NYE METODER

Anmodning om vurdering av legemiddel i Nye metoder

Skjema for leverandører

En leverandør som ønsker offentlig finansiering av et legemiddel/legemiddelindikasjon i den norske spesialisthelsetjenesten, skal anmode om vurdering i Nye metoder ved å fylle ut dette skjemaet.

Utfylt anmodningsskjema sendes til Nye metoder: nyemetoder@helse-sorost.no

Leverandøren skal på anmodningstidspunktet både ha et forslag til type helseøkonomisk analyse og en plan for når de leverer dokumentasjonen. Merk at dokumentasjon i henhold til oppdraget fra Bestillerforum for nye metoder må leveres inn senest 12 måneder etter anmodningstidspunktet.

Hele anmodningsskjemaet skal fylles ut. Mer informasjon og veiledning finnes i artikkelen For leverandører (nyemetoder.no)

Merk: Skjemaet vil bli publisert i sin helhet på nyemetoder.no.

Innsender er klar over at skjemaet vil bli publisert i sin helhet (må krysses av): ☒

Fyll ut dato for innsending av skjema: 30.07.2026

1 Kontaktopplysninger	
1.1 Leverandør (innehaver/søker av markedsføringstillatelse i Norge)	Orphalan SA, 226 Boulevard Voltaire, 75011 Paris, France. Orphalan SA is the applicant for marketing authorisation for Kizfizo (temozolomide oral suspension, 40 mg/ml). The product entered the group through the acquisition of Orphelia Pharma on 1 December 2025.
1.2 Navn kontaktperson	Robert-Jan van Son
1.3 Stilling kontaktperson	General Manager BeNeLux and Nordics
1.4 Telefon	+31-631787983
1.5 E-post	robert-jan.vanson@orphalan.com
Ekstern representasjon - vedlegg fullmakt	
1.6 Navn/virksomhet	Oslo Economics AS, Christoffer Bugge. The request is submitted on behalf of Orphalan SA under a Power of Attorney. The Power of Attorney is attached.
1.7 Telefon og e-post	Telephone: +47 986 36 221 E-mail: cbu@osloeconomics.no

2 Legemiddelinformasjon og indikasjon	
2.1 Hva gjelder anmodningen? *Kryss av for hva anmodningen gjelder*	Et nytt virkestoff ☐ En indikasjonsutvidelse / ny indikasjon ☐ En ny styrke eller formulering ☒

2.2 Hvilken indikasjon gjelder anmodningen? *Indikasjonen skal oppgis på norsk. Hvis prosess for godkjenning pågår, oppgi også indikasjon på engelsk.* *Merk: Leverandør skal anmode om vurdering av hele indikasjonen som de har fått godkjent eller søker om godkjenning for. Dersom leverandør foreslår en avgrensning til undergrupper, må dette begrunnes og leverandør må levere dokumentasjonen som trengs for å foreta en vurdering av undergruppen i tillegg til dokumentasjonen for hele indikasjonen.*	The request covers the full indication for which marketing authorisation is being sought. Indication in Norwegian (as required by this field): 1) Barn fra ett år til under sju år, samt dysfagiske barn over sju år, ungdom og voksne pasienter med malignt gliom, slik som glioblastoma multiforme eller anaplastisk astrocytom, med residiv eller progresjon etter standardbehandling. 2) Voksne dysfagiske pasienter med nydiagnostisert glioblastoma multiforme, samtidig med strålebehandling og deretter som monoterapi. Indication in English (wording applied for in the ongoing EMA procedure): 1) Children from the age of one year to less than seven years, and dysphagic children above seven years, adolescents and adult patients with malignant glioma, such as glioblastoma multiforme or anaplastic astrocytoma, showing recurrence or progression after standard therapy. 2) Adult dysphagic patients with newly diagnosed glioblastoma multiforme concomitantly with radiotherapy (RT) and subsequently as monotherapy treatment.
2.3 Handelsnavn	Kizfizo. Also referred to during clinical development as Kimozo, Ped-TMZ and ORP-005.
2.4 Generisk navn/virkestoff	Temozolomide
2.5 ATC-kode	L01AX03
2.6 Administrasjonsform og styrke *Oppgi også forventet dosering og behandlingslengde* *Skriv kort*	Oral suspension, 40 mg/ml. Ready to use and taste-masked. Supplied as a kit with a bottle (18 ml) and a dosing syringe graduated to 5 ml in 0.1 ml increments. Can be administered orally or via a nasogastric tube. Dosing follows the established temozolomide regimen. Concomitant phase in newly diagnosed glioblastoma in adults: 75 mg/m2 daily for 42 days concurrently with focal radiotherapy (60 Gy in 30 fractions). Monotherapy phase: from four weeks after the concomitant phase, up to six cycles of 150–200 mg/m2 on days 1–5 of 28-day cycles (150 mg/m2 in cycle 1, increased to 200 mg/m2 if tolerated). In recurrence or progression of malignant glioma: temozolomide monotherapy according to established protocols.
2.7 Farmakoterapeutisk gruppe og virkningsmekanisme.	Antineoplastic agents, other alkylating agents (ATC L01AX03). Temozolomide is a prodrug that converts spontaneously

