# Forslag til nasjonal metodevurdering

Innsendte forslag til nasjonale metodevurderinger vil bli publisert i sin helhet. Dersom forslagsstiller mener det er nødvendig informasjon for utfylling av skjemaet som ikke kan offentliggjøres ta kontakt med sekretariatet før innsending.

Forslagsstiller er klar over at skjemaet vil bli publisert i sin helhet (kryss av): ☒

## Kontaktinformasjon:

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Roche Norge AS

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**Sted og dato:**

Oslo, 11.03.2015

**1. Tittel på bestillingen:**

The pharmaceutical product Gazyvaro (obinutuzumab) for the indication relapsed, rituximab refractory follicular lymphoma

**2. Kort beskrivelse av metoden som foreslås vurdert:**

Gazyvaro (obinutuzumab) for relapsed, rituximab refractory follicular lymphoma

Indication pending approval:

Gazyvaro in combination with bendamustine, followed by Gazyvaro maintenance for the treatment of patients with follicular lymphoma who did not respond to or who progressed during or up to 6 months after treatment with rituximab or a rituximab-containing regimen. Gazyvaro is for treatment at hospital setting.

Gazyvaro has been granted orphan designation for follicular lymphoma indication in Europe from 19th June 2015.

**3. Kort beskrivelse av dagens tilbud** (Hvilken metode(r) brukes nå? Status for metoden (gir kurativ behandling, forlenget levetid etc.) Vil metoden som foreslås vurdert erstatte eller komme i tillegg til dagens tilbud?)

In the current Norwegian treatment guidelines (Nasjonalt handlingsprogram med retningslinjer for diagnostikk, behandling og oppfølging av maligne lymfomer) there are a few options mentioned for relapsing patients:

- Retreatment with rituximab is recommended when the previous remission lasted for at least 6 months. Studies indicate that at least 50% of these patients will have a new remission that will last longer than the first line treatment.
- Responses of median 1 year are seen in patients treated second line treatment, but lower for patients with high tumor loads.

Rituximab dose used is 375 mg/$m^2$ once weekly for 4 weeks .Nordic trial experience show that 4 additional treatments will give added benefit.

- Relapsing patients should be evaluated for participation in clinical trials according to the guidelines. The mentioned trial in the guidelines (MabCute), is no longer recruiting patients.
- R-CHOP is mentioned as an alternative and gives higher benefit than CHOP alone and is specially advised for patients that did not receive rituximab in the first line.
- Bendamustine with or without rituximab has also shown good results in several phase 2 studies, in relapsed patients. The efficacy is most likely comparable to CHOP and with less toxicity.

The proposed method, Gazyvaro in combination with bendamustine , followed by Gazyvaro maintenance is an add-on to the existing, recommended bendamustine treatment scheme, that has shown a more than double improvement in progression free survival and clinically meaningful increase in overall survival in patients with relapsed, refractory to rituximab follicular lymphoma compared to bendamustine alone. This is the first time clear benefit is demonstrated in a robust phase III study in the rituximab refractory follicular lymphoma setting.

The proposed method is an additional alternative for patients who no longer benefit from rituximab based treatments.

| **4. Hva gjelder forslaget?** | **Ja** | **Nei** |
|---|---|---|
| En helt ny metode? | ☐ | ☒ |

| | | |
|---|---|---|
| Et nytt bruksområde, eller en ny indikasjon for en etablert metode? | ☒ | ☐ |
| En sammenligning mellom flere metoder? | ☐ | ☒ |
| Er metoden tatt i bruk? | ☐ | ☒ |
| Hvis ja – metode tatt i bruk i klinisk praksis? | ☐ | ☐ |
| Hvis ja – metode tatt i bruk innen forskning/utprøving? | ☐ | ☐ |

This is a new, not yet authorized indication.

Gazyvaro is used and approved for one other indication:

Gazyvaro in combination with chlorambucil is indicated for the treatment of adult patients with previously untreated chronic lymphocytic leukaemia (CLL) and with comorbidities making them unsuitable for full-dose fludarabine based therapy

**5. Hva omfatter metoden** (flere kryss mulig)**?**

| | |
|---|---|
| Legemiddel | ☒ |
| Medisinsk utstyr/teknologi | ☐ |
| Prosedyre | ☐ |
| Screening | ☐ |
| Høyspesialiserte tjenester/nasjonale tilbud | ☐ |
| Organisatorisk oppsett av helsetjenesten | ☐ |
| Annet (beskriv) | ☐ |

"Klikk her og beskriv. Inkluder eventuelt hvem som er ansvarlig for utvikling av metoden"

**6. Metodens bruksområde:**

| | |
|---|---|
| Forebygging | ☒ |
| Utredning og diagnostikk | ☐ |
| Behandling | ☒ |
| Rehabilitering | ☐ |

| | |
|---|---|
| Spesialisthelsetjenesten | ☒ |
| Primærhelsetjenesten | ☐ |

Gazyvaro in this particular indication will not prevent cancer, but will have an impact on cancer progression - increase progression free survival for the patients with rituximab refractory follicular lymphoma

