5.6 million. |
| In sheer economic terms, is there a loss to the economy if chickenpox brings a loss of working hours, loss of working hours due to caring demands for a child who becomes infected or a pregnant woman might be at added risk of miscarriage with loss of work days during an actual miscarriage that may have been provoked by exposure to the infection in the first trimester? | When examining the costs of chickenpox from a societal perspective, there is a loss associated with absence from paid work due to the illness. In this HTA, a societal perspective was adopted for the economic analysis where the productivity loss associated with absence from paid work for both parents caring for children with chickenpox and for individuals of working age sick with chickenpox was included. The productivity loss associated with absence from paid work due to miscarriage caused by chickenpox in the pregnant woman was not included in the analysis. The report has been updated to note this limitation (section 7.5.2). |
| Each strategy has its merits. It is however unclear to me on reading the document how the short interval strategy is truly dominant. | In the economic evaluation (section 7.4.2), the term 'dominant' refers to an intervention that is less costly and more effective than the comparators. From the societal perspective, the two-dose short interval strategy is the least costly and most effective strategy. It generates the greatest cost savings and the greatest QALY gains, and is therefore deemed the 'dominant' strategy. |
| I believe one potential flaw in the HIQA analysis is assigning equivalency to the administration costs in the shorter and longer interval schedules. Further consideration might be given to the analysis addressing selection of a shorter or longer interval strategy. | The two-dose short interval strategy is based on both vaccine doses being administered in the general practice setting, while the two-dose long interval strategy is based on the first dose being administered in the general practice setting and the second dose being administered as part of the school immunisation programme. The cost of administering the second dose of the vaccine in the school setting is just one of a range of model input parameters that are uncertain and that potentially impact the overall certainty of the results of the economic evaluation. This uncertainty is acknowledged in the economic evaluation (section 7.3.1.8.6) and was examined in the sensitivity analysis and a number of scenario analyses where the base case assumption was adjusted (section 7.4.2.3). The cost-effectiveness results of the uncertainty analysis are presented in Table 7.16 and indicate a lower cost-effectiveness ratio for the two-dose long interval strategy, compared with the one-dose strategy, and a higher cost-effectiveness ratio for the two-dose short interval strategy, relative to the two-dose short interval strategy, when the cost of administering the second dose is lowered.<br><br>The uncertainty around the cost of administering the vaccine is also discussed in chapter 10 where it is highlighted that the difference in cost effectiveness between the long and short interval two-dose strategies is sensitive to the cost of administering the vaccine. Additionally, the justification for the |