Skriv kort	at physiological pH to the active compound MTIC (monomethyl triazeno imidazole carboxamide). MTIC methylates DNA, primarily at the O6 and N7 positions of guanine. The resulting damage triggers futile mismatch repair, leading to arrest of cell division and apoptosis. Activity of the repair enzyme MGMT counteracts this effect, and methylation of the MGMT promoter is associated with better response to treatment.

3 Historikk – virkestoff og indikasjon

3.1 Har Nye metoder behandlet metoder med det aktuelle virkestoffet tidligere? *Hvis ja, oppgi ID-nummer til metoden/metodene i Nye metoder*	Ja ☒ Nei ☐ ID-nummer: Temozolomide has not been assessed as a method in its own right within Nye metoder. The active substance forms part of the combination treatment in ID2018_053 and ID2022_119 (tumour treating fields, Optune, in combination with temozolomide in glioblastoma), where temozolomide constitutes the basis for comparison.
3.2 Er du kjent med om andre legemidler/virkestoff er vurdert i Nye metoder til samme indikasjon? *Hvis ja, oppgi ID-nummer til metoden/metodene i Nye metoder*	Ja ☒ Nei ☐ ID-nummer: ID2021_056 (sitoiganap for the treatment of glioma). In addition, methods classified as medical devices have been assessed for the same indication: ID2018_053 and ID2022_119 (tumour treating fields, Optune, in glioblastoma).
3.3 Er du kjent med om det er gjennomført en metodevurdering i et annet land som kan være relevant i norsk sammenheng? *Hvis ja, oppgi referanse*	Ja ☐ Nei ☒ Referanse: The supplier is not aware of any completed health technology assessments of Kizfizo in other countries. The product does not hold marketing authorisation in any country. Kizfizo was granted early access in France in March 2022 (autorisation d'accès précoce), but for relapsed and refractory high-risk neuroblastoma, that is, an indication other than the one covered by this request.

4 Status for markedsføringstillatelse (MT) og markedsføring

4.1 Har legemiddelet MT i Norge for en eller flere indikasjoner? *Hvis ja - skriv inn dato for norsk MT for den første indikasjonen*	Ja ☐ Nei ☒ Dato for MT for første indikasjon: Not applicable

