Dexamethasone sodium phosphate (EryDex) for ataxia telangiectasia – first line

Target group

Background
A-T is an autosomal recessive, multi-system disorder resulting from defects in the ataxia telangiectasia mutated (ATM) gene and is characterised by severe progressive neurodegeneration, including cerebellar ataxia (upper and lower limbs), speech difficulties and abnormal eye movements. There is also variable immunodeficiency, impaired organ maturation, hypersensitivity to ionising radiation, ocular and cutaneous telangiectasia and predisposition to malignancies.\(^1\)\(^,\)\(^a\). Onset of symptoms usually occurs between 1-2 years with abnormal head and eye movements and loss of balance. Typically, patients inevitably require wheelchair-assistance by their early teens and life expectancy is not likely to extend beyond early twenties.\(^2\)\(^,\)\(^a\).

Technology description
Dexamethasone sodium phosphate (EryDex; Dex 21-P) is designed for encapsulation into human erythrocytes. Blood is withdrawn from patients and their erythrocytes are loaded with dexamethasone sodium phosphate using a specialised Red Cell Loader before re-introduction via intravenous (IV) infusion.

Due to the hydrophilicity of its phosphate group, dexamethasone sodium phosphate is retained intracellularly within erythrocytes until it is slowly dephosphorylated to its active form, dexamethasone. This is able to more easily diffuse through erythrocyte cell membranes and into the circulation. It is thought that by providing patients with a lower but constant plasma concentration of dexamethasone, beneficial anti-inflammatory effects will be observed with a concomitant reduction in adverse effects associated with long-term glucocorticoid therapy. 50ml of blood is used during the encapsulation and re-infusion procedure in a process taking less than 2 hours. The treatment is given once every 28 days at 500mg in the phase II clinical trial.\(^3\)

Dexamethasone sodium phosphate has also been in phase II trials for ulcerative colitis and cystic fibrosis.

Innovation and/or advantages
If licensed for this indication, dexamethasone sodium phosphate may provide a new treatment option for this patient group, who currently have limited effective therapeutic options.

Developer
EryDel S.p.a

Availability, launch or marketing dates, and licensing plans
In phase II clinical trials.

\(^a\) Expert personal communication.
NHS or Government priority area
This topic is relevant to the National Service Framework for Long-term (Neurological) Conditions (2005).

Relevant guidance

Clinical need and burden of disease
Epidemiological data regarding progressive A-T in the UK is limited, however studies have suggested a diagnosed prevalence in those aged ≤50 years of 1 in 514,000 and a birth frequency of around 1 in 300,000 in the West Midlands, whilst figures from the USA suggest a prevalence of 1 in 100,000. It is estimated that around 200 patients in the UK suffer from A-T. As the ATM gene plays a pivotal role in the repair of DNA damage, A-T patients are at an increased risk of developing cancer. These occur in about 20% of A-T patients, with lymphomas and leukaemias accounting for around 70% of such cases in the UK. Other common cancers in A-T patients include: stomach, brain, ovary, skin, liver, larynx and breast. Patients with A-T do not usually survive beyond their early twenties with mortality usually attributable to recurrent respiratory infections or malignancies.

In 2010-2011 there were 77 admissions for A-T in England, resulting in 103 bed days and 77 finished consultant episodes (ICD10 G11.3).

Existing comparators and treatments
There are currently no licensed therapies for A-T. Treatment is directed against specific symptoms including:
- Physical therapy and exercises to help improve movement – beta-blockers may also be used to improve motor function.
- Speech therapy.
- Gamma-globulins to supplement the immune system.
- Antibiotics for recurrent infections.
- Dietary supplements.
- Radiotherapy and chemotherapy regimens for the treatment of cancers are used with caution.

Efficacy and safety

<table>
<thead>
<tr>
<th>Trial</th>
<th>IEDAT-01, NCT01255358; dexamethasone sodium phosphate; phase II.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sponsor</td>
<td>EryDel S.p.a</td>
</tr>
<tr>
<td>Status</td>
<td>Complete but unpublished.</td>
</tr>
<tr>
<td>Source of information</td>
<td>Trial registry' and manufacturer.</td>
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<tr>
<td>Location</td>
<td>EU.</td>
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<tr>
<td>Design</td>
<td>Single arm.</td>
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<tr>
<td>Participants and schedule</td>
<td>n=22; ≥ 3 years of age; proven molecular diagnosis of A-T; neurological signs of A-T. Once monthly infusions using 500mg dexamethasone sodium phosphate and 50ml of blood (equivalent of 5-15mg/infusion).</td>
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<tr>
<td>Follow-up</td>
<td>Active treatment period 6 months; follow-up 30 days after last infusion.</td>
</tr>
</tbody>
</table>

' Expert personal communication.
Estimated cost and cost impact
The cost of dexamethasone sodium phosphate (EryDex) is not yet known.

Claimed or potential impact – speculative

Patients
- Reduced mortality or increased length of survival
- Reduction in associated morbidity or improved quality of life for patients and/or carers
- Quicker, earlier or more accurate diagnosis or identification of disease
- Other:

Services
- Increased use: IV administration, monitoring.
- Decreased use
- Other:

Costs
- Increased unit cost compared to alternative
- New costs: new treatment option.
- Increased costs: more patients coming for treatment
- Increased costs: capital investment needed
- Savings:
- Other:

Other issues
- Clinical uncertainty or other research question identified:

References

2 Orphanet. Ataxia-telangiectasia. http://www.orpha.net/consor/cgi-bin/Disease_Search.php?lng=EN&data_id=104&Disease_Disease_Search_diseaseGroup=telangiectasia&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group of diseases=Ataxia-telangiectasia&title=Ataxia-telangiectasia&search=Disease_Search_Simple

ICARS – International Cooperative Ataxia Rating Scale; 100-point semiquantitive scale offering a compartmentalised quantification of 4 subscores: posture and gait disorders, kinetic functions, speech disorders and oculomotor disorders.

VABS – Vineland Adaptive Behaviour Scale; One of the various assessment tools that can be used to help diagnose and evaluate special needs. Test focuses on adaptive behaviours, including the ability to cope with environmental changes, to learn new everyday skills and to demonstrate independence.
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