| Comment | Response |
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| | approach adopted, and the implications for cost effectiveness if the cost of administering the second dose in the school setting is lower than the base case assumption are discussed (section 10.3.4). |
| It is unclear from the health technology assessment whether a two-dose short interval option, with vaccinations administered at 12 months and 13 months, has been considered. The current varicella vaccine available in Ireland, VARIVAX®, can be given to children aged 12 months to 12 years, with at least a 1-month interval between doses. Utilising the existing 12 and 13 month vaccine appointments may be more cost-effective compared to the proposed 12 and 15 month vaccination schedule, and potentially more clinically effective than the two-dose long interval option suggested. This approach may ensure that children are fully immunised at a younger age. We believe it is essential to consider this option in the health technology assessment, as it is a common question among GP and practice nurse colleagues who have been informed about the proposal to add varicella to the immunisation schedule, and who would play a key role in its administration. Alternatively, could consideration be given to adjusting the timing of the existing 13 month vaccines (e.g. to 14 months) to include the varicella vaccine without creating an extra visit? | As agreed with the Department of Health, and stated in chapter seven, three plausible alternative vaccination strategies, were considered in the economic evaluation as follows:<br>▪ one-dose administered at 12 months of age<br>▪ two-dose short interval administered at 12 months and 15 months of age<br>▪ two-dose long interval administered at 12 months and five years of age.<br><br>The selection of these three strategies for inclusion in the economic evaluation ensured that both one- and two-dose strategies with both short and long intervals were considered. While a two-dose short interval strategy with vaccines administered at 12 months and 13 months was not considered in the economic evaluation, its cost effectiveness would unlikely be substantially different to a two-dose strategy administered at 12 months and 15 months. Any decision taken by the Department of Health on the introduction of a varicella vaccination programme and the timing of the administration of each vaccine would not necessarily be strictly limited to the dosing schedule considered in the economic evaluation. As outlined in chapter eight, organisational issues around programme implementation and health service capacity, as well as the impact on the existing immunisation programme, would also be key considerations in decision making regarding the specific strategy. |
| We have queries regarding the presentation of the third option, the two-dose long interval approach. The way the costing has been reported may make this option appear more attractive than it truly is. There is a fear that if this option is selected, it may turn out to be more expensive than the proposed two-dose short interval (12 and 15 months) or the suggested 12 and 13 month option when the full programme is up and running and all costs are taken into account. Moreover, the two-dose long interval option is clinically less effective. Therefore, beyond a five-year timeframe, it is possible that option three could become more costly than option two, leading to a potential desire to switch approaches. Such a switch in strategy could undermine public confidence and impact vaccine uptake rates. Therefore, it is crucial to | The economic evaluation examined both the budget impact of three different varicella vaccination strategies over a five year time horizon and the longer term cost effectiveness of the three varicella vaccination strategies over an 80 year time horizon (section 7.3.1.7).<br><br>As outlined in section 7.4.3.1, from year five onwards the difference in budget impact between the two-dose strategies (short and long interval) should only reflect the difference in cost (if any) between administering the vaccine in the GP practice setting and the school setting.<br><br>From a cost-effectiveness perspective, an 80 year time horizon was adopted for the cost-effectiveness analysis, ensuring that the long term costs and effects (beyond five years) of each of the three strategies were modelled and incorporated into the analysis (section 7.3.1.7). The cost-effectiveness ratios presented in the report include both the costs and clinical effectiveness of each strategy (including |

| Comment | Response |
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| discuss the risks associated with selecting option three more extensively in this health technology assessment. | parameters such as waning immunity with one dose) over 80 years and therefore incorporate estimated long term differences between the three strategies.<br><br>Additionally, waning immunity for one dose was varied in the sensitivity analysis with the cost-effectiveness results presented for both the two-dose long interval strategy compared to one-dose strategy (section 7.4.2.2.2) and the two-dose short interval strategy compared with the two-dose long interval strategy (section 7.4.2.2.3). The report highlights that the cost-effectiveness ratio for the two-dose short interval strategy, relative to the two-dose long interval strategy, was most sensitive to changes in the waning immunity rate of one dose (section 7.4.2.2.3 and figure 7.5). |
| **Organisational issues** | |
| The potential seriousness of varicella and herpes zoster needs to be part of the education and public awareness programme (Section 8.5.3). | While the potential for complications is detailed in chapter 3 (Epidemiology and Burden of Disease), section 8.5.3 has been updated to include further detail on the purpose of an information and awareness campaign for parents. |
| One issue that is not covered in any great depth in the report, relates to monitoring of the impact of vaccination. Hard end points in the process will obviously include the degree of uptake within selected age groups. However, total cases of vaccine preventable diseases, for which there are primary schedule vaccines, are statutorily notifiable under the relevant Infectious Disease Regulations. Surveillance of varicella relates only to hospitalised cases. Given that the reporting of hospitalised cases may involve a degree of underreporting, I think it would be important that there was an initiative to ensure that reporting of hospitalised varicella cases was as complete as possible, supported by bespoke studies to determine any degree of under ascertainment. | Monitoring the impact of any vaccination programme is challenging, particularly given the movement of population in and out of the country where exposure is not solely due to immunity in Ireland. As noted, data on incidence of varicella are typically under-estimates as many people will not consult with a GP when their child has varicella.<br><br>Bespoke studies are a potential route to determine under-ascertainment of disease incidence. Whether these are necessary may depend on whether the interest is in changes in incidence of varicella or of severe disease. The latter, which in many respects is the primary outcome of interest, should be relatively well measured in the hospitalisation (HIPE) data.<br><br>Section 8.6.1 has been updated to include monitoring incidence to determine the impact of adding varicella to the childhood immunisation schedule. |
| **Vaccination catch-up programme** | |
| Please consider a catch up schedule for the under 5s | The Department of Health's request to HIQA for this HTA did not include a catch-up programme and therefore such a programme has not been included in this assessment. It should be noted that a catch-up programme could be logistically challenging to implement unless it was able to leverage off existing scheduled immunisation visits. |
| I think a once-off vaccine to older children should also be offered to catch any who have not yet had chickenpox. For example, my daughter is almost nine years old and has not yet | |