4.2 Markedsføres legemiddelet i Norge?	Ja ☐ Nei ☒
4.3 Har legemiddelet MT i Norge for anmodet indikasjon? *For alle metoder: Fyll ut prosedyrenummer i EMA (det europeiske legemiddelbyrået)* *Hvis metoden ikke har MT i Norge, fyll ut forventet tidspunkt (måned/år) for CHMP opinion i EMA.* *Hvis metoden har MT i Norge, fyll ut dato for MT*	MT i Norge: Ja ☐ Nei ☒ Prosedyrenummer i EMA: To be forwarded.
	Hvis metoden ikke har MT: Forventet tidspunkt for CHMP opinion i EMA (måned/år): January 2027 Forventet tidspunkt for markedsføringstillatelse (MT) for den aktuelle indikasjonen i Norge (måned/år): February 2027
	Hvis metoden har MT: Dato for MT i Norge for den aktuelle indikasjonen: Not applicable
4.4 Har legemiddelet en betinget markedsføringstillatelse for anmodet indikasjon? *Hvis ja, fyll ut en beskrivelse av hva som skal leveres til EMA og når.*	Ja ☐ Nei ☒ Beskrivelse: Not applicable. The application is a hybrid application under Article 10(3) of Directive 2001/83/EC, supported by bioequivalence with the reference product Temodal.
4.5 Har anmodet indikasjon vært i «accelerated assessment» hos EMA?	Ja ☐ Nei ☒
4.6 Har legemiddelet «orphan drug designation» i EMA? *Hvis ja, fyll ut dato*	Ja ☒ Nei ☐ Dato for «orphan drug designation»: 21.08.2019

5 Ordning for forenklet vurdering av PD-(L)1-legemidler

5.1 Er legemiddelet registrert i Nye metoders ordning «Forenklet vurdering av PD-(L)1-legemidler"?	Ja ☐ Nei ☒

6 Sammenlignbarhet og anbud	
6.1 Finnes det andre legemidler med lignende virkningsmekanisme og /eller tilsvarende effekt til den aktuelle indikasjonen?	Ja ☒ Nei ☐ Kommentar: Yes. Temozolomide capsules (Temodal and generics) and temozolomide powder for solution for infusion contain an identical active substance and have the same effect. These are the same medicine in other pharmaceutical forms. For patients who cannot swallow capsules, the current alternatives are to open the capsules and mix the contents into soft food, or to administer temozolomide intravenously. No other ready-to-use, age-appropriate oral formulation holds marketing authorisation.
6.2 Vurderer leverandør at legemiddelet i anmodningen er sammenlignbart med et eller flere andre legemidler som Nye metoder har besluttet å innføre til den samme indikasjonen? *Hvis ja, hvilke(t)? Oppgi ID-nummer på metoden/metodene i Nye metoder*	Ja ☐ Nei ☒ Legemiddel og ID-nummer: No, not in the sense in which the comparability scheme is framed. The scheme applies to medicines that Nye metoder has decided to introduce for the same indication, whereas temozolomide is established standard treatment predating the system and has not been the subject of a decision by Beslutningsforum.
6.3 Er det eksisterende anbud på terapiområdet som kan være aktuelt for legemiddelet?	Ja ☒ Nei ☐ Kommentar: Yes. Temozolomide is included in the oncology tenders run by Sykehusinnkjøp HF, where the capsule formulation is available generically. Kizfizo would fall within the same therapeutic area, but is directed at a defined patient group unable to use the capsule formulation

7 Nordisk samarbeid JNHB (Joint Nordic HTA-bodies)	
7.1 Er anmodet indikasjon aktuell for utredning i det nordiske HTA-samarbeidet JNHB? *Hvis nei, begrunn kort*	Ja ☐ Nei ☒ Begrunnelse: The request concerns a new pharmaceutical form of a well-established active substance, not a new active substance or a new indication. There is no new efficacy documentation to be assessed; the documentation base is pharmacokinetic. The patient

	population in the Nordic countries is also limited. In the supplier's assessment, a joint Nordic assessment would not add value proportionate to the resources required.