7. **Involverer metoden bruk av stråling** (ioniserende/ikke-ioniserende)**?** ☐

(Kort beskrivelse av type strålekilde, utstyr og stråleeksponering.)

| |
|---|
| |

8. **Hvilke fagområde(r) gjelder metoden, og hvilke pasienter berøres?** (Får metoden evt. også konsekvenser for andre grupper (som personell, pårørende?)

| |
|---|
| Oncology area<br>Follicular lymphoma patients who are refractory to rituximab |

9. **Hvilke aspekter er relevante for vurderingen?** (flere kryss mulig)

| | |
|---|---|
| Klinisk effekt | ☒ |
| Sikkerhet/bivirkninger | ☐ |
| Kostnader/ressursbruk | ☒ |
| Kostnadseffektivitet | ☒ |
| Organisatoriske konsekvenser | ☐ |
| Etiske | ☐ |
| Juridiske | ☐ |

10. **Foreslå hva som bør være hovedproblemstilling(er) for metodevurderingen, samt eventuelle underproblemstillinger** (i samsvar med pkt. 8):

Assessment of the cost-effectiveness and budget impact of the Gazyvaro treatment relative to the treatment it will replace.

**11. Gi en kort begrunnelse for hvorfor det er viktig at metodevurderingen som foreslås bør gjennomføres:**

To investigate if the drug for this indication can be implemented into treatment.

**12. Kommenter metoden som forslås vurdert mht. følgende punkter:**

Alvorlighetsgraden på tilstanden metoden er ment for

Relapsed refractory follicular lymphoma is rare and a very serious disease with poor prognosis. Patients who do not benefit from a rituximab containing regimen have a median progression-free survival of less than one year and although limited treatment options do exist, prognosis remains poor for these hard to treat patients.

Gazyvaro and bendamustine in combination, followed by Gazyvaro maintenance has shown a more than double improvement in progression free survival and clinically meaningful increase in overall survival in patients with relapsed, refractory to rituximab follicular lymphoma compared to bendamustine alone. This is the first time when clear benefit is demonstrated in a robust phase III study in the rituximab refractory follicular lymphoma setting.

Forventet effekt

Summary abstract from L.H. Sehn et al., J Clin Oncol 33, 2015 (suppl; abstr LBA8502)

Data from the Gadolin trial shows, that Gazyvaro combined with bendamustine followed by Gazyvaro maintenance significantly improved progression-free survival vs bendamustine alone (120 mg/m$^2$) in rituximab refractory Non-Hodgkin Lymphoma. Independently assessed risk of progression, relapse or death for patients was reduced by 45% in the Gazyvaro + bendamustine arm (HR 0.55, 95% CI 0.4–0.74; p = 0.00011). Median progression-free survival was more than double (14,9 vs 29,2 months) in the Gazyvaro + bendamustine arm.

Sikkerhet (beskriv kort opplysninger om kjente risikoforhold, sikkerhetsaspekter og bivirkninger)

Summary abstract from L.H. Sehn et al., J Clin Oncol 33, 2015 (suppl; abstr LBA8502)

Overall, similar number of adverse events where reported between treatment arms, although, there were fewer Grade ≥ 3 adverse events with bendamustine (B) than Gazyvaro + bendamustine (GB) (62.1% B vs 68% GB), notably neutropenia (26.3% B vs 33.0% GB) and infusion-related reactions (3.5% B vs 8.8% GB), but more Grade ≥ 3 thrombocytopenia (16.2% B vs 10.8% GB), anemia (10.1% B vs 7.7% GB) and pneumonia (5.6% B vs 2.6% GB).

Totalt antall pasienter i Norge metoden er aktuell for

We assume that there are 10-20 relapsed/refractory patients per year.

Konsekvenser for ressursbruk i helsetjenesten

No impact.

Behov for revisjon av eksisterende nasjonale faglige retningslinjer, evt. utarbeidelse av nye

Yes

13. **Oppgi referanser til dokumentasjon om metodens effekt og sikkerhet (eks. tidligere metodevurderinger).** (Inntil 10 sentrale referanser oppgis. Ikke send vedlegg på dette trinnet i prosessen.)

L.H. Sehn et al., J Clin Oncol 33, 2015 (suppl; abstr LBA8502)

14. **Oppgi navn på produsenter/leverandører vedrørende metoden (dersom aktuelt/tilgjengelig):**

Roche Norge AS

15. **Status for markedsføringstillatelse (MT) eller CE-merking:** (Når forventes MT- eller CE-merking? Eventuelt opplysning om planlagt tidspunkt for markedsføring).

Marketing Authorization is expected in Q3 2016

16. **Fritekstrubrikk** (Supplerende relevant informasjon, inntil 300 ord.)

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