**Nusinersen (Spinraza®) for the treatment of 5q Spinal Muscular Atrophy**

Package advice of the *Zorginstituut Nederland* (National Health Care Institute, the Netherlands) dated 7 February 2018

*Zorginstituut Nederland* carried out an assessment on the medicinal product nusinersen (Spinraza®), whereby they came to the following conclusion.

*Zorginstituut Nederland* has completed its assessment of nusinersen (Spinraza®) for the treatment of 5q spinal muscular atrophy (SMA). This is a summary of the advice of the *Zorginstituut*, as sent to the Ministry of Health, Welfare and Sport (VWS), on including nusinersen in the basic package, and the considerations on which our advice is based. In addition, we also discuss the lack of societal accountability of manufacturers, which is seriously hampering our assessment of orphan drugs such as nusinersen.

**Package advice on nusinersen (conclusion)**
Nusinersen is an orphan drug that underwent the accelerated assessment programme of the EMA for the treatment of 5q spinal muscular atrophy (SMA), a rare, inherited, progressive muscular disease. No alternative treatment for SMA currently exists other than symptomatic treatment and compensating the loss of functions. Roughly speaking, four types of SMA can be differentiated, based on the appearance of the first symptoms and motor milestones that have been reached. The younger a person is when the first symptoms occur, the more severe will be the course of the disease.

The *Zorginstituut* assessed nusinersen based on the four package criteria: effectiveness, cost-effectiveness, necessity and feasibility. The assessment shows that the drug is effective (i.e. complies with established medical science and medical practice) for three groups of patients:

- SMA with *infantile-onset (symptom onset before 6 months of age)* whose disease was diagnosed less than 26 weeks before the start of treatment.
- SMA with *later childhood-onset (symptom onset 6-20 months of age)* in children who were diagnosed no more than 94 months before the start of treatment.
- *pre-symptomatic infants* genetically diagnosed with 5q spinal muscular atrophy and with 2 or 3 SMN2-copies.

Nusinersen is not cost-effective. The *Zorginstituut*'s estimate of the cost-effectiveness (ICER) for use in the three groups of patients on whom the product is effective far exceeds the relevant reference value of €80,000 per high-quality life-year gained (QALY). The *Zorginstituut* estimated the ICER for type 1 SMA patients at about €600,000 per QALY and for type 2/3a patients at about €1,700,000 per QALY.

Based on the above-mentioned groups of patients, in 2020 the additional costs of including nusinersen in the package would amount to €30.1 million in total. This took into account the costs of administering nusinersen via a lumbar puncture**.**

Based on the assessment, the *Zorginstituut* advises the Ministry of VWS not to include nusinersen in the insured package as addition to best supportive care, unless the cost-effectiveness of this treatment can be improved, and its impact on

the care budget reduced by means of price negotiation. The price of nusinersen would have to be reduced by at least 85% in order for it to be considered cost-effective.
We should point out that uncertainty exists about the effectiveness of nusinersen in the long term for the groups for which we conclude that the product complies with established medical science and medical practice. For this reason we advise the Ministry of VWS to investigate whether a *pay-for-performance* arrangement can be concluded with the manufacturer. Under this type of arrangement, the medicine will only be reimbursed if it is actually effective for patients. In relation to this, we should comment that further elaboration of this must not be allowed to delay decision-making on the reimbursement and availability for patients.

If price negotiations lead to inclusion in the basic insurance, the *Zorginstituut* will conclude an orphan drug arrangement that records agreements on appropriate use (e.g. start and stop criteria and, if possible, a European register for monitoring the effect on Quality of life). Furthermore, the *Zorginstituut* will actively monitor its use and costs in the orphan drugs monitor. Initiatives of the SMA centre of expertise for appropriate use offer good leads in this respect. This is to support the policy of the government and health care insurers, and to promote appropriate use.

Apart from the insured package, we advise the Ministry of VWS to make agreements with the manufacturer about research into the effectiveness of nusinersen for all groups of SMA patients, so that - for them too – a statement can eventually be issued on reimbursement. Until then, the costs of research and of the medicine must be borne by the manufacturer. We also took into consideration that the manufacturer is working under the umbrella of European patent protection. This is intended as legal protection against unrestrained competition and serves the public interest, namely: the development of innovative medicines. We feel that, in exchange for this protection, the manufacturer should be prepared to further promote the appropriate use of nusinersen. Our advice is emphatically in line with the ambition expressed by the manufacturer during the meeting of the Insured Package Advisory Committee (ACP): to give patients with SMA a central role.

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*The original text of this excerpt from advice of Zorginstituut Nederland was in Dutch. Although great care was taken in translating the text from Dutch to English, the translation may nevertheless have resulted in discrepancies. Rights may only be derived on the basis of the Dutch version of Zorginstituut Nederland's advice.*
*Furthermore, Zorginstituut Nederland points out that only the summary of this report was translated. A proper understanding of all relevant considerations and facts would require familiarity with the Dutch version of this report, including all appendices.*