8 Europeisk samarbeid om vurdering av relativ effekt og sikkerhet (HTAR)	
8.1 Er anmodet legemiddel/indikasjon omfattet av regelverket for utredning av relativ effekt og sikkerhet i europeisk prosess (HTAR)? *Hvis ja, fyll ut dato for søknad om MT til EMA*	Ja ☐ Nei ☒ Dato for søknad til EMA: Not applicable

9 Helseøkonomisk dokumentasjon og forslag til helseøkonomisk analyse	
9.1 Hvilken type helseøkonomisk analyse foreslår leverandøren? *F.eks. kostnad-per-QALY analyse eller kostnadsminimeringsanalyse.* *Begrunn forslaget*	Cost-minimisation analysis. Rationale: Kizfizo contains the same active substance as the reference product Temodal and has documented bioequivalence with temozolomide capsules in a crossover study in adults (ORP-TMZ-I-a). Where bioequivalence is established, equal clinical efficacy and safety are assumed, and there is neither a basis nor a need to model a difference in effect. The relevant difference between the alternatives lies in the pharmaceutical form, and in the resources required to deliver temozolomide to patients who cannot swallow capsules. Where no age-appropriate liquid formulation is available, capsules must be opened and the contents dispersed before administration. This may generate differences in resource use and in the burden on patients and caregivers, such as cytotoxic handling and administration. These differences do not concern the active substance, which is well established, but whether treatment can be delivered accurately and safely to patients who cannot swallow capsules. We therefore suggest that the commission to DMP covers (i) the population defined by inability to swallow capsules, and (ii) the resource use associated with current preparation and administration practice.

9.2 Pasientpopulasjonen som den helseøkonomiske analysen baseres på, herunder eventuelle undergrupper.	Patients covered by the applied-for indication, that is, patients with malignant glioma (glioblastoma multiforme, anaplastic astrocytoma) who cannot swallow capsules: children from the age of one year to less than seven years, dysphagic children above seven years, and dysphagic adolescents and adults. The analysis covers both the recurrence and progression population and adult dysphagic patients with newly diagnosed glioblastoma treated concomitantly with radiotherapy and subsequently as monotherapy. No separate subgroup analyses are planned beyond a possible split between children and dysphagic adults, since dosing in both cases follows body surface area.
9.3 Hvilken dokumentasjon skal ligge til grunn? (H2H studie, ITC, konstruert komparatorarm etc.) *Angi det som er relevant med tanke på hvilken type analyse som foreslås.*	Bioequivalence study against the reference product (ORP-TMZ-I-a, NCT04467346) as the basis for the assumption of equal efficacy and safety. Population pharmacokinetics, acceptability (CAST) and safety in children from TEMOkids (ORP-TMZ-I-b, NCT04610736). Efficacy documentation for temozolomide in malignant glioma rests on the established evidence base for the reference product, principally EORTC 26981-22981/NCIC CE.3 (Stupp et al. 2005). No indirect treatment comparison or constructed comparator arm is required.
9.4 Forventet legemiddelbudsjett i det året med størst budsjettvirkning i de første fem år.	[TO BE COMPLETED: requires a price assumption from Orphalan.] The estimate is calculated as the number of eligible patients per year multiplied by the medicine cost per patient at the established dosing by body surface area and treatment duration. Given the limited patient population covered by the indication (see section 10.7), the budget impact is expected to be modest, but quantification requires a confirmed price.
9.5 Forventet tidspunkt (måned og år) for levering av dokumentasjon til Direktoratet for medisinske produkter og/eller Sykehusinnkjøp HF. *Tidspunkt må oppgis*	[TO BE COMPLETED/CONFIRMED: month and year.] The supplier is aware that documentation in accordance with a commission from Bestillerforum must be delivered no later than 12 months after the date of the request, and that DMP must be notified of the submission date (week number) no later than three months before submission.

