International Journal of Pharmaceutics 479 (2015) 159–162

Contents lists available at ScienceDirect

International Journal of Pharmaceutics

journal homepage: www.elsevier.com/locate/ijpharm

Note

Investigation into the dosage form attributes of currently UK licensed cardiovascular and Parkinson's disease drug products

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ARTICLE INFO

Article history:
Received 29 September 2014
Accepted 26 December 2014
Available online 30 December 2014

Keywords:
Older people
Dosage form
Cardiovascular disease
Parkinson's disease
Polypharmacy
Excipient

ABSTRACT

Globally, there is a continuous rise in the older population (over 65 years), particularly in developed countries. As many diseases are age-related, older adults represent a highly heterogeneous cohort. This presents a major challenge for both the pharmaceutical industry and healthcare professionals. The purpose of this research was to attract attention towards the appropriateness of geriatric formulations by investigating the dosage form attributes of currently UK licensed cardiovascular and Parkinson's disease drug products. Medication available in the UK for cardiovascular disorders and Parkinson's disease were screened and the available formulations, packaging and patient information leaflets of these medicines were analysed, with the goal of raising awareness of the need to cater for elderly patients with increasing difficulty in managing their medication. It emerged that although cardiovascular disorders and Parkinson's disease are more prevalent in older people, many treatment options have not been optimised for this cohort. In particular, older patient centred dosage forms, specific dosing requirements, excipients, patient-friendly packaging and easy-to-follow patient information were highlighted as areas to be considered in order to optimise health outcomes in the ageing population.

Older people, defined as individuals over 65 years old, represent approximately 17.2% of the total community population in the United Kingdom (UK) and this is expected to increase to 22.4% by 2032 (AgeUK, 2014). Similarly, older people constitute around 17% of the total community population in Europe and this is predicted to increase to 30% in 2050 (European Medicines Agency, 2013). According to the Age UK 2014 report on later life, cardiovascular disease (CVD) is the greatest cause of death in the UK in people over 65 years (AgeUK, 2014). Parkinson's disease (PD) is another fatal disease that is prevalent in the older population, with almost two thirds of all PD cases reported in those over 70 years old (Meara, 2000). Therefore, in the present study, pharmaceutical products listed in the British National Formulary (BNF) for CVD and PD were screened in order to determine the suitability of the formulations and associated information for older people. It has been previously reported that up to 50% of patients do not use their medication as prescribed (National Collaborating Centre for Primary Care, 2009). By screening the available information on formulations from two areas of particular importance in prescribing for older patients, this research aims to assess the appropriateness of dosage forms with respect to the older population.

All products listed in the Cardiovascular System and Parkinsonism and Related Disorders sections of the BNF (Joint Formulary Committee, 2013) were included for analysis. The available data were then compiled from relevant UK reference sources - the BNF, Summary of Products Characteristics (SmPC) and Patient Information Leaflets (PILS) (Joint Formulary Committee, 2013). In the BNF, 262 products were listed under cardiovascular system and 41 products were listed under Parkinsonism and related disorders. The SmPCs as well as relevant PILs were screened and aspects considered significant in the optimisation of formulations for CVDs (Table 1) and PD (Table 2) in elderly patients were identified for analysis.

The classification of dosage forms for CVD and PD drug products are presented in Table 3. Of the listed cardiovascular drug products, 48% specified general posology adjustment guidelines based on both renal and hepatic function (Fig. 1). Posology adjustments of the cardiovascular formulations were mainly based on renal and hepatic impairment. Renal and hepatic functions are often reduced in older patients, affecting drug metabolism and clearance (Mangoni and Jackson, 2004). However, there are other age-related changes that can influence the pharmacokinetic and pharmacodynamic parameters of medication. For example, older

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http://dx.doi.org/10.1016/j.ijpharm.2014.12.065
0378-5173/

Table 1
Pharmaceutical formulation aspects considered significant in the screening of dosage forms with respect to elderly patients receiving medication for cardiovascular disorders.

BNF classification
Therapeutic indication(s)
Active pharmaceutical ingredient(s)
Available dosage forms
Therapy type (mono or fixed dose combinations (FDCs))
Dose frequency (mono- or multi- dose)
Potential "risky excipients" (propylene glycol, sodium)
Tablet scoring/ability to be halved
Drug release profile (immediate/modified release)
Coating type
Age range
Minimum age
Elderly-specific section
Packaging type
Storage conditions
Name of marketing authorisation holder
Information source and additional comments

