NHS
Pan Mersey
Area Prescribing Committee

VORICONAZOLE (VFEND®) or POSACONAZOLE (Noxafil®) for allergic bronchopulmonary aspergillosis

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of VORICONAZOLE or POSACONAZOLE, by GPs or specialists, for allergic bronchopulmonary aspergillosis.

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Neither voriconazole nor posaconazole is licensed for the treatment of allergic bronchopulmonary aspergillosis (ABPA).

Voriconazole is licensed for the treatment of invasive aspergillosis. Posaconazole is licensed for invasive aspergillosis in patients with disease that is refractory to amphotericin B or itraconazole or in patients who are intolerant of these. Patients with invasive aspergillosis are critically ill and are managed in intensive care[1].

Treatment of chronic pulmonary aspergillosis is managed by the National Aspergillosis Centre in Wythenshawe Hospital and is commissioned by NHS England. NHSE commissions voriconazole and posaconazole for patients with chronic pulmonary aspergillosis but not for ABPA.

Allergic Bronchopulmonary Aspergillosis (ABPA) manifests as poorly controlled asthma, and other symptoms are haemoptysis, fever, malaise, and expectoration of mucous plugs. If untreated, it can lead to permanent lung damage through the development of bronchiectasis[1,2,3]. Although inhaled fungal conidia are normally removed from the airways, defective clearance in patients with asthma and cystic fibrosis allows conidia to germinate and produce hyphae. These hyphae induce the production of inflammatory cytokines which are responsible for the development of symptoms.

Hypersensitivity to *Aspergillus* is reflected by elevated *Aspergillus* – specific IgE levels or by a positive aspergillus skin test. Patients are managed by respiratory teams in secondary care and may be treated with itraconazole which is licensed for treatment of aspergillosis.

Evidence for use of voriconazole and posaconazole in patients with ABPA who have failed treatment with itraconazole is limited and comes from a retrospective review of 25 adult asthmatic patients with either ABPA (n=20) or severe asthma with fungal sensitisation (SAFS)(n=5) who were treated at the National Aspergillosis Centre[3]. All patients had received itraconazole previously for durations between 6 months and 10 years, but it was discontinued due to lack of efficacy, adverse effects, low serum concentration or fungal resistance. 24 patients started with voriconazole, 12 of whom still had a clinical response at 12 months. 1 patient started on posaconazole and 8 voriconazole patients were switched to posaconazole. 7 of these 9 patients still had a clinical response at 12 months.

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

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APC administration provided by Midlands and Lancashire Commissioning Support Unit

SUPPORTING INFORMATION

VORICONAZOLE (VFEND®) or POSACONAZOLE (Noxafil®) for allergic bronchopulmonary aspergillosis

Effectiveness Use is unlicensed in patients with ABPA who have previously been treated with itraconazole that has been discontinued due to lack of efficacy, adverse effects, fungal resistance or the patient is unable to achieve therapeutic serum levels. Evidence is limited to a retrospective review of 25 patients treated at the National Aspergillosis Centre. 12 of 24 patients treated with voriconazole maintained a clinical response at 12 months. 7 of 9 patients treated with posaconazole (including 8 who had failed with voriconazole) maintained a clinical response at 12 months[3]. The study concludes that larger prospective studies are required, and that the possibility of adverse effects linked to voriconazole needs to be taken into account and monitored.	**Safety** Contraindicated in patients prescribed some CYP3A4 substrates, including ergot alkaloids. Both voriconazole and posaconazole are associated with QT prolongation. LFTs should be monitored throughout therapy with both drugs. Patients should avoid exposure to direct sunlight while on voriconazole therapy. Long-term treatment with voriconazole > 6 months should be carefully evaluated as there is a risk of squamous cell carcinoma. Risk of prolonged sedation and respiratory depression if posaconazole is co-prescribed with benzodiazepines that are metabolised by CYP3A4.
Cost Cost for one year of therapy: Voriconazole £10,180 - £15,241 depending on dose[4]. Posaconazole £27,311. Numbers are expected to be very low. The National Aspergillosis Centre case review included all known cases at the time. This was 25 patients nationally. Currently there is one known patient in the Pan Mersey area to date.	**Patient factors** Voriconazole and posaconazole are PbR – excluded drugs and prescribing is not recommended.

Prescribing information and Implementation notes

Prescribing is not recommended.

References

1. Kosmidis C, Denning DW. The clinical spectrum of pulmonary aspergillosis. Thorax Published Online First 29 October 2014. https://thorax.bmj.com/content/thoraxjnl/early/2014/10/29/thoraxjnl-2014-206291.full.pdf
2. Orphanet monograph for APBA. https://www.orpha.net/consor/cgi-bin/OC_Exp.php?lng=en&Expert=1164
3. Chishimba L et al. Voriconazole and Posaconazole Improve Asthma Severity on Allergic Bronchopulmonary Aspergillosis and Severe Asthma with Fungal Sensitisation. J Asthma 2012; 49(4): 423-433. http://www.life-worldwide.org/assets/uploads/files/Chishimba%20SAFS%20ABPA%20vori%20posa%20J%20Asthma%202012.pdf
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