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Brand names of Portuguese medication: understanding the importance of their linguistic structure and regulatory issues

Nomes de marca dos medicamentos Portugueses: sua estrutura linguística e aspetos regulatórios

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Abstract Among other regulatory requirements, medicine brands should be composed of single names without abbreviations to prevent errors in prescription of medication. The purposes of the study were to investigate the compliance of a sample of Portuguese medicine brand names with Portuguese pharmaceutical regulations. This includes identifying their basic linguistic characteristics and comparing these features and their frequency of occurrence with benchmark values of the colloquial or informal language. A sample of 474 brand names was selected. Names were analyzed using manual (visual analyses) and computer methods (FreP - Frequency Patterns of Phonological Objects in Portuguese and MS word). A significant number of names (61.3%) failed to comply with the Portuguese phonologic system (related to the sound of words) and/or the spelling system (related to the written form of words) contained more than one word, comprised a high proportion of infrequent syllable types or stress patterns and included abbreviations. The results suggest that some of the brand names of Portuguese medication should be reevaluated, and that regulation on this issue should be enforced and updated, taking into consideration specific linguistic and spelling codes. Key words Commercial medication brand names, Qualitative analysis, Language, Linguistics, Medication legislation

Palavras-chave Denominação comercial do medicamento, Análise qualitativa, Linguagem, Linguística, Legislação de medicamentos

Lisboa.

Resumo Entre outros requisitos regulatórios, o nome dos medicamentos de marca deve ser composto por um único nome e não integrar abreviaturas para evitar erros de medicação. Os objetivos do estudo foram: investigar a adequação de um grupo de nomes de medicamentos de marca portugueses à regulação farmacêutica do mesmo País; identificar as suas características linguísticas básicas e comparar essas características e a sua frequência com valores de referência da língua corrente ou informal. Foi selecionada uma amostra de 474 nomes. Os nomes foram analisados com recurso a métodos manuais (análise visual) e automáticos (FreP - Frequency Patterns of Phonological Objects in Portuguese e o MS word). Um número significativo de nomes (61,3%) não estava em conformidade com o sistema fonológico (relacionado com a forma sonora das palavras) e ortográfico do Português (relacionado com a forma de escrita das palavras), tinha mais de uma palavra, continha uma alta proporção padrões silábicos e acentuais raros, e incluía abreviaturas. Os resultados sugerem que alguns dos nomes das marcas medicamentos portugueses devem ser reavaliadas e os aspetos regulatórios atualizados, tendo em consideração as características específicas do sistema linguístico e ortográfico português.

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Introduction

The names of medicinal products must be clear, legible and not associated with information of a promotional nature, thus ensuring their safe use and avoiding medication errors^{1,2}. Preferably, these names should not contain²⁻⁴:

- . abbreviations, which might be ambiguous, unfamiliar, or unknown (and thus opaque) to the patients, pharmacists and/or prescribers,
- adjectives (e.g. 'rapid', 'hiper' in Portuguese or 'hyper' in English, etc.), which might suggest the existence of enhanced medicinal proprieties,
- symbols (e.g. '+'), which might also be ambiguous or misleading and, words with hyphens, because hyphens increase word extension and reflect morphologic or structural complexity⁵.

Considering the Portuguese regulation² the names of medicines may be classified according to one of the three following groups: 1) names of fantasy, 2) the common designation of the drug followed by a brand, or 3) the common designation of the drug followed by the name of the applicant or the Marketing Authorization Holder. In particular, "the fantasy name corresponds to a term without a proper meaning, fruit of the imagination, devoid of correspondence in the reality, which objective is only to allow the production of sounds based on the reading of certain combinations of letters." In this context, the brand names of medicines correspond to the group 1 - names of fantasy, the names of branded generics medicines correspond to group 2 - the common designation of the drug followed by a brand; and the names of the generic medicines correspond to group 3 - the common designation of the drug followed by the name of the applicant or the Marketing Authorization Holder². Also, in accordance with the Portuguese regulation (Law Decree 176/2006, article 3, available at: http://portalcodgdh.min-saude.pt/images/c/cf/ DL176-2006.pdf), "a medicine is any substance or associations of substances with preventive or curative proprieties on human diseases or on their symptoms through exerting a pharmacological, immunological or metabolic action to restoring, correcting or modifying physiological functions, or that might be used or administered in humans to establish a medical diagnostic."

In general, medicine brand names should be formed by just a single word^{2,4}, thus making it easier to recall¹. Despite the fact that there are reports cited in health written materials of patient deaths as a consequence of misunderstandings related to the interpretation of abbreviations⁶,

