Alfacalcidol for the treatment of hypocalcaemia due to hypoparathyroidism in adults (One-Alpha®)

Amber with shared care

Shared Care Guidelines: For the treatment of hypocalcaemia due to hypoparathyroidism in adults

AREAS OF RESPONSIBILITY FOR THE SHARING OF CARE

This shared care agreement outlines suggested ways in which the responsibilities for managing the prescribing of medicine name and indication shared between the specialist and general practitioner (GP). GPs are **invited** to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it. Patients with the condition are under regular specialist follow-up, which provides an opportunity to discuss drug therapy.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

RESPONSIBILITIES and ROLES

	Specialist responsibilities
1	Diagnosis of hypoparathyroidism & assessing the patient's suitability for treatment.
2	Review patient's symptoms and signs.
3	Perform baseline blood tests before initiating treatment: serum calcium, albumin, phosphate and alkaline phosphatase.
4	Specify target dose, monitoring and review dates at clinically relevant time intervals for both the GP and specialist team and any other patient specific information.
5	Record the patient's confirmation of understanding of the risks, benefits and consent.
6	Initiate treatment and provide at least 28 days' supply.
7	Discuss the benefits and side effects of treatment with the patient.
8	Ask the GP whether he or she is willing to participate in shared care, and agree with the GP as to who will discuss the shared care arrangement with the patient.
9	Supply GP with summary within 14 days of a hospital out-patient review or in-patient stay.
10	Review the patient's condition at least 12 monthly. Monitor response to treatment regularly where indicated.
11	Give advice to the GP on when to stop treatment.
12	Report adverse events to the MHRA
13	Ensure that clear backup arrangements exist for GPs to obtain advice and support.

	General Practitioner responsibilities
1	Reply to the request for shared care as soon as practicable.
2	Prescribe medicine at the dose recommended and monitor as recommended.
3	Review patient's symptoms and signs, especially for signs of hypercalcaemia (muscle and bone pain, muscle weakness, confusion, dehydration, anorexia, fatigue, nausea and vomiting, constipation, polyuria, sweating, headache, polydipsia, hypertension and somnolence) and hypocalcaemia due to under-treatment (muscle weakness, perioral tingling, cramps and tetany) and do further monitoring (p.3) to establish if there is a problem.
4	Report to and seek advice from the specialist on any aspect of patient care that is of concern to the GP and may affect treatment.
5	Conduct an annual face to face medication review or more frequent if required (e.g. in elderly patient).
6	Stop treatment on the advice of the specialist.
7	Report adverse events to the specialist and MHRA.

	Patient's role
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Share any concerns in relation to treatment with medicine.
3	Report any adverse effects to the specialist or GP whilst taking the medicine.
4	Attend GP/specialist appointments for regular monitoring and be aware that treatment will be stopped it they do not attend for monitoring.

BACK-UP ADVICE AND SUPPORT

Contact details	Telephone No.	Bleep:	Fax:	Email address:
RUH specialist via consultant connect	-	7059	-	-

SUPPORTING INFORMATION

Summary of condition and licensed indications.

- Hypocalcacemia due to hypoparathyroidism (most commonly after thyroid or parathyroid surgery) in adults

Alfacalcidol is also used in patients with CKD with secondary hyperparathyroidism. This guideline should not be used for this indication. The specialist renal teams will provide monitoring guidance on monitoring for those patients.

A shared care agreement for use from the renal & transplant directorate at North Bristol NHS Trust can be found here for patients under their care:
https://www.bnssgformulary.nhs.uk/includes/documents/Alfacalcidol%20prescribing%20guidance%20NBT%20Feb16.pdf

Background Information

Alfacalcidol is a very potent short-acting vitamin D analogue with high risk of side-effects (see below). Other less potent vitamin D preparations should be used for prevention and treatment of osteoporosis in those with normal renal function.

Alfacalcidol is a form of activated vitamin D which should only be prescribed under the advice of a specialist.