10 Sykdommen og eksisterende behandling	
10.1 Sykdomsbeskrivelse for aktuell indikasjon *Kort beskrivelse av sykdommens patofysiologi og klinisk presentasjon / symptombilde, eventuelt inkl. referanser*	Malignant gliomas are fast-growing, infiltrating tumours arising from glial cells in the central nervous system. Glioblastoma multiforme (CNS WHO grade 4) is the most common and most aggressive form in adults, characterised by marked cell proliferation, microvascular proliferation and necrosis. Anaplastic astrocytoma (grade 3) follows a somewhat less aggressive course. The tumours infiltrate surrounding brain tissue diffusely, so that complete surgical resection is not achievable in practice, and recurrence is the rule. Clinical presentation depends on tumour location and growth pattern, and includes focal neurological deficits, epileptic seizures, cognitive changes and symptoms of raised intracranial pressure such as headache, nausea and vomiting. Diagnosis is made by MRI and confirmed histopathologically, with molecular classification including IDH status and MGMT promoter methylation status. Dysphagia is a frequent symptom throughout the disease course and affects approximately one third of adult glioma patients (IJzerman-Korevaar et al., J Neurooncol 2018;140:485–96), making administration of solid oral dosage forms difficult. In the youngest children, swallowing capsules is not possible in any event.
10.2 Fagområde *Angi hvilket fagområde som best beskriver metoden*	Velg fagområde fra menyen: Kreftsykdommer
10.3 Kreftområde *Hvis metoden gjelder fagområdet Kreftsykdommer, angi hvilket kreftområde som er aktuelt*	Velg kreftområde fra menyen: Kreft i sentralnervesystemet
10.4 Dagens behandling *Nåværende standardbehandling i Norge, inkl. referanse*	Standard treatment for newly diagnosed glioblastoma in adults is maximal surgical resection where feasible, followed by the Stupp regimen: focal radiotherapy 60 Gy in 30 fractions with concomitant temozolomide 75 mg/m2 daily, then up to six cycles of adjuvant temozolomide 150–200 mg/m2 on days 1–5 of 28-day cycles. In recurrence or progression of malignant glioma, temozolomide monotherapy is used.

	Reference: the Norwegian Directorate of Health national action programme with guidelines for the diagnosis, treatment and follow-up of diffuse gliomas in adults. For patients who cannot swallow capsules, that is, the youngest children and dysphagic patients, temozolomide is currently administered by opening the capsules and mixing the contents into soft food, or as intravenous temozolomide. Both approaches have drawbacks: respectively, inaccurate and poorly reproducible dosing together with a risk of cytotoxic exposure for children, parents and healthcare staff, and availability and cost.
10.5 Prognose *Beskriv prognosen med nåværende behandlingstilbud, inkl. referanse*	The prognosis in glioblastoma is serious, and the disease is incurable. In the pivotal study of the Stupp regimen, median overall survival was 14.6 months with radiotherapy plus temozolomide versus 12.1 months with radiotherapy alone, with two-year survival of 26.5 % and 10.4 % respectively (Stupp et al., N Engl J Med 2005;352:987–96). The five-year analysis showed 9.8 % versus 1.9 % surviving (Stupp et al., Lancet Oncol 2009;10:459–66). Patients with a methylated MGMT promoter have a substantially better prognosis than those without. Norwegian registry data show stable glioma incidence and improved survival over the past two decades, but long-term survival in glioblastoma remains very low (Skaga et al., Acta Oncol 2024;63:83–94). Anaplastic astrocytoma carries a somewhat better prognosis, with median survival in the range of three to five years. In recurrence or progression after standard therapy the prognosis is generally poor, and treatment is principally life-prolonging and palliative.
10.6 Det nye legemiddelets innplassering i behandlingsalgoritmen	The oral suspension does not replace temozolomide treatment as such; it is an alternative pharmaceutical form of the same active substance. It comes in addition to the capsule form and is directed specifically at patients who cannot swallow capsules, that is, children from the age of one year to less than seven years and dysphagic patients of any age. In practice it would replace the current unsuitable practice of opening and mixing capsules, and reduce the need for intravenous temozolomide in this group. It

