EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

21 February 2013
EMA/116843/2013

Agenda and list of questions for the workshop on paediatric investigation plans in Type 2 Diabetes Mellitus

25 February 2013, at EMA London, room 4B; 08:30 to 17:30 UK time

Objectives:

1. Identifying elements for agreeing Paediatric Investigation Plans (PIP) in Type 2 Diabetes Mellitus (T2DM) in line with good clinical practice and delivering conclusive outcomes.
2. Identifying elements to facilitate trial recruitment; approaches to enhance feasibility of paediatric T2DM trials.

Chair: David Dunger

Co-chairs: Carine de Beaufort and Janina Karres

Topic	Topic leader	Time
Registration		08:15
Welcome and introduction	David Dunger / Janina Karres	08:30-08:45
Problem statement. T2DM PIP overview – number, stage of development, number of modifications Meeting objectives	Janina Karres	08:45-09:00
Prevalence of paediatric Type 2 Diabetes and current therapeutic approaches • Current guidelines • Europe • US	Carine de Beaufort / David Dunger / William Tamborlane	09:00-10:00
Key elements in current T2DM PIPs.	Janina Karres	10:00-10:15
Trial recruitment issues- a company perspective.	Philip Ambery / Pamela Zee	10:15-10:30
Coffee break		10’
Questions related to randomized placebo controlled paediatric trials with new investigational medicinal products for T2DM- Part I: **Patient population**	Janina Karres / Carine de Beaufort	10:45-13:15

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Topic	Topic leader	Time
1. Do you consider inclusion of treatment naïve patients feasible and compatible with good clinical practice? 2.a Do you consider inclusion of paediatric patients on stable insulin background therapy (without additional metformin background therapy) feasible and compatible with good clinical practise? 2.b Is there a potential need for triple pharmacotherapy (novel glucose lowering agent on top of metformin and insulin) in children to achieve glycaemic control? 3. Depending on the duration of prior insulin therapy, how long should a wash out period at least be before including paediatric patients, weaned off insulin prior to inclusion, into a trial? 4. Which minimum and maximum HbA1c levels do you deem adequate for pharmacotherapy naïve patients, patients on metformin or on combined metformin/insulin treatment? **Trial duration** 5. Should a paediatric study demonstrate sustainability of treatment effect or rather proof similar size of treatment effect as in adults? 6. What study duration (placebo controlled phase) could provide information on the sustainability of glucose lowering effects in children (3, 6 or 12 months, longer)? 7. Is it ethically justified to have a placebo controlled trial period of more than 3 or 6 or 12 months within paediatric T2DM studies if children with HbA1c up to 11% are included (naïve and metformin or insulin treated patients)?		
Lunch break		13:15-13:45
Questions related to randomised placebo controlled paediatric trials with new investigational medicinal products for T2DM- Part II: **Endpoints** 8. Which primary and key secondary endpoints do you consider most appropriate for a paediatric T2DM trial (HbA1c, FPG, other)? 9. What is considered a minimally important clinical difference in terms of glucose lowering properties (% HbA1c lowering) of an investigational glucose lowering agent? Can we define responder criteria? 10. If a glucose lowering agent has a potential effect on beta cell preservation, which endpoints, study duration, laboratory test parameters and patient population would you consider most appropriate?	Janina Karres / Carine de Beaufort	13:45-14:30

Topic	Topic leader	Time
Discussion on Enpr-EMA Diabetes/Endocrinology Network Establishing a European Network Questions: A. Would you be interested in supporting/participating in a European paediatric/endocrine research network? B. Which data are captured/available from current European diabetes registries? C. Could current European diabetes registries be used by a European paediatric/endocrine research network to capture patient outcome data and deliver long term surveillance of safety/efficacy around new glucose lowering drugs? D. Do specialised study centres have access to all potentially eligible paediatric T2DM patients?	 David Dunger / Peter Helms	14:30-15:15
Questions on innovative clinical trial approaches Innovative clinical trial approaches Multi-arm trial design Meta-analysis Quantitative Extrapolation in Type 2 Diabetes Mellitus in Paediatrics **Study designs** 11. In light of limited patient population, is a multi-company, multi-agent, academic led, pharma funded, CRO managed study considered feasible (comparison of several agents in the same class (Gliptin, GLP-1 analogues etc.) with one control group)? 12. In light of limited patient population, do you consider cross-over designs potentially appropriate for paediatric trials with investigational glucose lowering agents?	David Dunger / James Wason / Jack Bowden Ron Portman	15:15-16:30
Conclusions and next steps • Have we met our meeting objectives? • List of research topics that will help address our current knowledge gaps.	Paolo Tomasi	16:30-17:30

List of Participants

Participants

Agnes Gyurasics (Hungary, PDCO and CHMP member)

Alan Kerr (France, Sanofi)

Carine De Beaufort (Luxembourg, PDCO member)

Daniel Brasseur (Belgium, PDCO chair)

David Dunger (UK, University of Cambridge Metabolic Research Laboratories)

Douglas Lee (UK, Takeda)

Hanne Brokopp (Belgium, Merck Sharp & Dohme)

Henrik Mortensen (Denmark, Glostrup University Hospital),

Jack Bowden (UK, MRC Biostatistics Unit)

Jacqueline Carleer (Belgium, PDCO member)

James Wason (UK, MRC Biostatistics Unit)

Kolbeinn Gudmunsson (Iceland, CHMP)

Lieke Kusters (Switzerland, Hoffmann-La Roche)

Lilia Marinova (US, Pfizer)

Lori Laffel (US, Harvard Medical School)

Luis Castaño (Spain, Hospital Cruces)

Mark Turner (UK, University of Liverpool)

Nanette Schloot (Germany, Lilly)

Pamela Zee (US, AstraZeneca/Bristol-Myers Squibb)

Paula Hale (US, Novo Nordisk)

Peter Helms (UK, Enpr-EMA chair)

Philip Ambery (UK, GSK)

Przemyslawa Jarosz-Chobot (Poland, Medical University Katowice)

Ronald Portman (US, Bristol-Myers Squibb)

Stefan Kaspers (Germany, Boehringer Ingelheim)

Susan Sandler (UK, PAREXEL)

Thomas Pieber (Austria, Medical University Graz)

Timothy Barret (UK, Birmingham Children's Hospital)

Wieland Kiess (Germany, University Leipzig)

Will Treem (US, Janssen)

William Tamborlane (US, Yale Center for Clinical Investigation)

Barbara Njie (Canada, Health Canada)

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