Treatment aims

- Vitamin D replacement post parathyroidectomy
- Corrected calcium levels in the range 2.0-2.2mmol/l in patients with hypoparathyroidism
- Patients being free of symptoms or signs of hypocalcaemia

Treatment Schedule (including dosage and administration)

Maintenance doses generally range between 0.25 to 1microgram daily. Alfacalcidol should be prescribed a maximum of ONCE daily.

Higher doses may occasionally be required in acute hypocalcaemia in specialist care. If doses higher than 2 micrograms seem to be required in the non-acute setting seek specialist advice. Patients with normal renal function with significant hypoparathyroidism will usually require calcium supplements as well as Alfacalcidol, usually 1-2g per day.

In patients who have normal serum calcium without calcium supplementation consideration should be given to whether Alfacalcidol treatment can be stopped (seek advice).

Concomitant Drug Therapy:

- Many patients will be taking levothyroxine (T4) as well as Alfacalcidol. Ensure that these patients know not to take their levothyroxine at the same time as their calcium supplements as it interferes with the absorption of the levothyroxine.
- Some patients may be Vitamin D deficient as well as hypoparathyroid. Therefore all patients on alfacalcidol due to hypoparathyroidism will be initiated onto a daily oral Vitamin D3 supplement as advised by the specialist.

Good prescribing principles for Alfacalcidol:

- Micrograms and nanograms should not be abbreviated
- Avoid the use of decimals by using alternative units of measure (e.g. use 250 nanograms instead of 0.25 micrograms).
- Take additional care with Alfacalcidol oral drops, 2 micrograms/mL; one drop contains approximately 100 nanograms.

Pregnancy and breastfeeding.

Patients planning pregnancy or found to be pregnant should have serum calcium and renal function measured at the earliest opportunity as well as being referred to a specialist antenatal clinic. Alfacalcidol is unlikely to be harmful in pregnancy as long as serum calcium in target range (2.0 – 2.2 mmol/l). Risk to the foetus is likely to be greater if the therapy is discontinued through risk of maternal hypocalcaemia. Hypercalcaemia during pregnancy may produce congenital disorders in the offspring.

Although it has not been established, it is likely that increased amounts of 1,25-dihydroxyvitamin D will be found in the milk of lactating mothers treated with Alfacalcidol. This may influence calcium metabolism in the infant. Please seek specialist advice.

Contra-indications and precautions for use

NPSA Safety alert for Alfacalcidol: Highlighting issues with patients developing renal failure due to lack of monitoring of their calcium levels whilst taking Alfacalcidol. It states the necessity for the monitoring of bloods to minimise the chance of associated renal problems.

Please note: One-Alpha capsules contain sesame oil as an excipient and generic capsules may also contain sesame oil. Sesame oil may rarely cause severe allergic reactions.

Side-effects (not covered by specific monitoring requirements)
The most frequent adverse effects are serum hypercalcaemia and skin rashes.
Signs of hypercalcaemia are muscle and bone pain, muscle weakness, confusion, dehydration, anorexia, fatigue, nausea and vomiting, constipation, polyuria, sweating, headache, polydipsia, hypertension and somnolence. Severe hypercalcaemia can cause cardiac dysrythmias.
Persistent hypercalcaemia due to over-treatment with Alfacalcidol can cause irreversible nephrocalcinosis and end-stage renal failure.
Hypocalcaemia due to under-treatment can cause marked symptoms (muscle weakness, perioral tingling, cramps and tetany) and when severe can cause convulsions or cardiac arrythmias.
Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the MHRA.

Monitoring
Alfacalcidol must not be prescribed without monitoring of serum calcium and renal function. If monitoring is not possible, specialist advice should be sought and consideration given to use of alternative therapies.
GPs will only be asked to monitor Alfacalcidol treatment once the need for long-term therapy has been established (in surgical hypoparathyroidism 3-6 months post-operatively) and the patient is on a stable dose of therapy.