	does not change the treatment algorithm for patients who can swallow capsules.
10.7 Pasientgrunnlag *Beskrivelse, insidens og prevalens av pasienter omfattet av aktuell indikasjon* i Norge, inkl. referanse.* *Antall norske pasienter antatt aktuelle for behandling med legemiddelet til denne indikasjonen.* ** Hele pasientgruppen som omfattes av aktuell indikasjon skal beskrives*	The full patient group covered by the indication comprises patients with malignant glioma who cannot swallow capsules. The estimates below are approximate and should be verified against the Cancer Registry of Norway and the Norwegian Childhood Cancer Registry. The subgroup unable to swallow capsules is not registered separately. Adults with newly diagnosed glioblastoma in Norway: on the order of 300 new cases per year, corresponding to an incidence of approximately 5.3 per 100,000 (Skaga et al., Acta Oncol 2024;63:83–94). The proportion with dysphagia at diagnosis or treatment start is smaller, estimated on the order of 45 patients (cf. Madhavan, LaGorio and Carnaby 2016 on the prevalence of dysphagia). The proportion with dysphagia increases over the disease course and has been estimated at approximately one third of glioma patients overall (IJzerman-Korevaar et al. 2018), so that the number of eligible patients at recurrence or progression is higher than at diagnosis. Malignant glioma in children is rare. The number of children covered by the indication is uncertain, but is estimated at approximately 1–2 per year.

11 Studiekarakteristika for relevante kliniske studier

	Studie 1	Studie 2	Studie 3
11.1 Studie-ID *Studienavn, NCT-nummer, hyperlenke*	ORP-TMZ-I-a (NCT04467346)	TEMOkids (ORP-TMZ-I-b, NCT04610736)	EORTC 26981-22981 / NCIC CE.3 (the Stupp trial)
11.2 Studietype og -design	Phase I, randomised, open-label, multicentre crossover study. Single-dose bioequivalence study.	Phase I, open-label, single-arm multicentre study.	Phase III, randomised, open-label, multicentre study.

11.3 Formål	To demonstrate bioequivalence between temozolomide oral suspension 40 mg/ml and temozolomide capsules (Temodal) in adults.	To investigate the pharmacokinetics (population PK), acceptability and safety of temozolomide oral suspension in children.	To demonstrate the efficacy of temozolomide given concomitantly with and adjuvant to radiotherapy in newly diagnosed glioblastoma. The study constitutes the efficacy basis for the reference product, and thereby for the active substance in this request.
11.4 Populasjon *Viktige inklusjons- og eksklusjonskriterier*	36 adult patients with glioblastoma multiforme or lower-grade glioma, treated with temozolomide 200 mg/m2 as monotherapy. The study was conducted at multiple centres in France under fasting conditions. Note that the bioequivalence study was carried out in a glioma population, that is, the indication covered by this request.	43 patients aged 1–17 years with cancer for which temozolomide is indicated. The study mainly enrolled patients with neuroblastoma and mixed paediatric CNS tumours, with only a small glioma subset. The study therefore supports formulation, pharmacokinetics, acceptability and safety, not efficacy in glioma.	573 adult patients with newly diagnosed, histologically confirmed glioblastoma and WHO performance status 0–2.
11.5 Intervensjon (n) *Dosering, doseringsintervall, behandlingsvarighet*	Temozolomide oral suspension 40 mg/ml, single dose of 200 mg/m2. Crossover design in which each patient received the suspension and capsules on two consecutive days, in randomised order. n = 36.	Temozolomide oral suspension 40 mg/ml dosed by body surface area (mg/m2) according to established temozolomide regimens. n = 43.	Radiotherapy 60 Gy in 30 fractions with concomitant temozolomide 75 mg/m2 daily, followed by up to six cycles of adjuvant temozolomide 150–200 mg/m2 on days 1–5 every 28 days. n = 287.

