

Horizon Scanning Technology Summary

*National
Horizon
Scanning
Centre*

**Cyanocobalamin
nasal spray (Nascobal)
for vitamin B12
deficiency**

April 2007



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BIRMINGHAM**

This technology summary is based on information available at the time of research and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes.

Cyanocobalamin nasal spray (Nascobal) for vitamin B12 deficiency

Target group

- Maintenance of normal haematological status in pernicious anaemia - following initial stabilisation with intramuscular vitamin B12.
- Supplement for other vitamin B12 deficiencies including:
 - Dietary vitamin B12 deficiency in strict vegetarians (vegans).
 - Malabsorption of vitamin B12 resulting from structural or functional damage to the ileum e.g. from Crohn's disease or ileal resection.
 - Inadequate secretion of intrinsic factor resulting from structural or functional damage to the gastric mucosa and stomach e.g. from HIV infection and gastric atrophy.
 - Competition for vitamin B12 by intestinal parasites.
 - Inadequate utilisation of vitamin B12 e.g. during the treatment of malignancy with antimetabolites of vitamin B12.

Background

Prolonged vitamin B12 or folate deficiency account for most cases of megaloblastic anaemia in the UK, and about 80% of megaloblastic anaemias are caused by vitamin B12 deficiency resulting from pernicious anaemia. Pernicious anaemia is a chronic condition caused by an autoimmune gastritis resulting in reduced or absent acid production and absent intrinsic factor, which is necessary for the absorption of vitamin B12 from the ileum (the distal small intestine).

Other causes of vitamin B12 deficiency are rare in the UK, but include strict vegan diets, gastrectomy or gastric bypass surgery, other causes of intestinal malabsorption such as ileal resection and Crohn's disease, and HIV infection.

In the UK intramuscular hydroxocobalamin (rather than cyanocobalamin) is used as the vitamin B12 supplement of choice. However injections can lead to peaks and troughs in serum vitamin levels with the potential for sub-therapeutic levels between injections.

Technology description

Nascobal spray, a solution of cyanocobalamin - a synthetic form of vitamin B12, is administered once a week to the nasal mucosa in one nostril at a dose of 500µg cyanocobalamin (one spray from the spray pump). Each spray pump contains 2 months' supply. Nascobal nasal spray is rapidly absorbed through the nasal mucosa with peak serum levels within 1-2 hours. Blood tests are recommended 1 month after commencing nasal supplementation to check adequacy of therapy, then every 3-6 months.

Innovation and/or advantages

Nasal spray would avoid the need for 3-monthly intramuscular hydroxocobalamin injections with their associated health service staff and administration costs. Nasal self-administration may also increase patient compliance, although some elderly people may have difficulty with administration.

Developer

QOL Medical

Place of use

- | | | |
|---|---|--|
| <input checked="" type="checkbox"/> Home care e.g. home dialysis | <input type="checkbox"/> Community or residential care e.g. district nurses, physio | <input checked="" type="checkbox"/> Primary care e.g. used by GPs or practice nurses |
| <input type="checkbox"/> Secondary care e.g. general, non-specialist hospital | <input type="checkbox"/> Tertiary care e.g. highly specialist services or hospital | <input type="checkbox"/> Emergency care e.g. paramedic services, trauma care |
| <input type="checkbox"/> General public e.g. over the counter | <input type="checkbox"/> Other: | |

Availability, launch or marketing dates, and licensing plans:

Nascobal spray is available in the UK on a named patient basis. European licensing and distribution of the nasal spray is anticipated in 2008/09.

Nascobal spray was approved by the FDA in January 2005 and launched in the USA in March 2006.

Nascobal nasal gel was approved in Sweden and Israel, but has now been discontinued.

NHS or Government priority area:

- | | | |
|--|--|--|
| <input type="checkbox"/> Cancer | <input type="checkbox"/> Cardiovascular disease | <input type="checkbox"/> Children |
| <input type="checkbox"/> Diabetes | <input type="checkbox"/> Long term neurological conditions | <input type="checkbox"/> Mental health |
| <input checked="" type="checkbox"/> Older people | <input type="checkbox"/> Public health | <input type="checkbox"/> Renal disease |
| <input type="checkbox"/> Women's health | <input type="checkbox"/> None identified | <input type="checkbox"/> Other: |

This topic relates to the National Service Framework for Older People.

Relevant guidance

- Prodigy guidance. Anaemia – macrocytic. Reviewed August 2004.

Clinical need and burden of disease

Pernicious anaemia occurs in all races, but is most common in northern Europe. The incidence in Caucasians is estimated at 127 per 100,000 (about 66,000 people in England and Wales).¹ Peak incidence occurs at 60 years of age, and there is a female to male ratio of 1.6 to 1.

Symptoms of pernicious anaemia include tiredness, breathlessness, headache, lack of concentration, a swollen and sore tongue, pins and needles, and numbness. Pernicious anaemia is often associated with other autoimmune conditions such as hypothyroidism, hyperthyroidism, Addison's disease and vitiligo.