according to some regulation their use might be acceptable in medicine brand names when they provide additional information on the characteristics of the medicinal product (e.g. route of administration)^{2,7}. The regulation on the formal characteristics of medicine brand names, such as those from the National Medicines Agency IN-FARMED, I.P. - Autoridade Nacional do Medicamento e Produtos de Saúde, I.P. (the Portuguese medicine authority of medicines and health products)², the European Medicines Agency⁷, or the Australian Medicines Agency8, does not include any specific recommendation on the adequate number or types of syllables, letters, or other characters (e.g. symbols). However, the Food and Drug Administration (FDA) (the United States Department of Health and Human Services agency that among other is also responsible for assuring the safety and efficacy of the medicines) is somewhat more specific in this respect: (a) the applicant or sponsors are encouraged to provide a written transcription of the intended pronunciation of the brand (e.g. using the phonetic alphabet, that is an alphabet internationally accepted to transcribe all sounds/languages in non-ambiguous way, which might be consulted in the following link https://www.langsci.ucl. ac.uk/ipa/IPA_chart_(C)2005.pdf), because this might impact on how the names are pronounced in practice, to promote their precise identification and the prevention of medication errors, and (b) modifiers (e.g. abbreviations) need to be explained/detailed, because their use might suggest different meanings to health professionals or patients. Furthermore, the FDA critically reviews all proposed names, for instance using databases and computational linguistic methods to evaluate similar spellings, and orthographic or phonological similarities, that are similarities related to the written or sound form of the words, respectively. In these evaluations, attributes are screened such as: identical prefix (the use of an affix at the beginning of a word), infix (the use of an affix inside the word), suffix (the use of an affix at the end of a word), length, stress, and number of syllables9. The affix might be considered a segment (or a specific part of a word) that act as a modifier^{5,9}.

The length of brand names, for instance, is a fundamental issue for their development and conception. In general, short names are more easily spelled, pronounced and recalled (e.g. names with 4 or less letters in the case of English words, as tall, ball call, etc.). Nevertheless, overly short names are also not advisable, because

these words are more likely to present common sounds or similar orthographic parts (e.g. phonological neighbors, which are words containing at least one common sound/part, such as Actos® and Actonel®4,10-13. According to Lambert et al.14, 32,748 names of branded medicines from a database of medicines marketed in the United States, contained an average of 1.7 words, 3.5 syllables, and 10.3 letters (SD = 6.74). Another source reports that the most common US brand names comprised 8 letters¹². Word size in number of letters has been shown to impact on subjects' word recognition. This has been shown for instance in the English Lexicon Project (ELP). ELP is a multicenter study that among other aims to collect a large number of data on behavioral tasks with words and non-words and that enrolls presently six testing Universities (http://elexicon.wustl. edu/). In this project, 33,006 words (with 3 to 13 letters) were evaluated and 816 participants were enrolled in a lexical decision task, that is an experimental task in which the participants had to recognize different words^{15,16}. Results from this study support that, irrespective of the lexical frequency (the probability of using a word in a certain language), the number of syllables, and the number of neighbors (different names that are almost identical in terms of their sound form), the accuracy and reaction time in the recognition of words correlate with the number of letters of the word. In particular, an inhibitor effect in word recognition was detected on words with 8 to 13 letters, with these words taking longer to be recognized than shorter ones¹⁵. In another study (140 participants), specifically conducted on Portuguese, three disyllabic words (words with two syllables), as tema in Portuguese (syllabic division: te.ma) or 'theme' in English, and three trisyllabic words (words with three syllables), as tomada in Portuguese (syllabic division: to.ma. da) or 'capture' in English, were tested, in an auditory and oral task (first the words were orally produced and then the participants had to orally reproduce all their segments or sounds). It was found that longer words were more prone to be orally produced with errors: 46% of the disyllabic words were orally produced correctly vs. 30% of the trisyllabic words¹⁷.

Discrepancies between the general sound patterns of the language and the sound patterns found in medicine brand names may also increase readability problems. There are a number of properties that characterize words in European Portuguese. In what follows we describe some basic features of the language that will allow us

determining the extent to which medicine brand names may deviate from the common sound patterns found in European Portuguese words.

In European Portuguese, word stress may occur in one of the three final syllables in a word^{18,19}. Depending on stress location, words are classified as: (a) oxitone (stress on the last syllable), (b) paroxitone (stress on the penultimate syllable) and, (c) proparoxytone (stress on the antepenultimate syllable)19-21. Portuguese words with penultimate and final stress are more frequent than words with antepenultimate stress (74% and 22.8% vs 3.2 %, respectively)²⁰. Importantly, word stress is a fundamental issue to the appropriate processing, understanding, and intelligibility of speech, as has been shown in several studies on stress patterns^{22,23}. For example, in a recognition task of spoken English words, it was found that both native (English-speakers) and non-native English speakers (Dutch speakers) used stress patterns to identify the relevant words22.

Other basic linguistic features that influence how words are processed, read, or written, include: (a) the phonetic segments, or the elementary sounds of the language, that compose words, such as consonants (C), vowels (V), nasals (N) (vowel and vowel-like sounds that are produced with nasal resonance) and glides (G) (vowel-like sounds that must occur with a vowel that functions as a syllable nucleus) and (b) the patterns of combinations of sounds within the syllables the patterns of combinations of sounds within the syllables that compose words - e.g. the Portuguese word medicamento in Portuguese or 'medicine' in English is formed of 5 syllables (syllabic division: me.di.ca.men.to), but only 2 syllable types, 4 of the type CV (me, di, ca and to) and 1 of the type CVN $(men)^{5,24,25}$.