11.6 Komparator (n) *Dosering, doseringsintervall, behandlingsvarighet*	Temozolomide capsules (Temodal), single dose of 200 mg/m2. Crossover design, that is, the same 36 patients received both formulations on two consecutive days in randomised order. n = 36.	No comparator. Single-arm study, with comparison against established pharmacokinetic data for temozolomide capsules.	Radiotherapy alone, 60 Gy in 30 fractions. n = 286.
11.7 Endepunkter *Primære, sekundære og eksplorative endepunkter, herunder definisjon, målemetode og ev. tidspunkt for måling*	Primary endpoints: AUCt and Cmax for temozolomide. Bioequivalence defined as the 90 % confidence interval for the ratio between formulations falling within 80–125 %. Secondary endpoints: other pharmacokinetic parameters together with safety and tolerability.	Primary: pharmacokinetics, including population PK and exposure measured as AUC. Secondary: acceptability measured using CAST (Chronological Acceptability Score Test) and safety/tolerability, including local tolerability in the oral cavity.	Primary endpoint: overall survival. Secondary endpoints: progression-free survival, safety and health-related quality of life.
11.8 Relevante subgruppeanalyser *Beskrivelse av ev. subgruppeanalyser*	Not applicable.	Analyses by age group. Dosing by body surface area gave comparable exposure down to one year of age with no need for dose adjustment, and acceptability (CAST) was assessed specifically in children aged 1–11 years.	Analyses by MGMT promoter methylation status showed the greatest effect in patients with a methylated promoter (Hegi et al., N Engl J Med 2005;352:997–1003).

11.9 Oppfølgingstid *Hvis pågående studie, angi oppfølgingstid for data som forventes å være tilgjengelige for vurderingen hos Direktoratet for medisinske produkter samt den forventede/planlagte samlede oppfølgingstid for studien*	Completed. Single-dose study with pharmacokinetic sampling; no long-term follow-up.	Completed. Pharmacokinetic sampling was performed during treatment; the study objectives were pharmacokinetics, acceptability and safety, and no long-term efficacy follow-up was planned.	Median follow-up of 28 months in the primary analysis. Five-year follow-up published in 2009.
11.10 Tidsperspektiv resultater *Pågående eller avsluttet studie? Tilgjengelige og fremtidige datakutt*	Completed study. Results are available and published.	Completed study. Results are available, were assessed by the CHMP in assessment report EMA/96948/2025 and were presented at SIOP 2023.	Completed study. Final results are available, including five-year data.
11.11 Publikasjoner *Tittel, forfatter, tidsskrift og årstall. Ev. forventet tidspunkt for publikasjon*	A Multicenter Randomized Bioequivalence Study of a Novel Ready-to-Use Temozolomide Oral Suspension vs. Temozolomide Capsules. Pharmaceutics 2023;15(12):2664.	Results presented at the 55th SIOP Annual Congress, Ottawa, October 2023, and assessed in the CHMP assessment report EMA/96948/2025. [TO BE COMPLETED: any peer-reviewed publication.]	Stupp R, et al. Radiotherapy plus concomitant and adjuvant temozolomide for glioblastoma. N Engl J Med 2005;352:987–96. Stupp R, et al. Effects of radiotherapy with concomitant and adjuvant temozolomide versus radiotherapy alone on survival in glioblastoma in a randomised phase III study: 5-year analysis of the EORTC-NCIC trial. Lancet Oncol 2009;10:459–66.

12 Igangsatte og planlagte studier

12.1 Er det pågående eller planlagte studier for legemiddelet innenfor samme indikasjon som kan gi ytterligere informasjon i fremtiden?	Ja ☐ Nei ☒

Hvis ja, oppgi forventet tidspunkt	No ongoing or planned clinical studies with Kizfizo within the requested indication are known to the submitter at the time of this request. The documentation package rests on bioequivalence with the reference product and on the established evidence base for temozolomide in malignant glioma.
12.2 Er det pågående eller planlagte studier for legemiddelet for andre indikasjoner?	Ja ☒ Nei ☐ Kizfizo was developed for relapsed and refractory high-risk neuroblastoma, and has been available in France through the early access scheme (autorisation d'accès précoce) for that indication since March 2022. Efficacy and safety data for temozolomide in neuroblastoma include BEACON-Chemo and RETRO-TMZ.

