



This presentation is intended to facilitate continuing medical education.

The views expressed in this presentation are those of the presenter and do not necessarily reflect the views of Sanofi.

Sanofi does not recommend the use of its products in any manner inconsistent with that described in the local package insert.

Before using any product mentioned here-in please refer to the full local prescribing information.



Mucopolysaccharidosis II: A South African Case Study

DR GJM WOLMARANS

28 FEBRUARY 2015

Patient T.R.

- ▶ 4 years 3 months old boy
- ▶ Only child
- ▶ Known to me since 2011
- ▶ Family history:
 - ▶ Father – Burkitt lymphoma
- ▶ Past medical history:
 - ▶ 2011: Admission - # Gastroenteritis
 - ▶ 2011: Admission - # Severe upper respiratory tract infection with vomiting
 - ▶ 2011: # Mitral valve regurgitation secondary to mitral valve prolapse
 - ▶ 2013: Admission - # Bronchopneumonia
 - ▶ 2013: # Mucopolysaccharidosis II (Hunter syndrome) – enzyme studies, confirmed with 2 subsequent PCR tests

Medication

- ▶ Started in October 2014
- ▶ Portocath 1st week of December 2014
- ▶ Allergic reaction on 14 January 2015

Signs and symptoms

- ▶ Growth:
 - ▶ Currently on 50th centile
- ▶ Performance:
 - ▶ Hyperactive
- ▶ Craniofacial:
 - ▶ Coarsening of facial features
 - ▶ Full lips
 - ▶ Macrocephaly
- ▶ Joints and skeletal:
 - ▶ Stiff partial contracture of joints
 - ▶ Claw hand
 - ▶ Short neck
- ▶ Neurological / Development:
 - ▶ Speech delay
- ▶ Other:
 - ▶ PSM over apex
 - ▶ Umbilical hernia



Figure 2 - MPS patient: Type II (5y).

Diagnosis: Screening

Parameter	Result	Reference range	
Lysosomal Enzymes from Dried Blood			
alpha-Iduronidase (MSMS)	1198.87	350 - 2614	pmol/spot*20h
iduronate-2-sulfatase	0	– 0,02 - 0,25	nmol/spot*21h
Arylsulfatase B	0.26	0,14 - 0,7	nmol/spot*21h
beta-galactosidase	0.69	0,5 - 3,2	nmol/spot*21h



Evaluation

Dear colleague,

the activity of iduronate-2-sulfatase is below its reference range. This may be in agreement with an MPS II and confirms the previous findings. We recommend a molecular genetic assay for final confirmation.

The other enzyme activities above are within their respective reference ranges. Thus, there is no indication of MPS I and MPS VI.

If you have any questions feel free to contact us anytime.

A handwritten signature in black ink.

Diagnosis: Confirmation

<i>Indication:</i>	MPS II	Sample material: Dried blood spot
<i>Methods:</i>	DNA extraction, PCR and sequencing of exons 1, 2, 4, 6-9 and flanking intronic regions. Official symbol: IDS Gene ID: 3423 Reference sequence: ENST00000340855 (ENST00000247933)	
<i>Result:</i>	The following mutation was detected: c.[1509G>A] (p.[Trp502*])	
<i>Interpretation:</i>	The c.1509G>A results in a nonsense mutation (premature stop) and confirms MPS II in your patient.	

MPS II in South Africa: Reality?

- ▶ Patient
- ▶ Parents
- ▶ Diagnosis
- ▶ Treatment
- ▶ Medicine Control Council
- ▶ Medical Aids
- ▶ Follow-up
- ▶ Relationship between Pharmaceutical companies and clinicians

Patient

- ▶ Early onset of signs
- ▶ Difficult diagnosis
- ▶ Rare condition
- ▶ Complications or co-existing conditions
- ▶ Side effects of treatment
- ▶ Prevention of progression
- ▶ Death before 15 years

Parents

- ▶ Denial
- ▶ Counselling
- ▶ Parent discussions
- ▶ Lifestyle changes
- ▶ Impact on employment
- ▶ Support structure

Diagnosis

- ▶ Expense
- ▶ Acceptance of diagnosis
- ▶ Delay between diagnosis and start of treatment

