Fluticasone furoate/fluticasone propionate – different drugs with
different properties
Keith Biggadike

The similarity in the names of the recently introduced intranasal glucocorticoid
fluticasone furoate (FF; Veramyst®, GlaxoSmithKline/Avamys®, GlaxoSmithKline UK,
Uxbridge, UK) and the earlier fluticasone propionate (FP; Flonase®/Flixonase®,
GlaxoSmithKline) has led many to assume that the two compounds have the same
active principle (fluticasone) (e.g. 1, 2). This has been compounded by FP commonly,
and incorrectly, being abbreviated to fluticasone. The purpose of this letter is to
highlight that FF and FP are completely different drugs with FF showing distinct and
superior properties (3), and hence prevent any misprescription of these drugs in the
future.

This confusion clearly stems from the unusual assigned glucocorticoid nomenclature
which splits these molecules into the steroidal backbone (fluticasone) and the ester
substituent (furoate/propionate). This naming convention does suggest that these
derivatives could be ester prodrugs of fluticasone. In fact, a number of topical
glucocorticoid esters are indeed ester prodrugs releasing the active parent glucocorticoid
in the body. However, fluticasone 17α esters are remarkably stable and remain attached
to the fluticasone backbone even during metabolism. Their pharmacological activity is
mediated by the entire molecule (backbone + ester) and they share no common
metabolites – neither FF nor FP is metabolised to fluticasone. FF and FP are therefore
structurally distinct drug substances with distinct properties.

The furoate and propionate moieties are far from inert appendages but serve to
significantly enhance the glucocorticoid activity of fluticasone, which has never itself
been developed. Key interactions of FF with the glucocorticoid receptor have been
elucidated by X-ray crystallography which shows the ester derived from 2-furoic acid
occupying a discrete pocket on the receptor much more completely than does the
smaller propionate ester of FP (4). The resulting enhanced affinity of FF for the target
receptor is reflected in the lower daily dose of Veramyst (110 µg) compared with
Flonase (200 µg).

The ester group also contributes to the physicochemical characteristics of the molecule
which impact on solubility, dissolution rate, tissue affinity, and hence pharmacokinetic
and pharmacodynamic properties. Thus, the ester derived from 2-furoic acid in FF
confers higher affinity for both nasal and lung tissue compared with FP (5, 6) and recent
studies with inhaled FF have shown that this translates to enhanced lung residency and
once-daily efficacy in asthma (7, 8). There is already some evidence that the characteristics of FF may result in superior symptom reduction compared with FP (9, 10) or similar improvements in symptoms at less frequent dosing schedules (11), which could result in reduced health-care costs/concomitant medication use (12); however, prospective, randomised, head-to-head studies are required to provide a definitive answer. With new inhaled products containing FF in Phase III trials (Relovair®, GlaxoSmithKline) it is important for prescribers to understand that this is a novel glucocorticoid, not to be confused with FP. Moreover, the practice of abbreviating FP and FF to fluticasone should be discouraged (Clin Respir J. 2011 July; 5(3): 183–184.).

References
5. Valotis A, Hogger P. Human receptor kinetics and lung tissue retention of the enhanced-affinity glucocorticoid fluticasone furoate. Respir Res. 2007;8:54. [PMC free article] [PubMed]