The frequency of segments and syllable types may influence word processing. For instance, in studies involving word naming and lexical decision tasks, it has been found that words including more frequent syllable types were recognized faster than words with less frequent types of syllables^{24,25}. In European Portuguese, like in other languages, segments (for the most of the categories C and V) are grouped into syllables depending on their sound properties. Some rare consonantal sequences constitute ill-formed consonant clusters, and they trigger the insertion of a vocalic position (a V-Slot). This vocalic position allows segments to be parsed into syllables that conform to the language general laws for syllable formation. For example, while a consonant cluster like tr yields a well-formed syllable in Portuguese (as in the word dentro in Portuguese or 'inside' in English, which is syllabified as den.tro), a consonant cluster like ft in the Portuguese word afta or 'aphthous stomatitis' in English yields a ill-formed syllable structure (because in the Portuguese sound system ft cannot start a syllable, as in a.fta, and f cannot close a syllable either, as in af.ta). In the latter type of cases, a vocalic position emerges between the two consonants (a V-slot). V-slots allow the syllabification of words containing problematic consonant sequences, as in a.fV.ta, which then exhibits the typical syllabic pattern of the language (the pattern where syllables are formed of one consonant and one vowel, which is the most frequent syllable type in Portuguese)19. As a result, the word afta may be realized as afeta (or, to be more precise, ['afite] using the international phonetic alphabet).

The frequency of V-slot in available corpora of European Portuguese (or databases of texts of common language), such as the TQT (comprises 22994 words) and TA90PE1¹ (comprises 64757 words), is very low, corresponding to 0.07% and 0.2%, respectively. Both the corpus TA90PE and TQP are formed by common words, since the first is the result of the transcription of colloquial interviews from the different regions of Portugal, and the second is formed by transcriptions of oral samples collected in the Terra Quente Transmontana (a region in the North of Portugal)¹8,26. What is important for us here is that the presence of a V-slot in a word indicates that a given consonantal string is rare and phonologically problematic¹8,26.

Rare syllable types in European Portuguese include VG or CVGC. For instance, in the corpora just cited, these syllable types have been reported to account for only 1.51% and 1.21% of the total number of occurring syllables, respectively.

Importantly, above 90% of syllables found in Portuguese corpora belong to a very small subset of syllable types, composed of only 10 syllables types (including CV, CVC, CCV)²⁷.

Using a large sample of Portuguese medicine brand names, the purposes of this study were:

- 1. to investigate the compliance/agreement of medicine brand names with Portuguese regulation.
- 2. to characterize some of their basic linguistic and orthographic features,
- 3. to compare their basic linguistic features with reference frequency values of common language, thus assessing the extent to which the form of medicine brand names may deviate from the most common sound patterns found in European Portuguese.

Method

A random sample of Portuguese medicine brand names was obtained from the Portuguese prescribing guide²⁸. Approximately 25% of all medicine brand names available in this guide (531 brand names) were randomized, of which 57 were excluded for either being repeated (to avoid redundant analysis), or for comprising international nonproprietary names or the generic names used worldwide (to assure that only brand names were included in this study). The main reasons for not selecting generic names were the following: (a) generic and brand names present different structures, because generic names are formed by international nonproprietary names in association with the name of the marketing authorization holder and brand names are formed by invented names2, and (b) linguistic and orthographic rules are already available to adapt to Portuguese the names of generic medicines that are internationally marketed^{29,30}. For instance, for the translation of the name of active substances (e.g. generic names) the American Association of Physicians recommends: the use of i, t, f and e instead of y, th, ph and ae respectively, and to avoid k and w^{29} . These rules are very similar to those of the World Health Organization^{30,31}, and they are respected in the translation of Portuguese generic names which follow these general rules (e.g. the i is used instead of y, in the case of 'hydrocortisone' in English vs. hidrocortisona in Portuguese)30. Consequently, it was considered that the name of generic medicines should be studied in an autonomous investigation.

The assessments of the legal requirements were based on the criteria set out in the pharmaceutical regulation(e.g. names should comprise only one word and preferably not contain abbreviations)^{2,7,8}.

The medicine brand names were manually classified into 4 groups: Group 1 comprised names that might be considered as not being written in accordance with the orthographic system of European Portuguese³², Group 2 comprised names not written in accordance with that system, while Group 3 and 4 comprised names written in accordance with that system. This classification was performed taking into account the new Portuguese orthographic rules, given the inclusion of the letters k, y and w, as belonging to the Portuguese alphabet. However, it is important to highlight that these new rules only started to be mandatory for Brazil in 2009 and in Portugal they will only become mandato-

ry in 2016 (www.portaldalinguaportuguesa.org/ acordo.php). These three letters (k, y and w) were introduced in the Portuguese alphabet essentially because of the large scale introduction in the language of proper names and loan words from English origin (as currently happens in other languages of the world as well). In general, the use of these words only represented a very limited part of the Portuguese corpora. For instance, this can be seen searching the corpus CETEM-Publico (a database with 190 millions of words and specifically formed by journalistic texts, freely available at www.linguateca.pt/ACDC, where words like 'Hollywood' or 'Gulbenkian' clearly display a deviant orthographic shape). Given this, Group 1 includes names containing letters that were not part of Portuguese alphabet until recently (k, y, w). Group 2 includes names containing combinations of letters not allowed in the European Portuguese orthographic system (e.g. strings with double letters such as tt or zz, or ending with consonants different from r, l, s, m, n or x, such as t or d, and so forth). Group 3 includes names written in accordance with the European Portuguese orthographic system and excluding the names that comprise the letters k, y and w (in accordance to the rules of the previous orthographic convention legally approved) and Group 4 includes names integrating rare segments, such as names ending in n or x, or names containing V-slots (names containing unusual sequences of consonants such as $ft)^{27}$.

