Vurdering av byttbarhet – Abasaglar og Lantus

Preparat (biotilsvarende og referanse) (Fra SPC):	Biotilsvarende: **Abasaglar** • KwikPen injeksjonsvæske, oppløsning i ferdigfylt penn Hver penn inneholder 3 ml injeksjonsvæske, som tilsvarer 300 enheter insulin glargin. Styrke: 100 enheter/ml MT innehaver: Eli Lilly Referanseprodukt: **Lantus** • Injeksjonsvæske, oppløsning i ferdigfylt penn Hver penn inneholder 3 ml injeksjonsvæske, som tilsvarer 300 enheter insulin glargin. Styrke: 100 enheter/ml MT innehaver: Sanofi-Aventis	
Kommentar	Byttegruppen anser administrasjonsutstyret som likeverdig.	
Virkestoff (Fra EPAR – European Public Assessment Report):	**Insulin glargin** "Insulin glargin is a long-acting insulin analogue administered as a subcutaneous injection for the treatment of type 1 and type 2 diabetes mellitus.	
Kommentar produksjon	Både Abasaglar og referanselegemidlet Lantus er produsert i E. coli.	
ATC-kode	A10A B04	
Søkegrunnlag	10(4) biotilsvarende	
Kvalitativ sammensetning (Fra SPC):	Biotilsvarende: **Abasaglar** Sinkoksid Metakresol Glyserol Saltsyre (for pH-regulering) Natriumhydroksid (for pH-regulering) Vann til injeksjonsvæsker	Referanse: **Lantus**, Sinkklorid Metakresol Glyserol Natriumhydroksid (til pH-justering) Saltsyre (til pH-justering) Vann til injeksjonsvæsker
Indikasjon (Fra SPC):	Behandling av diabetes mellitus hos voksne, ungdom og barn fra 2 år og eldre.	
Biotilsvarende vurdering av kvalitet og biologisk funksjon (fra EPAR):	"Physicochemical and biological aspects relevant to the uniform clinical performance of the product have been investigated and are controlled in a satisfactory way. Overall, comparability between LY2963016* and the reference medicinal product Lantus, approved in the EU, has been satisfactorily demonstrated from the quality perspective." *Abasaglar	
Biotilsvarende vurdering av klinikk (PK (farmakokinetikk), PD (farmakodynamikk), effekt og sikkerhet) (fra EPAR):	"PK and PD (clamp studies) equivalence of Abasaglar and Lantus has been established based on an extensive comparability exercise performed in five studies, which tested several dose levels and were conducted in healthy volunteers as well as patients with type 1 diabetes.	

	For the purpose of the clinical biosimilarity exercise for biosimilar insulin products, the CHMP is of the view that the evaluation of HBA1c is not a sensitive endpoint and therefore efficacy studies evaluating HBA1c are not generally anticipated (EMEA/CHMP/BMWP/32775/2005). However, the applicant has conducted two phase III non-inferiority studies comparing the test and reference product in order to investigate how PK/PD features of the biosimilar product translate into clinical parameters relevant for the management of patients with Type 1 and 2 DM. Furthermore, both efficacy studies provide the safety and immunogenicity datasets that are still required by the CHMP guideline. Two clinical studies conducted in patients with type 1 and 2 diabetes demonstrated that Abasaglar is non-inferior to Lantus in achieving HBA1c at week 24 and therefore provided strong supportive evidence about the comparability of the two products. The safety profile of Abasaglar has been well characterised in the context of the biosimilarity exercise. It appeared comparable to the safety profile of Lantus in the clinical studies and in line with the profile established and documented with the reference product. There were no major safety findings or signals identified in the clinical program."
Vurdering av immunogenisitet (fra EPAR):	"The proportion of patients with detectable antibodies was comparable throughout both studies, with the exception of a significant overall difference in the subgroup of patients with T2DM that were previously treated with Lantus (pre-existing antibodies). The median antibody levels remained low throughout both studies, with no significant differences between treatment arms regardless of previous insulin treatment. Furthermore, extensive immunogenicity evaluation in two large studies, which covered both types of diabetic population, showed that the antibody profiles of Abasaglar and Lantus were comparable."
Totalvurdering (fra EPAR, benefit/risk)	"For a biosimilar, the benefit-risk balance is based on the totality of evidence collected from the quality, non-clinical, and clinical comparability exercise. Minor quality differences are expected to be observed between a biosimilar and its reference product; they are acceptable as long as they do not impact on efficacy and safety. All major physicochemical characteristics and biological activities of Abasaglar were shown to be comparable to those of Lantus, with only small differences observed which are attributed to the presence of low levels of citrate in Lantus. Furthermore, an extensive clinical programme, including five PK/PD studies and two efficacy/safety studies, did not reveal any relevant difference between Abasaglar and Lantus. Several PK/PD studies, which are considered the cornerstone of the clinical comparability exercise for insulin analogues, have established equivalence between the PK and PD profiles of Abasaglar and Lantus.

	In addition, two clinical studies conducted in patients with both types of diabetes mellitus have confirmed that the efficacy, safety and immunogenicity profiles of the two products were comparable. Based on the CHMP review of data on quality, safety and efficacy, the CHMP considers by consensus that the risk-benefit balance of Abasaglar in the treatment of diabetes mellitus in adults, adolescents and children aged 2 years and above is favourable and therefore recommends the granting of the marketing authorization."
Opptak på byttelisten i henhold til retningslinjene	Abasaglar er vurdert av EMA til å være biotilsvarende med Lantus. Komparabilitets- og funksjonelle analyser viser at insulin glargin fra Abasaglar og Lantus er meget like både mht. kvalitet, biologisk funksjon og klinikk, og de små forskjellene som er påvist, er vurdert til ikke å ha noen betydning verken for effekt, sikkerhet eller immunogenisitet. Kommentarer om administrasjonsutstyret: De ferdigfylte pennene vurdert som likeverdige av Byttegruppen. Lege kan reservere pasienten mot bytte dersom det er individuelle medisinske forhold knyttet til pasientens situasjon som taler mot bytte. **Konklusjon:** Legemiddelverket anbefaler opptak på byttelisten.