Treatment

- ▶ Idursulfase 0.5 mg/kg per week
- ▶ Weekly infusion
- ▶ Permanent port for infusion
- ▶ Bone marrow transplant
- ▶ Risk of anaphylaxis
- ▶ International Guidelines helpful
- ▶ Expensive

Medicine Control Council

- ▶ Forms (16 pages)
- ▶ Reapply every 6 months
- ▶ Progress report every 6 months
- ▶ Fee with every application
- ▶ Quick response





health

Department:
Health
REPUBLIC OF SOUTH AFRICA

MEDICINES CONTROL COUNCIL
The Registrar of Medicines, Private Bag X828, PRETORIA, 0001

Tel:
Fax:

Enquiries:
Reference:

FAX AND MAIL
TO:

Dr GJM Wolmarans
Akasia Medical Centre
P O Box 14739
Sinoville

0129

Fax: 0125490953

Dear Dr Wolmarans,

REQUEST TO USE UNREGISTERED MEDICINE IN TERMS OF SECTION 21 OF THE MEDICINES AND RELATED SUBSTANCES CONTROL ACT, 1965 (ACT 101 OF 1965):

Your application 13 Feb 2015 refers

- A. STATUS: Approved.
B. APPLICANT: Dr GJM Wolmarans
C. IMPORTING COMPANY: Sanofi-aventis South Africa (Pty) Ltd
D. PATIENT(S): [REDACTED]
E. UNREGISTERED MEDICINES:
GENERIC NAME: idursulfase
TRADE NAME: [REDACTED]
QUANTITY: 10-18 vials per month x 6 months
F. APPROVAL NUMBER: N2/19/9/1 [REDACTED] 05/07/2015

We acknowledge receipt as proof of payment.

PROGRESS REPORTS

Both the supplier and the Medicines Control Council should receive a full Progress Report at the time of termination of treatment (31 July 2015). In the case of long term treatment a follow-up report must be submitted every six months. A new authorisation number must be obtained every six months

Yours faithfully,

Dr S Munbodh
for and on behalf of REGISTRAR OF MEDICINES

MISS BOITUMELO MAHLANGU

ELAPRASE
05/07/2015

Datum - Date

23 February 2015

Tel: 0123958196
Fax: 0862743073

Please include this letter with any future correspondence to our offices to facilitate efficient processing of your documentation

MCC SECTION 21 REFERENCE NO: S150213/30

Medical Aids

- ▶ Applications for:
 - ▶ Chronic medicine
 - ▶ Prescribed Minimum Benefits (PMB)
- ▶ Approval takes a long time
- ▶ Contact person
- ▶ Involvement of the Rare Diseases Society

Follow-up

- ▶ Medication
- ▶ Pathology
- ▶ Radiology
- ▶ Other specialities and associated health services

Follow-up: Medication

- ▶ Weekly infusions = 52 per year
- ▶ Requirements:
 - ▶ 2 vials of Idursulfase
 - ▶ 0.9% Saline 100 ml
 - ▶ Jelco Catheter
 - ▶ Syringes and Needles
 - ▶ Infusion set
- ▶ Apply for everything separately as part of PMB
- ▶ Home infusions / Infusion Centres / In-hospital

Follow-up

Pathology

- ▶ Urinary GAGs – twice a year

Radiology

- ▶ Abdominal ultrasound – twice a year
- ▶ X-ray: Pelvis, lateral spine and neck – twice a year
- ▶ Echocardiogram – twice a year
- ▶ MRI Craniocervical junction (if radiological changes on X-ray) – once a year

Follow-up: Other specialities and associated health services

- ▶ Paediatrician – twice a year
- ▶ Paediatric Neurologist – twice a year
- ▶ Paediatric Pulmonologist – twice a year
- ▶ Ophthalmologist – twice a year
- ▶ Paediatric Cardiologist – twice a year
- ▶ Apnoea / Hypopnoea index – once a year
- ▶ Sleep study – once a year
- ▶ Audiology – once a year

Relationship between Pharmaceutical Companies and clinicians

- ▶ Information regarding these rare diseases
- ▶ Measurements
- ▶ Section 21 applications
- ▶ Screening and confirmation testing
- ▶ Support
- ▶ Contact with Medical Aids



Thank you!