Nye metoder: Innspill til metoder (forslag/metodevarsler/oppdrag)

Alle har anledning til å komme med tilleggsopplysninger til en metode som er foreslått for nasjonal metodevurdering. Det er ønskelig at innspill kommer inn så tidlig som mulig i prosessen, fortrinnsvis før behandling i Bestillerforum RHF.

Bruk dette skjemaet for å gi innspill til forslag, metodevarsler og oppdrag. På nyemetoder.no vil nye forslag/metodevarsler ha statusen «Forslag mottatt/åpent for innspill» før behandling i Bestillerforum RHF. Utfylt skjema sendes nyemetoder@helse-sorost.no.

NB: **Punkt 1-3 og 11 fylles ut av alle.** Punkt 4-9 fylles ut avhengig av rolle og kjennskap til metoden.

Jeg er klar over at skjemaet vil bli publisert i sin helhet på nyemetoder.no (kryss av): ☒
Har du informasjon du mener ikke kan offentliggjøres, ta kontakt med sekretariatet før innsending.

Jeg har fylt ut punkt 11 nedenfor «Interesser og eventuelle interessekonflikter» (kryss av): ☒

1.Hvilken metode gjelder innspillet?	
Metodens ID nummer*:	ID2020_029
Metodens tittel:	Elexakaftor, tezakaftor og ivakaftor

*ID-nummer finner du på metodesiden på nyemetoder.no og har formen ID2020_XXX

2. Opplysninger om den som gir innspill	
Navn	Stefan Frenning
Eventuell organisasjon/arbeidsplass	Vertex Pharmaceuticals
Kontaktinformasjon (e-post / telefon)	Stefan_frenning@vrtx.com / +46 70 563 8245

3. Oppsummert innspill til metoden (besvares av alle)

Input to Bestillerforum's assessment of elexacaftor/tezacaftor/ivacaftor (ID2020_029) – Ordering Forum Meeting May 25th 2020

Background

Vertex Pharmaceuticals (Vertex) would like to provide input to Bestillerforum's assessment of elexacaftor/tezacaftor/ivacaftor (ID2020_029). Elexacaftor/tezacaftor/ivacaftor (the Triple Combination) is a new treatment for cystic fibrosis (CF) currently under review by the EMA.

CF is a severe genetic disease leading to pre-mature mortality and morbidity. Until the relatively recent approval of CFTR (cystic fibrosis transmembrane conductance regulator) modulators, which treat the underlying cause of the disease, the only treatments available for CF patients were symptomatic. The launch of the new class of medicines, including elexacaftor/tezacaftor/ivacaftor, has meant a significant step-change in the treatment of CF providing clinical benefits to patients and their families. Clinical trials suggest that in addition to making more patients eligible for treatment with a CFTR modulator, the triple combination further enhances the treatment effect achieved by currently approved CFTR modulators.

Specific comments to the Horizon Scanning Report ("Metodevarsel") for elexacaftor/tezacaftor/ivacaftor

Vertex would like to comment on the following key points of the report.

Indication. The indication Vertex has applied for, and is currently being assessed by the EMA, is broader than assumed in the Horizon Scanning Report. The indication now being assessed by the EMA is similar to the indication approved in the US (https://www.accessdata.fda.gov/drugsatfda_docs/label/2019/212273s000lbl.pdf). The indication would, if approved, cover all patients 12 years and older with at least one F508del mutation in the CFTR gene.

Standard of care. Vertex would like to highlight that CFTR modulators are in fact a key element of the standard of care for CF in the growing number of countries across Europe where broad patient access for CFTR modulators has been granted (UK, Ireland, Denmark, Sweden, France, Spain, Germany, Austria, Netherlands), as well as in the US.

Comments on the appropriateness of the assessment methodology

The committee for Health and Care services in the Norwegian parliament has pointed out that there is a need to facilitate for the special features of Rare Disease treatments. More specifically the committee has emphasized the need for a less rigid demand for clinical documentation, and a higher willingness to pay for severe congenital disease such as CF. The committee restated this principle when the financing of Rare Diseases was transferred to the Health Regions in 2018.

When considering the Health Technology Assessment (HTA) of rare diseases, and CF in particular, the application of traditional cost-effectiveness methods has proven to be very challenging. Vertex believes that the methodology applied by most HTA-bodies, including the Norwegian Medicines Agency (NoMA), is not suitable for evaluating transformative medicines for rare diseases, and there is a need for assessment to be flexible for innovative technologies that offer substantial breakthroughs. The main reason is that the methodology has inherent biases against innovative medicines, such as CFTR modulators, developed and intended for lifelong chronic conditions where the health benefits are accrued far in the future.

There are three key elements we would like to emphasize and ask Bestillerforum to consider for the assessment of elexacaftor/tezacaftor/ivacaftor.

Assuming constant pricing over time. Norway has a well-defined system for pricing of generic versions of branded medicines. We believe this method should be applied in the cost-effectiveness assessment of Vertex branded medicines, one reason being that the treatment in question are tablets. Applying no price decrease following anticipated generic entry should, in our opinion, be considered the least likely and realistic future scenario. In our opinion a more plausible option would include price decreases at least of the magnitude the Norwegian system

requires at anticipated loss of exclusivity. The implication of not applying such price decreases is that the value of the medicine undergoing assessment turns out lower than it should be.

Discounting at same rate for costs and health benefits. The current method of discounting is also problematic in this situation because of the discount rate used and the asymmetry in the timing of cost versus benefits of the treatment. The full product costs are accrued from day 1 while the benefits in the form of increased survival or quality of life (QoL) are not fully realized until years or decades later. A methodology, such as the one used in Norway, will influence the ICER denominator heavily due to the significant devaluation of future health benefits. Vertex would therefore like to suggest that NoMA use a more flexible approach, i.e. using a lower discount rate for health gains, when discounting the costs and benefits for treatments aiming to help patients with lifelong chronic conditions such as CF.