It was pre-defined that if a name were to cumulatively comprise the letters k, y and w (Group 1), combinations of non-canonical segments or combinations of letters non-existent in Portuguese (Group 2) and/or end in n or x or contain V-slots (Group 4), this name would be assigned as an element of Group 1, and that if a name were to cumulatively comprise combinations of non-canonical segments (Group 2) and/or end in n or x, or contain V-slots (Group 4), this name would be assigned as an element of Group 2. In both situations the names were classified in accordance to the situation that was considered as more deviant from the natural Portuguese patterns.

The variables studied are described in Chart 1, where the frequency of the type of syllables was also quantified. For our purposes, syllable types were classified as frequent or rare. The 10 more frequent syllabic of the Portuguese European referred to in the introduction section are the following CV, V, CVC, CVGN, CVN, VC, CVG, VN, CCV and VG^{26,27}. For the purpose of the present

study, syllable types were classified as frequent if they belong to the set of the ten most frequent syllable types in European Portuguese, or rare is they are not part of that set²⁷.

The linguistic variables 1 and 3 to 6 were quantified using the informatics tool FreP - Frequency Patterns of Phonological Objects in Portuguese³³. Given the algorithm used in this tool (a) the individual stress patterns of all the words that constituted the brand names were classified in accordance with the natural pronunciation patterns of Portuguese, therefore the possible existence of alternative non-Portuguese stress was not investigated – the rational here is that, by default, Portuguese users will pronounce medicine brand names following the general rules of the language for stress placement; (b) the letters y, k and w were respectively processed as i, c and v; and (c) the doubling of letters that does not exist in Portuguese was processed as just one letter, for instance tt was processed as t, because this corresponds to the way these letter sequences are pronounced by default. This way, none of the non-canonical names (foreign names not adapted to Portuguese) were analyzed in accordance to the phonologic and orthographic rules of others language. The options (a), (b), and (c) reflect the average European Portuguese reader, given that 41% of the Portuguese population self-report not to speak any other language³⁴: the Portuguese population is assumed to follow the natural phonological patterns of their native language when reading medicine brand names.

We should notice that European and Brazilian Portuguese present different phonologies. Thus, words may be read with different pronunciations and reference values for the frequency of occurrence of segments, syllables and stress patterns may also vary. Therefore, the results we report here cannot generalize to other varieties of Portuguese. We believe a specific evaluation of medicine brand names used in Brazil similar to the one developed here would be recommended.

MS Word 2010 for Windows 7 was used to quantify the number of: (a) letters (variable 2), (b) words with a hyphen (variable 7), and (c) expressions or words not allowed according to regulatory requirements (variable 9), applying the automatic search function of this program. Names containing abbreviations, numbers, or symbols (variable 8) were manually identified. Abbreviations may be classified as acronyms (or abbreviations susceptible of being read as a single word, e.g. PA, which English full correspondence is 'pressure aerosol' - see http://www.oxforddictionaries.com/

Chart 1. Variables studied.

Number of	Method	Objective(s) ^a	Citation(s)	
1 - Orthographic words (Tokens)	FreP	1, 2, 3	(Handler et al., 2004; Infarmed, 2012; Institute for safe medication practice, 2011) ^{1,2,4}	
2 - Letters	MS Word	2,3	(Lambert et al., 2005) ¹²	
3 - Syllables	FreP	2,3	(Food and Drug Administration, 2010; Vigário, Martins, & Frota, 2006) ^{9,26}	
4 - Syllable types	FreP	2,3	(Vigário, Martins, & Frota, 2006) ²⁶	
5 - Consonants, vowels, glides, and V-slots	FreP	2,3	(Lambert et al., 2005; Mateus & Andrade, 2000; Vigário, Freitas, & Frota, 2006) ^{12,19,27}	
6 - Words per stress position	FreP	2,3	(Aguiar & Vigário, 2010; Food and Drug Administration, 2010; Mateus & Andrade, 2000) ^{9,18,19}	
7 - Hyphenated words	MS Word	1, 2, 3	(Hyönä et al., 2004; Villalva, 2000) ^{3,5}	
8 - Words containing abbreviations (acronyms or initialims), numbers or symbols	Manual	1, 2, 3	(Mateus et al., 2004) ³²	
9 - Expressions or words not allowed according to the regulatory requirements ^b	MS Word	1	(Infarmed, 2012) ²	

^aObjectives: 1. to investigate the compliance of medicine brand names with regulations; 2. to characterize their basic linguistic features, and 3. to compare the values of their basic linguistic features with reference values for the language. ^b e.g. 'rapid', 'hiper'.

definition/english/acronym) or initialism (or an abbreviation susceptible of being read by pronouncing the initial letters, e.g. FML, which English full correspondence 'fluorometholone' – see http://www.oxforddictionaries.com/definition/english/initialism)³⁵. Thus, a qualitative analysis to distinguish between acronyms and initialisms was performed (Chart 1). This classification was done in the following way, one of the researchers read all abbreviations (acronyms or initialisms) and immediately after classified the abbreviation as an acronym or as an initialism. One expert in linguistics re-checked all the linguistic data, using the same procedure.

The occurrence of abbreviations in the names of prescription medicines and over-the-counter medicines (OTC) was specifically quantified and analyzed. This quantification was considered pertinent, because OTC might be acquired without the direct intervention of a health pro-

fessional^{36,37}, and this may increase the potential for problems originated from the presence of abbreviations in medicine brand names.