| Comment | Response |
|---|---|
| had chickenpox. I would love to get her the vaccine but cannot afford it now. If a once off vaccine was offered through the HSE that would be great. | |
| Health authorities should strongly consider implementing a parallel catch-up programme when adding the varicella vaccine to their national immunisation programme, particularly if the intended goal of the programme is to achieve varicella disease elimination. | |
| **Chickenpox in pregnancy** | |
| I have never had chickenpox and when I was pregnant, the worry of catching it and the possible impact was significant. My daughter, now 12 years old, also has never had chickenpox. If she is pregnant, risk of complications will remain. I have thought of getting her vaccinated but couldn't find much information. Your report has reference to complications in pregnancy but suggest more. | The purpose of this HTA was to examine the introduction of a universal varicella vaccination programme for children and assess the main direct benefit (reducing the incidence of varicella disease in children) of such a vaccination programme. However, in considering the epidemiology and burden of disease associated with varicella, the incidence and nature of disease in adults and specifically pregnant women, their foetus and neonate, as well as children targeted for vaccination, were reported (section 3.2.4). Additionally, the possible benefit of herd immunity for pregnant women who have not had varicella is recognised in the report (section 9.2.5.1). |
| Should women considering pregnancy be advised that contracting chickenpox around the time of conception or in the early stages of pregnancy, might bring risks to the viability of the foetus and possible long term damage to an unborn baby, if that could be a risk? | The assessment focused on the implications of varicella vaccination in the context of it not being part of the current childhood immunisation schedule.<br><br>The HSE has published information on chickenpox in pregnancy including the associated risks. In the event that varicella is introduced to the immunisation schedule, there will be an extended period before the majority of pregnant women will have been eligible for and offered varicella vaccination in childhood. The information on risks of varicella in pregnancy will continue to be required as not all pregnant women can or will have availed of vaccination in childhood. |
| Is it possible to check one's immunity to chickenpox while family planning? | |
| Is there clarity on protection during pregnancy for a foetus in a mother who had chickenpox versus chickenpox vaccine as a child? Are there equal levels of protection for the foetus in utero, or has this been studied? | We are not aware of evidence on this specific question. As part of this HTA, two overviews of reviews of the effectiveness and safety of varicella vaccination in immunocompetent children aged nine months to six years were conducted. Within these reviews, no studies were identified that examined the long term effectiveness of the vaccine, compared with the effectiveness of wildtype varicella, in protecting a foetus in utero. |

## Changes to the report from the consultation process

The following changes were made to the draft report in response to comments and feedback received through the consultation process:

