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REVIEW-THEMED SECTION

Developing patient-centric medicines for older people: Reflections from the draft EMA paper on the pharmaceutical development of medicines for use in the older population

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Increased global longevity requires a re-evaluation of current structures in society to adapt to the consequential demographic shift. As (very) old people are prone to impaired human organ and body functions resulting in, for example, multimorbidity, polypharmacy, hospitalisation and problems in medication management, it is increasingly acknowledged that re-evaluations should include the suitability of pharmaceutical patient care as one of the cornerstones of public health. Following the 2011 European Medicines Agency (EMA) Geriatric Strategy, in 2017 the EMA published the draft Reflection paper on the pharmaceutical development of medicines for use in the older population. The draft paper was opened for public consultation and specific attention and feedback (either supportive or with a proposal for revision) was asked on three design aspects: tablet breaking, drug administration through enteral feeding tubes and medication management. Following publication, the draft paper was presented at two public conferences attended by participants from different disciplines. This manuscript is intended to draw the attention of different stakeholder parties to the urgent need to collaborate on the emerging issues arising from increasing longevity and multimorbidity, and especially those associated with pharmaceutical patient care and drug product design, including the need for collaborative research into existing or emerging knowledge gaps. The manuscript focuses on the three aforementioned aspects of pharmaceutical development (tablet breaking, drug administration through enteral feeding tubes and medication management) as these highly relate to medication safety and efficacy and constitute persistent and typical challenges for older people, caregivers and healthcare professionals in daily clinical practice.

KEYWORDS

aged 80 and over [MeSH], clinical pharmacology, drug regulation, clinical pharmacology, health policy, clinical pharmacology, medication safety, drug development, drug delivery, European Medicines Agency (EMA), medication errors [MeSH], public health, regulations, technology pharmaceutical [MeSH]

1 | INTRODUCTION

Increased global longevity necessitates a re-evaluation of the way societies are organised to adapt to the social, economic, environmental and healthcare consequences of the associated demographic shift.[13] Where an optimal strategy in the provision of healthcare services would be characterised by a holistic vision and multi-, inter- and transdisciplinary work between, for example, medical and pharmaceutical care, drug development, accessibility, human factors, housing or social security, such a strategy cannot mature without domain-specific understanding of expected challenges, potential solutions and useful interim measures.[4,5]

In 2011, the European Medicines Agency (EMA) published its Geriatric Strategy to ensure that medicines for older people are well studied and of high quality, and that users are well informed about their use.[6] In the context of this strategy, the need to provide further recommendations to stakeholders on the way the drug product design could be tailored to address the specific needs of older people relevant for medication safety and efficacy was acknowledged in 2013 and the drafting of a reflection paper on the pharmaceutical development of medicines for use in older people was started.[7,8] During the drafting process, the World Health Organizations (WHOs) World Report on Ageing and Health was published, which describes a framework for action to promote healthy ageing and the concept of functional ability.[9] This report clearly supports the EMA incentive.

In 2017, the first draft of the reflection paper was published and opened for public consultation.[10] Subsequently, the paper was presented at the March 2017 APV Graz meeting Medicines for older adults: Getting prepared for the scientific and regulatory evolution, and the June 2018 DIA Basel Chemistry Manufacturing Controls (CMC) workshop on Medical Errors Due to Product Design and Development. Stakeholder feedback revealed a common agreement on the importance of adapting drug development and pharmaceutical product design to the needs of older patients to support medication safety and efficacy. It was also considered highly relevant to address the significant knowledge gap in developing senior-friendly medicines and resolve matters through multi-, inter- or transdisciplinary research.

Public health relies on adequate medical and pharmaceutical patient care to ensure medication safety and efficacy, and realise the desired health outcomes. This manuscript is intended to draw the attention of a wide stakeholder audience to the progress in regulation connected with the urgency to collaborate on the emerging issues arising from increasing patient longevity and multimorbidity, with a special emphasis on pharmaceutical patient care. The manuscript discusses the draft EMA reflection paper on the pharmaceutical development of medicines for use in the older population by summarising its history and focussing on the three main items of public consultation (tablet breaking, drug product administration through enteral feeding tubes and medication management) as these items are the most frequent challenges for patients, caregivers and healthcare professions in current daily clinical practice. It is believed that this approach will increase the awareness of urgency, promote discussion of the draft reflections by a wide stakeholder audience, initiate research into existing and emerging knowledge gaps, and foster regulatory submissions and subsequent marketing of high-quality and senior-friendly medicines.

What is already known about this subject

- Older people's opportunities to spend additional life years in good health and well-being vary among regions.
- Generally, ageing increases the demand for medical and pharmaceutical patient care.
- Medication safety is promoted by senior-friendly medicines.