Despite the recommendation to not use abbreviations in medicinal information, such as package leaflets, when they are used their full meaning should correspond to the official language of the country where the medicine is marketed (e.g. CR or 'Controlled-Release' for English)38. In addition, according to some regulation the use of abbreviations in medicine brand names might be acceptable if they add information about the medicine (for instance, the abbreviation S in the case of the medicine Kompensan S®, might be considered useful for patients and health professionals, as a way of noticing the presence of a particular substance; Simethicone, in this medicine)^{2,7}. For this reason, the following aspects were checked by a pharmacist: (a) presence/absence of the full meaning of abbreviations in the content of the package leaflet, and (b) presence/absence of abbreviations corresponding to a language other than Portuguese.

The full meaning of abbreviations was confirmed in the package leaflet, when present. In the cases where the full meaning of an abbreviation was not described in the package leaflet, the information was obtained in the official sites for medical abbreviations such as Medilexicon³⁹ for English abbreviations, or in the glossary of the National Prescribing Guide for Portuguese abbreviations²⁸. It was important to verify the full correspondence of English abbreviations because, contrary to what would be expectable, abbreviations with full correspondence in English were also found within the brand names of Portuguese medicines. The package leaflets were consulted using a public Portuguese data base: the Infomed (available at https://www.infarmed.pt/infomed/ inicio.php)40.The full meaning of abbreviations was not checked on the outer package of the respective medicines, because of economic and logistic constraints that restricted access to such a large number of packages.

Results

Distribution by the 4 classificatory groups

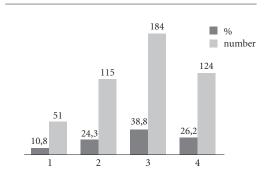
Overall, 24.3% of the names (115 of 474 names) were not written in accordance with the Portuguese orthographic system (Group 2). These names comprised non-canonical segments (or combinations of letters non-existent in Portuguese), such as the segments tt or ll, or the names ending in t, d or c (e.g. Nicotinell®, Novynette®, Atrovent®, Ronic® and Sinecod®). Also, 10.8% included the letter(s) k, y or w (e.g. Daktacort®, Alorexyl®, and Twinrix®) (51 of 474 names) (Group 1). Data are presented in Figure 1.

Names ending with t, d, and c were the most common in Group 2 (37.4%; 43 cases out of 115 names). Names ending in n were the most prevalent in Group 4 (63.7%; 79 cases out of 125 names). This group comprises names with rare structures in Portuguese, such as, the names ending in n (e.g. Rocephin®) or x (e.g. Dostinex®).

In the group of names comprising the letters k, y and w (Group 1), 8 names ended in n, 7 names contained more one letter of the type k, y or w, and 5 comprised V-slots. In the group of names containing non-canonical segments (or combination of letters that do not exist in Portuguese) (Group 2), 9 names ended in n, and 9

names comprised V-slots. The names were different in every case.

Among the 474 names: 384 (81%) were formed by one orthographic word, 64 (13.5%) by two words, and 89 (18.7%) by more than two words. A few names with 4, 6, and 9 orthographic words were also identified. Overall the 474 names comprised 615 words. The distribution of the number of words per name is presented in Figure 2.



- 1 Names containing the letters k, y and w
- 2 Names containing non-canonical segments
- 2 Names written in accordance with the Portuguese orthographic system
- 4 Names containing structures of low frequency in Portuguese

Figure 1. Percentage and names distributed by groups.

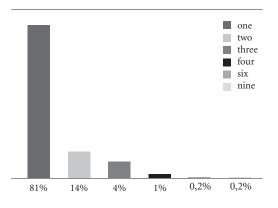


Figure 2. Percentage of the number of words in medicine brand names.

Word length: number of orthographic words, letters and syllables

The brand names contained 2 to 25 letters, of which 70.6% had 6 to 9 letters. Median of 8 and a mean of 8.7 (SD = 3.2) letters per name.

The average number of syllables per brand name was 3.7 (SD = 1.5). Among the 615 orthographic words that formed the 474 names, 96.1% contained 4 or less syllables, 11.4% a single syllable, 3.9% contained between 5 and 7 syllables and none contained more than 8 syllables.

Syllable types, segments, and V-slots

The ten most frequent syllable types in European Portuguese explain the syllabic structure of almost all brand names (93.2%; 1,649 of the 1,769 syllable occurrences). 116 names (24.5%) comprised at least one rare syllable type. Overall, 120 rare syllable types were identified: 13 (10.8%) in the names of Group 1, 28 (23.3%) in the names of Group 2, 29 (24.2%) in the names of Group 3, and 50 (41.7%) in the names of Group 4.

The 474 names were formed by 4,066 segments (with an average of 9 segments per word; SD = 3). The number of segments was determined by the sum of the number of consonants, vowels, and glides. The percentage of V-slots (n = 39, 2.2 %) was calculated in relation to the total number of syllables (n = 1,769), as a way of constituting an indicator of their occurrence. Data are presented in Table 1.

Number of words per stress position

The sum of words with final (385), penultimate (155) and antepenultimate stress (5) was 545. In general, final stress was predominant (70.6% of 545), when compared to penultimate (28.4% of 545), and antepenultimate (0.9% of 545) stress.

Hyphenated words

Hyphens were identified in 4.2% of names. A name with 2 hyphens was also found (Ben-uron®).

Table 1. Distribution of syllable types, segments, and V-slots in medicine brand names.