There were 1,651,100 hydroxocobalamin injections dispensed in England in 2005 at a cost of £4,063,700. If we assume 4 injections a year this would equate to 412,775 people.

There were 75,000 cyanocobalamin injections dispensed in England in 2005 at a cost of £125,400. If we assume 12 injections a year this equates to 6,250 people.

Existing comparators and treatments

Intramuscular vitamin B12

- Hydroxocobalamin 1mg 3 times a week for 2 weeks, then 1mg every 3 months (unless there is neurological involvement when the dose is 1mg every 2 months).

- Cyanocobalamin 1mg 10 injections at intervals of 2-3 days, then 1mg every month (not recommended on the NHS).

Oral vitamin B12

Although current practice in the UK is to prescribe intramuscular vitamin B12, there is limited evidence from a systematic review (2 randomised trials, n=108) that high daily doses of oral vitamin B12 (not currently available on the NHS) are as effective as intramuscular administration.²

Efficacy and safety

Trial name or code	Trial C02-016	
Sponsor	Nastech	Nastech
Status	Unpublished	Unpublished
Location	USA	USA, two site
Design	Randomised, cross-over trial	Open label
Participants	N=25 healthy volunteers (n=22 for per-protocol analysis). Three arms: nasal spray 500µg; intranasal gel 500µg; and intramuscular cyanocobalamin 100µg.	N=25 with documented vitamin B12 malabsorption. Intramuscular B12 100µg on day 1; nasal B12 500µg on days 29, 36, 43 and 50.
Follow-up	96 hours	1 week after 4 th intranasal dose.
Primary outcome	Bio-equivalence between nasal spray and gel (serum concentration C _{max} and area under curve). Relative bio-availability of intranasal versus intramuscular B12.	Pharmacokinetic profile - vitamin B12 levels measured weekly and prior to nasal doses.
Key results	Bio-equivalence between nasal spray and gel. Relative bio-availability between nasal spray and gel was 0.97; between spray and intramuscular was 0.61.	Serum vitamin B12 levels (including trough levels) were maintained above the therapeutic threshold by weekly intranasal B12. The co-efficient of variability for nasal B12 was lower than that for intramuscular B12.
Major adverse effects	All formulations well tolerated. Sneezing in one subject was the only adverse event judged to be drug-related.	More patients reported adverse effects with intramuscular than nasal B12. Of the events judged as 'possibly' relating to the drugs – headache, nausea and rhinitis were reported following nasal B12.

Estimated cost and cost impact

Nascobal costs about \$180 (£97) for a 60-day self-administered supply.

- Hydroxocobalamin costs £2.46 for 1mg. A year's supply of injections at 3 monthly intervals costs £9.84.
- Cyanocobalamin costs £1.67 for 1mg. A year's supply of injections at 1 monthly intervals costs £20.
- Depending on the staff and setting of the injection, administration costs may be in the region of £8 - £34 per injection.^{3,4}

Potential or intended impact – speculative

Potential savings include a reduction in patient visits to health services and in home visits by nursing staff to patients who are housebound, although compliance may be reduced.

Patients

- | | | |
|---|--|---|
| <input checked="" type="checkbox"/> Reduced morbidity | <input type="checkbox"/> Reduced mortality or increased survival | <input checked="" type="checkbox"/> Improved quality of life for patients and/or carers |
| <input type="checkbox"/> Quicker or more accurate diagnosis | <input type="checkbox"/> Earlier identification of disease | <input type="checkbox"/> Other: |

Services

- | | | |
|---|--|---|
| <input type="checkbox"/> Increased use e.g. length of stay, out-patient visits | <input type="checkbox"/> Service reorganisation required | <input type="checkbox"/> Staff or training required |
| <input checked="" type="checkbox"/> Decreased use e.g. practice nurse consultations, and district nurse visits to administer injections | <input type="checkbox"/> Other: | |

Costs

- | | | |
|---|---|---|
| <input checked="" type="checkbox"/> Increased unit cost compared to alternative | <input type="checkbox"/> Increased costs: more patients coming for treatment | <input type="checkbox"/> Increased costs: capital investment needed |
| <input type="checkbox"/> New costs: | <input checked="" type="checkbox"/> Savings: staff and administration costs of 3-monthly injections | <input type="checkbox"/> Other: |

References

¹ Prodigy guidance. Anaemia – macrocytic. Reviewed August 2004. Accessed 12 February 2007.

[Hhttp://www.prodigy.nhs.uk/anaemia_macrocyticH](http://www.prodigy.nhs.uk/anaemia_macrocyticH)

² Vidal-Alaball J, Butler CC, Cannings-John R et al. Oral vitamin B12 versus intramuscular vitamin B12 for vitamin B12 deficiency. Cochrane Database of Systematic Reviews 2005, Issue 3. Art. No.: CD004655. DOI: 10.1002/14651858.CD004655.pub2.

³ Curtis L, Netton A. Unit costs of health and social care 2006. Personal Social Services Research Unit, The University of Kent. 2006.

⁴ Department of Health. NHS Reference costs 2005/06. December 2006

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