From: **KPUR (Katrina Purcell)** kpur@novonordisk.com
Subject: CAS-154602-G9G8 Medical Information Request - Novo Nordisk - Saxenda
Date: 26 February 2019 at 9:42 am
To: Harsha Chandraratna drchandra@westnet.com.au
Cc: AUNR CCC aunrccc@novonordisk.com

Dear Dr Harsha Chandraratna,

Thank you for your medical information request for information on the use of Saxenda® have not been established in pediatric patients.[1] Saxenda® is not recommended for use in pediatric patients.

Phase 1 Pharmacokinetic Studies

Novo Nordisk has conducted two randomized, double-blind, placebo-controlled clinical pharmacology trials to assess the safety, tolerability, and pharmacokinetic/pharmacodynamic (PK/PD) profile of Saxenda® in both pediatric patients (ages 7 to 11 years; Mastrandrea *et al*) and adolescent patients (ages 12 to 17 years; Danne *et al*).[2,3]

***Mastrandrea et al*[3]**

- Twenty-four children were randomized to Saxenda® (n=16) or placebo (n=8) for at least 7 weeks (6 optional treatment weeks). Saxenda® was initiated at 0.3 mg and titrated weekly in 0.3 mg increments to 1.2 mg, titration above 1.2 mg occurred in weekly 0.6 mg increments to the targeted dose of 3 mg.
- The primary endpoint was the number of adverse events from the time of first dosing until completion of the follow-up visit in all children who received at least one dose of trial product.
- Five hypoglycemic episodes in 4 patients treated with Saxenda® and 1 episode in a patient on placebo were reported. Frequencies of adverse events overall was similar between Saxenda® and placebo treatment groups.
- The PK results for Saxenda® in children compared to adolescents or adults demonstrated similar dose-proportionality, apparent clearance (CL/F), $AUC_{0\text{-}24h}$ at steady state, and exposure (C_{avg}) when adjusted for body weight differences.
    - Saxenda® C_{avg} and $AUC_{0\text{-}24h}$ were both higher and CL/F was lower in children compared to adolescent and adult populations prior to adjusting for body weight.
- The PD results for children randomized to Saxenda® compared to placebo demonstrated reductions in BMI Z-score of -0.28 (95% CI: -0.47;-0.09), decreases in body weight of
  -3.3 lbs (95% CI: -7.79;1.19), and a minor reduction in fasting plasma glucose (FPG).
    - No differences were observed in serum insulin levels or HbA_{1c} between treatment groups.

***Danne et al*[2]**

- Twenty-one adolescents were randomized to Saxenda® (n=14) or placebo (n=7) for 5 weeks. Saxenda® was initiated at 0.6 mg and titrated to the targeted dose of 3 mg in weekly increments of 0.6 mg.
- The concentration-time profile of Saxenda® in adolescents was similar to that seen

in adults.

- Liraglutide exposure was slightly higher in adolescents than adults with an estimated ratio of 1.10 (90% CI: 0.93;1.31)
- Liraglutide exposure was 23% lower in male patients than female patients, and was reduced with increasing body weight

- The most common adverse events associated with Saxenda® were gastrointestinal disorders (i.e. abdominal pain, nausea, vomiting and diarrhea).
- Twelve hypoglycemic episodes in 8 patients treated with Saxenda® and 2 episodes in a patient on placebo were reported.

Additionally, there are two relevant clinical trials listed on clinicaltrials.gov. Information pertaining to those studies can be found in **Table 1**. Please refer to www.clinicaltrials.gov for more information.

Table 1: Saxenda® Clinical Trials on ClinicalTrials.gov in Pediatric Patients

Title	Age (years)	Total Patients (N)	Status*	ClinicalTrials.gov Identifier
Effect of Liraglutide for Weight Management in Pubertal Adolescent Subjects With Obesity	12-17	~228	Active, not recruiting	NCT02918279
Effect of Liraglutide for Weight Management in Paediatric Subjects With Prader-Willi Syndrome	6-18	~60	Recruiting	NCT02527200

*Status as of December 19, 2018

The above information is supplied to you as a professional service in response to your specific request. This letter is meant to supplement information you may have gathered from other sources.

Please let me know if you have any further questions,

Kindest regards,

Katrina

References

1. Saxenda® Product Information, Australia.
2. Danne T, Biester T, Kapitzke K, et al. Liraglutide in an Adolescent Population with Obesity: A Randomized, Double-Blind, Placebo-Controlled 5-Week Trial to Assess Safety, Tolerability, and Pharmacokinetics of Liraglutide in Adolescents Aged 12-17 Years. *J Pediatr.* 2016
3. Mastrandrea LD, Witten L, Carlsson Petri KC, et al. Liraglutide effects in a paediatric (7-11 y) population with obesity: A randomized, double-blind, placebo-controlled, short-term trial to assess safety, tolerability, pharmacokinetics, and pharmacodynamics. *Pediatr Obes.* 2019:e12495.

Katrina Purcell PhD
Medical Advisor

Novo Nordisk Pharmaceuticals Pty. Ltd.
Level 3

Level 3
21 Solent Circuit
Baulkham Hills NSW 2153
+61 2 8858 3600 (switchboard)

+61 2 8858 3749 (direct)
+61 417 201 541 (mobile)
kpur@novonordisk.com
www.novonordisk.com.au