	Number of occurrences	%
Total number of syllables	1769	100
(more frequent + rare)		
Ten most frequent syllabics types		
CV	863	48.8
V	147	8.3
CVC	393	22.2
CVGN	5	0.3
CVN	58	3.3
VC	36	2
CVG	8	0.5
VN	27	1.5
CCV	108	6.1
VG	4	0.2
Total (more frequent)	1649	93.2
Rare syllable types		
VGC	1	0.1
CCVC	34	1.9
CCVCC	9	0.5
CCVG	1	0.1
CCVN	13	0.7
CGVC	2	0.1
CGVN	1	0.1
CVCC	52	2.9
CVGC	2	0.1
VCC	1	0.1
Other rare	4	0.2
Total (rare)	120	6.8
Segments ^a and V-slots		
Consonants	2313	56.9
Vowels	1730	42.5
Glides	23	0.6
Total	4066	100
Segments average	9	
Standard Deviation	3	
V-Slot ^b	39	2.2

C: consoants; V: vogals; G: glides; N: nasal.

Names containing abbreviations, numbers and symbols, and abbreviations full meaning

Thirty-six brand names (7.6% of 474) contained abbreviations and in one case two abbreviations were found in a single name, hence 37 abbreviations were identified: 4 belong to OTC names, 3 might be read as acronyms, with the remaining being read as initialisms, and 8 present full correspondence in English instead of Portu-

 $^{^{\}rm a}$ Segments = consonants + vowels + glides, $^{\rm b}$ *V-slots* percentages were calculated in relation to the total number of syllables (n = 1769).

guese. In only 3 cases was the full meaning of the abbreviations described in the package leaflets.

With respect to the presence of numbers and symbols, 6 brand names contained numbers in their structure (1.3% of 474 names) and 1 brand name enclosed a symbol, namely '+' (see Chart 2).

Prohibited expressions

Eight prohibited expressions² were detected in 21 brand names (Chart 2).

Discussion

Letters only recently introduced to the Portuguese alphabet and non-canonical segments

In the present study, the occurrence of names with letters k, y and w or containing non-canonical segments (associations of letters that are non-existent in Portuguese, such as tt), was quite prevalent, affecting almost half of the names. Given that it is well documented that the mental processing of words is dependent on an orthographic and phonological code (respectively related

Chart 2. Abbreviations, names and expressions not recommended/allowed.

Chart 2. Abbreviations, names and expressions not reco	inniciaca/anowea.
Abbreviations included specifically in names of over- the-counters medicines	C = vitamin C
Abbreviations that might be read as acronyms	S = simethicone
	DM = diethylamine
	R = hoarseness
	CA = continuous ambulatory
	PA = pressure aerosol
.,,	LA = long action
Abbreviations with full correspondence not given in Portuguese	CR = controlled-releases
	PA = pressure aerosol
	CPAD = continuous ambulatory peritoneal dialysis
	OD = once daily
	SR = slow releases
	LA = long action
	MR = muscule relaxant
	DC = direct current
Abbreviations with full description in the package	CAPD = continuous ambulatory peritoneal dialysis
leaflet text	M3 = mixture three
	B = polybacterial lysates
Names comprising numbers	'HBO 12®'
	'Q10®'
	'Cerbon-6®'
	'Debridat 200®'
	'HUMULIN M3®'
	'CAPD/CAPD 17®'
Names comprising symbols	'Depot Medrol + Lidocaine®'
Names comprising prohibited expressions	'rapid'
	Forte or 'Strong'a
	'Plus'
	Hiper or 'Hyper' a
	Pediátrico or 'Pediatric'a
	Infantil or 'Infant'a
	Adulto or 'Adult'a
	Junior or 'Younger person'a

^a The Portuguese word in italic and the correspondent translation between quotation marks.

with the written or oral forms of the words)41,42, this type of letters and segments might have a negative impact on the adequate memorization, recall and pronounceability of words, and consequently not be suitable to form brand names for medicines to be used by the Portuguese speaking population. In Portuguese, orthography presents a close correspondence to the sound, i.e. each letter corresponds to one sound. The specific cases of names containing double letters, usually consonants (e.g. tt or zz), seems to increase reading complexity: not only these cases deviate from the orthographic rules of the language, but they are formed of more letters than those required, since two characters represent single sound. Overall, the fact that these orthographic patterns were different from those that the readers are familiar with might cause doubts as to the way words are correctly read, written or pronounced. In this context, brand names that cumulatively include linguistic features from different groups (e.g. names containing letters recently introduced in the Portuguese alphabet, such as the k, y and w plus non-canonical segments) are likely to be more complex and processed more poorly.

Number of orthographic words

A considerable number of names included at least two orthographic words. This might negatively influence their adequate pronunciation and memorization^{1,2,4,8,12,14,43}.

Word length: number of letters and syllables

Most of the names in this study contained up to three syllables, a pattern of distribution also found in the common/colloquial Portuguese, such as that represented in the TQP and TA90PE (see the introduction)^{26,27}. Thus, the word length patterns of the brand names also were very similar to those of others names available on European Portuguese databases corpora^{26,27}.