Willingness-to-pay linked to absolute shortfall. In Norway, the accepted cost for a quality-adjusted life year (QALY) is linked to the severity of disease measured by absolute shortfall. However, the accepted cost per QALY has a ceiling value once the absolute shortfall reaches a value of 20 QALYs. The implication is that severe diseases, where the absolute shortfall value is significantly higher, are not treated with parity compared with less severe diseases. To Vertex, this is counter-intuitive, as the opposite would be expected. In the example of CF, the absolute shortfall as assessed by NoMA is 50% higher than the threshold value mentioned above, we believe this should be taken into consideration in the assessment for elexacaftor/tezacaftor/ivacaftor.

Concluding remarks

Vertex has followed the Norwegian health care debate over the past few years. During 2019, we have noticed the public debate changing regarding the introduction of new pharmaceuticals. In particular, we've been closely following concerns related to access to rare disease medicines and the challenge of assessing rare diseases in the current system.

In December, Stortinget recommended, with a specific reference to rare diseases like CF, an evaluation of the entire system for introducing new methods in the hospital sector (Nye Metoder). Stortinget has also, when debating the Whitepaper on the Health Industry (Meld. St. 18 (2018–2019)), called for more pilots on innovative assessment and procurement of pharmaceuticals. Vertex obviously wants to contribute to the process of ensuring access to patients also in Norway, as achieved through innovative agreements in other countries like Denmark, UK and Switzerland.

Vertex believes that our suggestions above for the evaluation of elexacaftor/tezacaftor/ivacaftor could serve as a valuable pilot for customized, innovative models for assessment of advanced treatments for rare diseases. We fear that unless suitable models of assessment are developed and tested out, the accessibility to this and other new treatments for Norwegian patients with rare diseases will be severely hampered.

Nærmere informasjon om metoden og innspill til PICO*

*PICO er et verktøy for å formulere presise problemstillinger i metodevurderingsarbeid. PICO er en forkortelse for Population/Problem – Intervention – Comparison – Outcome. PICO brukes til å presisere hvilken populasjon/problem som skal studeres, hvilke(t) tiltak (metode/behandling) som skal vurderes, hvilket tiltak det er naturlig å sammenligne med, og hvilke utfall/endepunkter det er relevant å måle/vurdere. PICO er viktig for planlegging og gjennomføring av en metodevurdering.

4. Kjenner du til om metoden er i bruk i Norge i dag?
Er metoden i bruk utenom kliniske studier i dag: Nej Fra hvilket tidspunkt har den vært i bruk: Hvor er eventuelt metoden i bruk:

5. Hvilken pasientgruppe i den norske spesialisthelsetjenesten er metoden aktuell for? (PICO)
Beskriv kortfattet: Den ansökta indikationen för elexakaftor/tezakaftor/ivakaftor i kombination med ivakaftor omfattar behandling av patienter med cystisk fibros 12 år och äldre som har minst en F508del mutation i CFTR-genen. Det är dessa patienter som behandlingen är aktuell för i Norge, förutsatt att EMA godkänner denna.

6. Er du kjent med behandlingsalternativer til denne metoden og hvordan disse fungerer for pasientgruppen i dag? (PICO)
Beskriv kortfattet: Idag behandlas Norska patienter med cystisk fibros huvudsakligen med symtomlindrande behandling (se introduktionstext ovan). Vissa CF-patienter behandlas även med sjukdomsmodifierande läkemedel, genom den tidigare möjligheten med individuell refusjon, dvs med Orkambi eller Kalydeco. Kliniska data för elexacaftor/tezacaftor/ivacaftor visar att, utöver att ge fler patienter möjlighet till behandling med CFTR modulatorer, ger trippelkombinationen förbättrad effekt jämfört med hittills godkända CFTR modulatorer.

7. Har du innspill til hva som vil være viktig for pasienter som er aktuelle for behandling med metoden? (PICO)
Hva kan oppfattes som en fordel for pasienter og brukere med denne metoden sammenlignet med aktuelle alternativer? Hvilke endepunkter/resultater av behandlingen er det aktuelt å måle? Beskriv kortfattet: Elexacaftor/tezacaftor/ivacaftor ger, baserat på information från de kliniska studier som refereras i horizon scanning-rapporten, signifikanta förbättringar i

relevanta parametrar för patienter med cystisk fibros, t.ex. lungfunktion, svettklorider och livskvalitet.

8. Spesielt for medisinsk utstyr (besvares av leverandør): CE-merking
Foreligger det CE-merking for bruksområdet som beskrives i metoden? I så fall angi type og tidspunkt:

9. Spesielt for legemidler (besvares av leverandør): Markedsføringstillatelse (MT)
Har legemiddelet MT for indikasjonen som omfattes av metoden? Angi i så fall tidspunkt eller ventet tidspunkt for MT: Nej, marknadsföringstillstånd förväntas under 2020.

10. Andre kommentarer
Hur elexacaftor/tezacaftor/ivacaftor utvärderas är av största vikt, därför är kommentarerna i inledningen väsentliga för en rimlig värdering av denna produkt. Exempelvis är den modellerade överlevnadsvinsten är stor, men riskerar att nedvärderas med den metodik som idag används.

11. Interesser og eventuelle interessekonflikter Beskriv dine relasjoner eller aktiviteter som kan påvirke, påvirkes av eller oppfattes av andre å ha betydning for den videre håndteringen av metoden som det gis innspill på (for eksempel: økonomiske interesser i saken, oppdrag eller andre bindinger).
Beskriv kortfattet: Jag arbetar på företaget.