patients are often more sensitive to cardiovascular drugs such as digoxin and warfarin, both of which have a narrow therapeutic index, due to a reduction in apparent volume of distribution of these agents. This considerably increases serum concentration and therefore, toxicology and adverse effects. On the contrary, the efficacy of adrenoceptor blocking agents declines with age and careful dose titration is required. However, these factors were considered for less than half of the available cardiovascular dosage forms, with 30 providing neither specific adjustments for older patients nor any information regarding posology adjustments. This suggests that more academic and industrial efforts are required to optimise the efficacy of medicines for the older population (Ford, 2000; Mangoni and Jackson, 2004). Clinical trials often exclude older patients based on age, concomitant conditions, polypharmacy, frailty or the higher costs associated with recruiting and maintaining elderly during clinical trials. However, the extrapolation of clinical findings to include patients outside the tested age range does not offer a true representation of these groups. Clinical studies for older patients are required to maintain the safety of elderly participants and to obtain valid professional data regarding those patients that can be used by healthcare professionals (Cherubini et al., 2010; ICH Steering Committee, 2010).

Of the listed CVD products, 40% specified dose recommendations that were adjusted for older patients, taking into account factors such as comorbidity, polypharmacy, increased vulnerability to adverse effects and other age-related physiological changes that can impact the pharmacodynamic profile and tolerability of the patient. The prevalence of modified release formulations, fixed-dose combinations (FDCs) and "risky" excipients (for example propylene glycol or sodium) are also shown in Fig. 1. Polypharmacy

Table 2
Pharmaceutical formulation aspects considered significant in the screening of dosage forms with respect to elderly patients receiving medication for Parkinson's disease.

BNF classification
Therapeutic indication(s)
Active pharmaceutical ingredient(s)
Available dosage forms
Method of administration
Therapy type (mono or fixed dose combinations (FDCs))
Drug release (immediate/modified release)
Packaging
Elderly-specific section
Definition of elderly
Pictogram
Specific warnings for elderly

Table 3
Classification of screened dosage forms and route of administration for cardiovascular disorders (CVD) and Parkinson's disease (PD). Observations are reported as number of drug products (*n*) and percentage of oral, sublingual, parenteral, topical or other formulations (%).

Route of administration	CVD (*n* = 262)	PD (*n* = 41)
Oral,*n*(%)	198 (76)	33 (80)
Tablets, *n*	150	20
Chewable tablets, *n*	1	–
Dispersible tablets, *n*	1	1
Orally disintegrating tablet	–	1
Capsules, *n*	30	5
Liquid, *n*	13	6
Sachet/powder, *n*	3	–
Sublingual,*n*(%)	3 (1.1)	–
Tablet	1	–
Spray	2	–
Parenteral,*n*(%)	58 (22)	7 (17)
IV injection, *n*	17	–
IV infusion, *n*	14	–
IV injection or infusion, *n*	17	–
IV/SC injection or infusion, *n*	1	–
IV/IM injection, *n*	–	1
IM injection, *n*	3	3
SC injection, *n*	5	2
Intra-ocular injection, *n*	1	
Topical,*n*(%)	2 (0.76)	1 (2)
Ointment, *n*	1	
Patches, *n*	1	1
Other	1 (0.38)	1 (2)
Pulmonary, *n* (%)	1	–
Intestinal gel, *n* (%)	–	1

IV: intravenous; IM: intramuscular; SC: subcutaneous

is common in older patients. While multi-drug prescribing is often necessary in the treatment of age-related conditions including CVD, it can significantly increase the complexity of dosing regimens and contribute to non-compliance (Hilmer et al., 2007). FDCs allow multiple drugs to be delivered in a single entity. Increasing the number of licensed FDCs would be beneficial in reducing the number of medications required in conditions such as CVD, when the level of concomitant prescribing is high (Bangalore et al., 2007; Martial et al., 2013). Modified release formulations offer a prolonged action in the body, which in turn may reduce the frequency of dose administration, particularly in drugs with short biological half-lives. Reducing the complexity of drug regimens by minimising dose frequency has been shown to

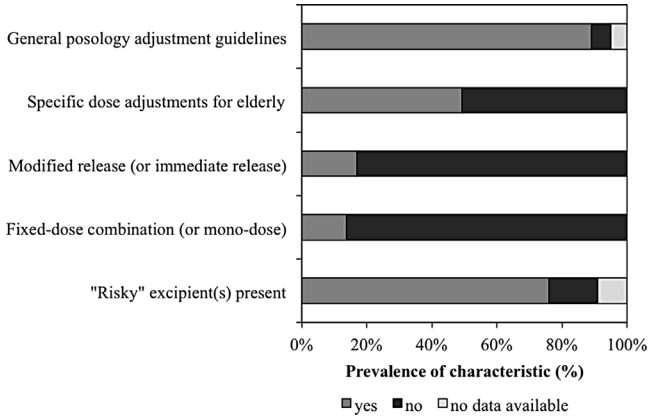

Fig. 1. Prevalence of key characteristics for each of the CVD formulations, presented as a percentage of the 262 formulations screened.