Although the average length of Portuguese brand names seems appropriate, as far we known there are no studies specifically on the appropriate length of Portuguese brand names. Therefore, it would be desirable to confirm the suitability of the brand names length before their marketing approval (e.g. through using experimental studies). A number of facts suggest, nevertheless, that the average length of the Portuguese brand names may be appropriate: 1) the brand names slightly longer than the average Portuguese

words (or the names with 3 or 4 syllables)^{26,27}, are possibly more appropriate to feature on the outer packaging and to use within the text of the package leaflets, because presumably these names will be better distinguished and less confusable, 2) overly long names (namely names with more than 4 syllables) are not advisable so as to assure their adequate memorization, recall and pronunciation¹⁰⁻¹², because longer words take more time to be identified (e.g. in reading tasks)44, and 3) too short names (or the names with less than 3 syllables) are also not advisable, because they are usually related with a greater number of phonological neighbors (different names that are almost identical in terms of their sound form)45. This situation probably increases the possibility of correspondences with other words and therefore the risk of confusion between similar names of medicines.

The Portuguese medicine brand names exhibit an average size in terms of number of letters and syllables very similar to those described in studies involving names of medicines marketed in other countries¹⁴. This was not surprising given that many of these medicines were also available in other countries with the exact same name, consequently confirming that it is very likely that these names were not initially invented/developed in Portuguese speaking countries⁴⁶.

Syllable types, segments, and V-slots

The predominance of the ten most frequent syllable types in European Portuguese²⁷ apparently confirms the existence of some similarity between the structure of brand names and the general Portuguese words. Nevertheless, it was possible to identify in the brand names a high proportion of syllable types that are rare in Portuguese (e.g. CVCC and CCVC)27. As expected the rare syllable types were much more prevalent (almost twice as many) in the group of names containing structures of low frequency, such as the names ending in n or x, because these deviant structures will indirectly promote the formation of rare syllable types. Again, deviant syllable structure might yield lower readability of some Portuguese medicine brand names.

A high prevalence of vowels and consonants was found in the sample of names, similar to those in other European Portuguese corpora (or databases of texts that are used to estimate the frequency of words, segments, letters, symbols, or punctuations signs in a certain language)^{18,26}. By contrast, a lower proportion of glides and a great-

er proportion of V-slots were found in relation to the common patterns. For instance, the segments were distributed as follows: 48% vowels, 46% consonants, 5.8% glides, and 0.2% V-slots in the corpus TAP90PE (22,994 words) (we recall that these are rare elements that emerge to break sequences of segments that do not form proper syllables in the language, as *dv* in the Portuguese word *advogado* or 'lawyer'in English)¹⁸. Assuming that V-slots, only emerge with segmental sequences that are not allowed by the general laws of the language for the combination of segments, the proportion of V-slots found in brand names also suggests the low readability of some Portuguese brand names.

Stress distribution

The frequency of the three stress patterns in the medicine brand names under observation was clearly different from that commonly found in the language^{18,26}. In fact, in our data words with final stress were more prevalent than words with penultimate stress. As we have seen in the introduction section, according the data available in a reference database of Portuguese, words with penultimate stress are more frequent than words with final stress (22.8%) and antepenultimate stress (3.2%), and similar results have been reported elsewhere 18,20,26.

Despite the proportion of the three stress patterns being clearly different from those in common language, it is not expected that this should produce a very significant negative impact on the readability of names, because the words with stress on the last syllable are also fairly common in Portuguese.

Names containing hyphenated words

The proportion of words with a hyphen was very limited in the sample of brand names. This seems to be a good result, given that the presence of hyphens increases word extension and correlates with a higher morphological complexity, since they indicate that the names are formed by associations of two or more words (as in *arco-tris* in Portuguese or 'rainbow' in English). Therefore the use of hyphenated word in medicine brand names probably also negatively impacts on their readability^{3,5}.

Names containing abbreviations

Various abbreviations were identified in the sample of brand names, although their use is not recommended^{1,2,4,12}. Additionally, many of these abbreviations referred to English technical terms (e.g. CR meaning 'controlled-release' or PA meaning 'pressure aerosol'), which might represent an additional issue to Portuguese monolingual speakers, and also to non-health professionals who are usually not familiarized with the use of technical terms. Unexpectedly, in many cases the full meaning of each abbreviation was also not detailed in the text of package leaflets. Therefore names containing abbreviations might be considered less readable and in some cases compromise the safe use of medicines^{6,47}.

In the case of OTC medicines, exceptionally some abbreviations used in their names might be considered compliant with the legal requirements, as a result of their potential advantageous². For instance: (a) in the case of Aspirin C® and Kompensan S®, the C and S probably promote a better differentiation relative to other medicinal products with similar names (Aspirin® and Kompensan®, respectively) or allow the composition of the medicine to be better identified, (b) in the case of Mentocaina-R®, the R (rouquidão in Portuguese or 'hoarseness' in English) constitutes a cue to identify one of the symptoms that the medicine treats, and (c) in the case of DM, the DM (dores musculares in Portuguese or 'muscle pain' in English) might also be associated with the treatment of a specific health issue. However, if the patients do not have any previous knowledge about the medicine, the use of these abbreviations is not likely to be beneficial, because they will not be able to assign any meaning to these abbreviations.

The fact that almost all abbreviations identified in this study were acronyms, presents even more readability problems, because the pronunciation of initialisms is easier than that of acronyms³⁴.

