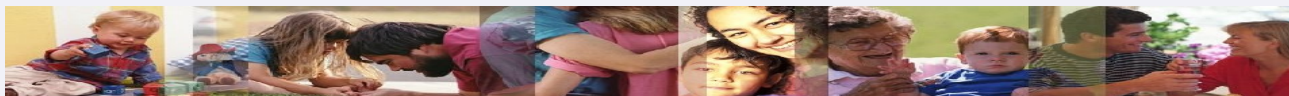


NEWSLETTER



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Oral Miconazole Gel and Warfarin Interaction

There have been several incidents recently where patients were admitted to hospital with bleeding events and increased INRs when co-prescribed warfarin and oral miconazole gel (Daktarin Oral Gel[®]). Some of these bleeding events had fatal outcomes.

The antifungal drug miconazole inhibits multiple P450 isozymes that heighten the anticoagulant effect of warfarin and lead to increase in patient INRs. Vaginal and topical administration of miconazole can also affect warfarin, but the oral route usually has a more profound effect because the oral gel is swallowed after use in the mouth.

For further information refer to Drug Safety Update, September 2017 <https://www.gov.uk/drug-safety-update>.



Action for prescribers:

- Miconazole oral gel should generally be avoided in patients taking warfarin. If the two have to be co-prescribed, exercise caution and ensure the INR is monitored carefully.

Action for community pharmacists:

- Over the counter miconazole oral gel is contraindicated in patients taking warfarin.
- If you receive a prescription for oral miconazole gel for a patient currently on warfarin, contact the prescriber to ensure that they are aware of the interaction and document the outcome of the intervention.

Advise patients taking prescription only miconazole oral gel and warfarin that if they experience symptoms of bleeding to stop using miconazole and seek immediate medical attention.

NI Formulary Choice: Adcal D3 Caplets[®]

Combination calcium plus vitamin D preparations vary in terms of strength, and hence the recommended daily dose. The first line choice of combination calcium plus vitamin D on the [NI Formulary](#) is **Adcal-D3[®] caplets**. For patients who are unable to swallow caplets, the 2nd line NI Formulary choice is **Calceos[®] chewable tablets**

Adcal D3[®] caplets are not equivalent to Adcal D3[®] chewable tablets, or Calceos[®] chewable tablets, or Natecal D3[®] chewable tablets — see table.

Action for prescribers:

- Ensure that patients prescribed Adcal D3[®] caplets are prescribed the correct dosage (usual dose is **TWO** tablets twice a day).
- For patients who require a chewable formulation, please ensure that Calceos[®] chewable tablets are prescribed.
- For patients currently prescribed a chewable preparation, it should be established at review if a chewable preparation is actually required. If not, a change to Adcal D3[®] caplets would be appropriate, being careful to ensure that the correct dose is prescribed.

| Product | Calcium | Vitamin D (colecalfiferol) | Usual daily dose |
|---|---|-----------------------------|--------------------------------|
| Adcal D3 [®] caplets | Calcium carbonate 750mg (equivalent to 300mg of calcium) | 200IU (5 micrograms) | TWO tablets twice a day |
| Calceos [®] chewable tablets | Calcium carbonate 1250mg (equivalent to 500mg of calcium) | 400IU (10 micrograms) | ONE tablet twice a day |
| Adcal D3 [®] chewable tablet | Calcium carbonate 1500mg (equivalent to 600mg of calcium) | 400IU (10 micrograms) | ONE tablet twice a day |
| Natecal D3 [®] chewable tablets [®] | Calcium carbonate 1500mg (equivalent to 600mg of calcium) | 400IU (10 micrograms) | ONE tablet twice a day |

Buccal Midazolam Preparations

Buccal midazolam products should be **prescribed by brand name** to reduce the risk of medication errors. The two available brands, Buccolam[®] and Epistatus[®], are not interchangeable and there is high risk of harm if patients receive the incorrect brand and strength of buccal midazolam. Prescribers should ensure that they are aware of the different buccal midazolam brands, preparations and strengths.

All strengths of Epistatus[®] were previously classified as unlicensed specials. However one preparation of Epistatus[®] - the midazolam 10mg in 1ml oromucosal solution pre-filled syringe — has recently been granted a UK marketing authorisation. In addition, Epistatus[®] continues to be available in two other unlicensed formulations and strengths. The alternative buccal midazolam preparation, Buccolam[®], is licensed for use in children from 3 months to less than 18 years. It is available in four colour-coded pre-filled oral syringes, each suitable for different age groups.

| Brands | Preparations |
|--|---|
| Buccolam [®] (10mg in 2ml) hydrochloride base Licensed: ages 3 months to <18 years | 2.5mg/0.5ml; 5mg/ml; 7.5mg/1.5ml; 10mg/2ml pre-filled syringes |
| Epistatus [®] (10mg in 1ml) maleate base Licensed: ages 10 to < 18 years | 10mg/ml pre-filled syringe |
| Epistatus [®] (10mg in 1ml) maleate base Unlicensed | 2.5mg/0.25ml; 5mg/0.5ml; 7.5mg/0.75ml pre-filled syringes |
| | Multi-dose 10mg/ml 30ml bottle (dose to be drawn up). Note: bottle contains overage |

Important Prescribing Points:

- Always prescribe buccal midazolam by brand.
- Prescribe the brand of buccal midazolam that is specified in the patient's Epilepsy Care Plan and which the carer has been trained to use.
- Patients should be reviewed to ensure that the preparation prescribed corresponds with the patient's Epilepsy Care Plan and that an incorrect preparation has not been inadvertently prescribed or dispensed.
- Counsel patients or carers about making sure they receive the same brand each time.
- Ensure that prescriptions comply with CD prescription-writing requirements as midazolam is a schedule 3 CD.
- Prescribe the dose in mg and ml.

NICE GUIDANCE — NORTHERN IRELAND SERVICE NOTIFICATIONS

Service Notifications have been issued in Northern Ireland for the following:

[NICE TA475](#) — Dimethyl fumarate for treating moderate to severe plaque psoriasis.

[NICE TA 477](#) — Autologous chondrocyte implantation for repairing symptomatic articular cartilage defects of the knee (review of TA89).

[NICE TA478](#) — Brentuximab vedotin for treating relapsed or refractory systemic anaplastic large cell lymphoma

[NICE TA479](#) — Reslizumab for treating severe eosinophilic asthma.

MANAGED ENTRY DECISIONS

The following medicines were considered in February as part of the Northern Ireland Managed Entry process. **Please refer to the Managed Entry section of the Northern Ireland Formulary website for full details on Managed Entry decisions:** <http://niformulary.hscni.net/ManagedEntry/MEDecisions/Pages/default.aspx>

Bezlotoxumab (Zinplava[®])
Brodalumab (Kyntheum[®])
Carbetocin (Pabal[®])
Ceftaroline (Zinforo[®])
Ceftazidime + avibactam (Zavicefta[®])

Ceritinib (Zykadia[®])
Ixazomib (Ninlaro[®])
Lesinurad (Zurampic[®])
Lenvatinib (Kisplyx[®])

This newsletter has been produced for GPs and pharmacists by the Regional Pharmacy and Medicines Management Team. If you have any queries or require further information on the contents of this newsletter, please contact one of the Pharmacy

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