- To ensure clarity, wording of a sentence in Chapter 2 and other relevant sections has been updated.
- Sections 2.3 and 3.3 have been updated to include skin scarring as a potential complication.
- Section 2.5.2 on the co-administration of varicella vaccines with other vaccines has been updated to remove the bullet point relating to meningococcal serogroup B (MenB) vaccine.
- Table 2.1 (Summary of key characteristics of the licensed varicella vaccines in Europe) has been updated with revised wording on the formulation for Varilrix®.
- Table 2.2 (Dosing schedules, age at vaccination and interchangeability for licensed varicella vaccines) has been updated with revised wording on the recommended dosing schedule for Varilrix®.
- Table 2.4 (Recommended childhood immunisation schedule in Ireland 2020) has been updated as follows:
    - Product manufacturer for Menjugate® updated
    - Priorix® and GSK added for MMR vaccine at 12 months and four/five years
    - Sources updated.
- The association between varicella and invasive Group A Streptococcus disease has been added to the key points in Chapter 3.
- A limitation has been added to section 7.5.2 which notes that the productivity loss associated with absence from paid work due to miscarriage caused by varicella in the pregnant woman, is not included in the economic analysis.
- Section 8.5.3 has been updated to include further detail on the purpose of an information and awareness campaign for parents.

- Section 8.6.1 has been updated to include the need to monitor incidence, using hospitalisation data or bespoke studies, to determine the impact of adding varicella to the childhood immunisation schedule.

In addition to the changes made above, the Advice to the Minister, an Executive Summary and a plain language summary are presented in the final report. Every attempt has been made to further emphasise issues of importance that were highlighted during the consultation process in the plain language summary, the Executive Summary and the Advice to the Minister.

# References

1. Health Information and Quality Authority. Draft HTA of expansion of the childhood immunisation schedule to include varicella (chickenpox). Dublin: HIQA; 2023 20 April 2023.

## Appendix A – Copy of submission feedback form

# Health Technology Assessment of expansion of the childhood immunisation schedule in Ireland to include varicella (chickenpox) vaccination

# For public consultation

## Consultation Feedback Form

Your feedback is very important to us. We welcome responses to all questions as well as any additional comments you would like to make.

When commenting on a specific section of a document, it would help if you can identify which element you are commenting on and the relevant page number.

**The closing date for consultation is 5pm on Monday 29 May 2023**

**You may email a completed form to us at consultation@hiqa.ie . You may also complete and submit your feedback online at https://hiqa.survey.fm/public-consultation-expanding-childhood-immunisation-schedule-to-include-chickenpox-vaccine**

# About you

| | |
|---|---|
| **Name** | |
| **You or your organisation's country** | |
| **Today's Date** | |

## General Information and Questions

You may provide us with feedback on the specific questions (see questions that follow), or alternatively you may provide us with general comments.

## Part 1

Are you replying in a personal capacity or on behalf of an institution or organisation?

☐ Personal capacity

☐ On behalf of an institution *Please name*

☐ On behalf of an organisation *Please name*

## Part 2

Please outline any general or specific feedback on the documents. In your response, where applicable, please specify the section to which you are referring.

*Please comment*

## Part 3

Please outline any issues with the clarity or presentation of the report. In your response, where applicable, please specify the section to which you are referring.

*Please comment*

# Thank you for taking the time to give us your views.

After the closing date, we will assess all feedback and use it to finalise our documents. The final documents and the Statement of Outcomes (a summary of the responses) will be published on http://www.hiqa.ie.

If you wish to do so, you can request that your name and/or organisation be kept confidential and excluded from the published summary of responses. Please note that we may use your details to contact you about your responses. We do not intend to send responses to each individual respondent.

Please return your form to us either by email:

consultation@hiqa.ie

or complete it online at: https://hiqa.survey.fm/public-consultation-expanding-childhood-immunisation-schedule-to-include-chickenpox-vaccine

If you have any questions you can contact the consultation team emailing consultation@hiqa.ie.

**Please return your form to us either by email or post before 5pm on Monday 29 May 2023**

Please note that the Authority is subject to the Freedom of Information Acts and the statutory Code of Practice regarding FOI.

For that reason, it would be helpful if you could explain to us if you regard the information you have provided as confidential. If we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances.

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