Names containing numbers and symbols

Some names were identified comprising numbers or symbols in this study. Although their use is not recommended because of the risk of patients' misinterpretation and low readability², it is possible to identify some possible positive reasons for their use: (a) it may facilitate patients' memorization and recall of medicine brand names by increasing their phonological

extension – in other words, the oral form of the name is longer than the correspondent oral form in the case of the symbol being omitted (e.g. Cerbon-6® is read as Cerbon-seis in Portuguese or 'Cerbon-six' in English; '+' is read as mais in Portuguese or 'more' or 'plus' in English); or (b) it may promote the distinction between similar brand names (e.g. the use of M3 probably helps to better distinguish between different types of Humulin® insulins). By contrast, their use might also be associated with negative reasons such as increasing the complexity of medicinal brand names, as well as constituting an element of promotional nature (e.g. if their use increases the memorization of medicine brand names in particular by healthcare prescribers). Overall the use of numbers and symbols in medicine brand names for possible reasons of a promotional nature should be adequately controlled and supervised by marketing authorization holders and health authorities.

Names containing prohibited expressions

Also some names containing legally unacceptable expressions were identified, such as Hiper in Portuguese (or 'Hyper' in English), 'Strong' and 'Plus', also contributing to the possible existence of non-adequate names. The use of these expressions might (a) incorrectly suggest that medicines exhibit enhanced therapeutic actions, (b) influence the prescription patterns of physicians, or the acquisition of OTC medicines by patients.² Although the expressions 'Rapid', 'Pediatric', 'Infant', and 'Adult' are also not recommended, their use might be explained by the following facts: (a) in the case of insulin, 'Rapid' might facilitate the distinction from insulin with prolonged action and similar names, and (b) 'Pediatric', 'Infant' and 'Adult' might facilitate the identification of the population group for which the medicinal product is intended².

Limitations

The formal similarity of medicine brand names, such as Dynapen® and Dynacirc®12, was not specifically evaluated, because as far we know there are no specific automatic tools that allow performing this task in Portuguese. This screening is very important, due to the risk of potential confusions between similar drug names, with potential harm to the patient 10-13. The same type of screening using the names of generic products,

medical devices, or other body-care products would also be advisable.

Practical Implications

Regulation should state/define the most adequate linguistic characteristics for each language to assure the readability of medicines names by the local relevant users.

The linguistic characteristics of brand names are very important to the commercialization and marketing of medicines, because these features might influence the adequate memorization and pronunciation of brand names by health professionals and patients. Also, the use of similar names might be misunderstood by patients12,14. Besides performing descriptive and qualitative studies, it is also advisable the realization of experimental studies with patients for defining the best word shapes for the adequate memorization, recall and design of brand names for each language. Furthermore, to date there are no specific golden rules for developing the name of brand medicines in Portuguese. The suitability of medicine brand names for a certain speaking/reading population should be investigated for each individual language, because linguistic rules and orthographic conventions vary cross-linguistically⁴⁸. Similar experimental studies are also recommended to the names of generic medicines.

Software tools specifically developed to study the characteristics of Portuguese brand names, such as the automatic detection of phonological neighbors (different names that are almost identical in terms of their sound form), should be developed in order to avoid the approval of too similar names. The adaption of the brand names written in accordance with the orthographic system of other languages to Portuguese (e.g. the use of the letters k, y and w or non-canonical segments) seems also advisable, for instance following a procedure similar to that applied to the names of generic medicines (e.g. use of i, t, f and e instead of y, th, ph and ae respectively, for instance in 1) Pentoxifilina in Portuguese, that in English is translated as 'Pentoxifylline', 2) Petidina in Portuguese that in English is translated 'Pethidine', 3) Morfina in Portuguese that in English is translated as 'Morphine' and 4) Hemocoagulase in Portuguese that in English is translated as 'Haemocoagulase')29,30.

Although the names of brand medicines were specifically investigated in this study, it is likely that the same or similar linguistic principles might be applicable to other Portuguese brands, such the brands of cosmetics, medical devices, food, generic medicines or herbal products^{49,50}.

Given that Portuguese is the fifth most widely spoken language in the world (spoken by approximately 273 million people)⁵¹, the occurrence of the letters k, y and w, that might be used within non-Portuguese words or non-canonical segments in the names of brand medicines might be especially important, because these names might also be marketed in many countries other than Portugal, where Portuguese is also the official language (e.g. Brazil, Angola, or Timor).

Moreover, the real impact of using certain orthographic patterns in the name of medicines is not completely clear/known (e.g. abbreviations/symbols), consequently more research on the topic is needed. Regulatory authorities should be more involved in the supervision of medicine brand clarity and pronounceability during the process of medicines approval². Besides of being involved in the creative process of inventing brand names, marketing authorization holders should assure their appropriateness.

Conclusions

Many issues were detected for the brand names in this study, which might promote a lower readability of Portuguese brand names. Overall, some names were formed by more than one word or contained letters only recently introduced in the Portuguese alphabet (y, k and w), as well as non-canonical segments (or associations of letters non-existent in Portuguese), rare syllabic types, V-slots (rare segments/parts of words that are deviant from the common patterns of the language), abbreviations, numbers, symbols, hyphenated words, and prohibited expressions according to the pharmaceutical legislation. These suggest that some Portuguese brand names might need to be reevaluated by marketing authorization holders or medicines authorities. Updating the pharmaceutical regulation on this issue is also advisable, given that the linguistic features of brand names are not detailed enough in the Portuguese and European regulation.

Collaborations

C Pires, M Vigário and A Cavaco contributed to the conception, design, development, analysis and writing-up of the manuscript.

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