13 Diagnostikk

13.1 Vil bruk av legemiddelet til anmodet indikasjon kreve diagnostisk test for analyse av biomarkør? *Hvis ja, fyll ut de neste spørsmålene*	Ja ☐ Nei ☒
13.2 Er testen etablert i klinisk praksis? *Hvis ja, testes pasientene rutinemessig i dag?*	Ja ☐ Nei ☐ Hvis ja, testes pasientene rutinemessig i dag? Ja ☐ Nei ☐
13.3 Hvis det er behov for en test som ikke er etablert i klinisk praksis, beskriv behovet inkludert antatte kostnader/ressursbruk	Not applicable. Diagnosis of glioblastoma and malignant glioma follows established practice with imaging and histopathology. MGMT promoter methylation status already forms part of the current work-up and is not a precondition for the use of this pharmaceutical form. Identifying patients unable to swallow capsules is a clinical assessment, not a test.

14 Andre relevante opplysninger

14.1 Har dere vært i kontakt med fagpersoner (for eksempel klinikere) ved norske helseforetak om dette legemiddelet/indikasjonen?	Ja ☐ Nei ☒ Klikk eller trykk her for å skrive inn tekst.

Hvis ja, hvem har dere vært i kontakt med og hva har de bidratt med? *(Relevant informasjon i forbindelse med rekruttering av fageksperter i Nye metoder)*	
14.2 Anser leverandør at det kan være spesielle forhold ved dette legemiddelet som gjør at en innkjøpsavtale ikke kan basere seg på flat rabatt for at legemiddelet skal kunne oppfylle prioriteringskriteriene? *Hvis ja, begrunn kort.* *Hvis ja, skal eget skjema fylles ut og sendes til Sykehusinnkjøp HF samtidig med at dokumentasjon til metodevurdering sendes til Direktoratet for medisinske produkter.* *Nærmere informasjon og skjema:* Informasjon og opplæring - Sykehusinnkjøp HF	Ja ☐ Nei ☒ No. The product is a new pharmaceutical form of a well-established active substance, and pricing is expected to be manageable within ordinary arrangements.
14.3 Andre relevante opplysninger?	Regulatory history The EMA refused marketing authorisation for Kizfizo in November 2024, confirmed after re-examination on 27 February 2025 (EMA/77307/2025, procedure EMEA/H/C/006169). That application concerned relapsed and refractory high-risk neuroblastoma, and the refusal was based on insufficient efficacy documentation in neuroblastoma. Pharmaceutical quality, the formulation and bioequivalence with the reference product were accepted by the CHMP. A new marketing authorisation application, for malignant glioma, has been accepted for review by the EMA with the formal procedure commencing on 22 January 2026. In malignant glioma the efficacy of temozolomide is already established through the reference product, so the uncertainty underlying the refusal in the neuroblastoma case does not apply in the same way. Orphan drug designation (section 4.6) Kizfizo holds orphan drug designation EU/3/19/2188, granted on 21 August 2019. The designation covers neuroblastoma, not the indication covered by this request. European cooperation, HTAR (section 8.1) The application is a hybrid application under Article 10(3) of Directive 2001/83/EC and concerns a known active substance, not a new active substance. The

	supplier therefore assumes that the product does not fall within the scope of the Joint Clinical Assessment (JCA) requirement under the European HTAR process. [TO BE CONFIRMED.] Scope of any commission The target population is defined by an inability to swallow capsules rather than by age, and includes dysphagic adults in addition to the youngest children. A commission from Bestillerforum should therefore not be limited to the paediatric population alone. Earlier submission The case was originally submitted using the proposal form (forslagsskjema). This request replaces that proposal. Representation and interests Oslo Economics AS submits this request on behalf of Orphalan SA under a Power of Attorney, and has a commercial consultancy relationship with the company. Should a health technology assessment be commissioned, it is likely that Oslo Economics would prepare the documentation.

Informasjon om Nye metoder finnes på nettsiden nyemetoder.no