Once on stable dose of Alfacalcidol, the following tests will need to be done every 3 months in primary care:

Test	Frequency
Serum calcium (corrected for protein binding)	Every 3 months, more frequently if symptoms of possible over or under-treatment
Magnesium	
Phosphate	
Renal function	

Please note that the SPC for Alfacalcidol actually states that when the dose is stabilized, serum calcium measurements may be taken every 2 - 4 weeks. However local specialist consensus is that the above tests should be done every 3 months. Monitoring will need to be continued indefinitely while taking the therapy.

The aim of treatment in general is to achieve serum corrected calcium 2.0 – 2.2 mmol/l (higher levels even within the normal range may increase the risk of nephrocalcinosis).
Always ensure patient is still taking their calcium supplements (see treatment schedule above).
If serum calcium results persistently outside target range, seek specialist advice (see table below). Please copy results to secondary care team if under active specialist follow up.

Further monitoring:

- Local specialists also recommend 24 hour urinary calcium every two years if stable.
- If there is a change in dose, a 24 hour urinary calcium within 3 months of dose change once stable.
- If 20% deterioration in creatinine (local specialist consensus), then 24 hour urinary calcium needs doing if not done recently and renal imaging (USS) should take place, and referral to specialist care.

How to adjust Alfacalcidol dose according to serum calcium levels:

Corrected serum calcium level	Action
1.7 to 2.0	Increase by 0.25-0.5 micrograms daily then check serum levels 1 wk post dose change
2.2 to 2.6	Check serum levels again in 1 wk. If still high, decrease by 0.25-0.5 micrograms daily, repeat serum calcium after one week on new dose.
>2.6	Reduce dose by 0.5 micrograms daily and repeat serum calcium in 2-3 days.
<1.7	If serum calcium <1.7 mmol/l or >3.0 mmol/l or patient markedly symptomatic (malaise, thirst, perioral tingling, cramps or tetany), seek specialist advice urgently or consider admission.
>3.0	

Information to be given to patient (by specialist & GP)

Hypoparathyroidism UK: PIL

- The need for long-term Alfacalcidol treatment has been established.
- On-going monitoring of serum calcium and renal function is required indefinitely. Once a stable dose of Alfacalcidol is achieved the GP will arrange blood tests every 3 months. If the patient has persistent symptoms he/she should contact the GP and have another blood test.
- Patients should be informed about the clinical symptoms connected with hypercalcaemia and to see their GP if these occur.
- Alfacalcidol treatment is usually accompanied by calcium supplementation.

Drug Interactions (refer to SPC for full list of interactions)

Alfacalcidol should be used with caution for:

- Patients being treated with cardioactive glycosides or digitalis as hypercalcaemia may lead to arrhythmia in such patients
- Patients taking barbiturates or anticonvulsants may require larger doses of Alfacalcidol to produce the desired effect due to the induction of hepatic detoxification enzymes.
- Concomitant administration of colestyramine may interfere with the intestinal absorption of Alfacalcidol.
- Use with caution in patients being treated with thiazide diuretics as they may have an increased risk of developing hypercalcaemia.

Cost

Current drug tariff prices (June 2018):

Alfacalcidol 250nanogram capsules x 30 £4.85
Alfacalcidol 500nanogram capsules x 30 £9.73
Alfacalcidol 1microgram capsules x 30 £13.58
Alfacalcidol 2micrograms/ml oral drops sugar free 10 ml £21.30

Full Prescribing Information

For full prescribing information please consult summaries of product characteristics and the current BNF.

References

- Summary of product characteristics One-Alpha: https://www.medicines.org.uk/emc/product/5516/smpc
- Prevention of harm with alfacalcidol preparations | Signal29 September 2011. Accessed via https://www.sps.nhs.uk/wp-content/uploads/2018/03/Prevention-of-harm-with-alfacalcidol-preparations-Sept-2011-1.pdf

The information contained in these shared care guidelines is issued on the understanding that it is the best available from the resources at our disposal at the time of issue.