What this study adds

- This manuscript describes the European draft reflections on senior-friendly product development.
- The manuscript is intended to increase awareness about current progress in regulation to promote interdisciplinary discussions and foster collaborative work, and initiate science into existing knowledge gaps

2 | EMA DRAFT REFLECTION PAPER

The draft reflection paper was based on a three-pillar approach to summarise the available data and promote discussion among stakeholder parties, ie, evaluation of (a) scientific literature and post-marketing data; (b) practical issues and medication errors reported by healthcare professionals; and (c) the need to ease/reduce the burden of medication use by patients and caregivers.[7,10]

As for paediatrics, the paper was adopted for public consultation together with a note calling for specific consideration and feedback (either supportive or with a proposal for revision) to specific topics.[11] The EMA was interested to know whether stakeholders agreed it would be best to publish the document as a reflection paper, a type of paper that is intended to summarise the available data and support stakeholder discussion, or whether it would be better to turn the document into a guideline intended to provide guidance that should be followed as soft law.[12] The anticipated advantage of a guideline was that every company would not only have to consider the document during drug development, but also ensure that the relevant conditions would be fulfilled at the time of marketing authorisation. A disadvantage could be that guidance based on limited data may discourage stakeholder discussions and hinder incentives for other (innovative) approaches.

Historically, quality guidelines and reflection papers were intended for industry or for industry and assessors. However, the draft reflection paper for older people clearly acknowledges that medication safety requires multi-, inter- and transdisciplinary work. Thus, as a second point, the EMA was interested in hearing if the reflection paper or guideline should involve stakeholders beyond the typical stakeholders from industry and regulatory authorities such as drug developers in academia, device experts, patient representatives, community and hospital pharmacists, medical doctors, lay caregivers, Health Technology Assessment (HTA) experts and others who could provide input as well as for whom the reflections could potentially be relevant.[10]

Besides a third point on preferred terminology (older patient/people/population versus the elderly), specific consideration and feedback was sought on tablet breaking, drug product administration through enteral feeding tubes and medication management. These items constitute typical challenges in daily clinical practice for patients, healthcare professionals and caregivers that are highly relevant to medication safety and efficacy.

3 | TABLET BREAKING

Tablet breaking is a well-known strategy for dose reductions in situations where a drug product is not commercially available in the lower dose and/or when the use of alternative dosage forms is not a feasible option. Tablet breaking is also commonly employed to ease the swallowing of the intact tablet dose or to reduce cost. Moreover, it is known that tablets may be crushed and mixed with food or drink to ease swallowing and/or cover taste. Tablet breaking is common in older people even though they may experience that tablet breaking is difficult, painful, or impossible without the use of a tablet splitter or other household tool as a coping strategy.[13,14]

Despite being a generally accepted handling in clinical practice, it is generally acknowledged that tablet breaking may affect medication safety and efficacy. Breaking may result in inaccurate doses when the tablet does not break into equal parts or when the active substance is not distributed homogeneously in the tablet itself.[1315] The stability of tablet parts may not be ensured in storage, resulting in reduced doses and potentially harmful impurities.[16] Patient acceptability and adherence may be reduced when taste masking is affected and the bad taste of the active substance becomes (more) apparent on swallowing.[17] Also, patients and caregivers may not realise that some tablets are not suitable for breaking because of their specific design aspects, meaning breaking may result in dose dumping or a lack of effect.[18] When tablet parts are mixed with food or drink, chemical or physical interactions may occur and the stability or bio-availability of the tablet parts may be affected.[19,20]

To ensure that marketed tablets are broken into equal parts when divided by hand, the European Pharmacopoeia (Ph. Eur.) developed a test for tablets for which the lower dose was authorised.[21] The test is well accepted, although some experts consider the criteria may be rather (too) relaxed for products where dosing is considered critical, eg, levothyroxine and anti-epileptics. Moreover, some experts consider it is not appropriate that companies do not need to comply with the test when breaking is only authorised for ease of swallowing. They consider that off-label use cannot be ignored, and it should be acknowledged that many tablets are broken for off-label dosing. Also, some experts question the prognostic validity of the test for the older patient population as the test can be performed by any operator whereas it is known that technicians break better than the general public and the general public has better hand motor function than older people.[22]

In the context of an increasing older population, some experts consider it is time to adapt the Ph. Eur. requirements to ensure that any marketed tablet with a break mark can be easily and accurately broken by the concerned patient population(s). However, companies may withdraw products from the market if they do not consider it worth the time and expense to comply with any new Ph. Eur. requirements. Where alternative trademarks and alternative presentations of a particular medicine do not exist, this may result in drug shortages, which will not only affect the (commonly older) patients in need of lower doses, but also the general public who are using the intact tablet. All this underpins the need for a timely review of requirements affecting new and marketed products to ensure safe and effective medication use by the vulnerable older patient population.

The draft EMA reflection paper states that companies may (but do not need to) refer to the ability of the break-mark to divide tablets into equal parts. This technical information is considered acceptable even in cases where the lower dose is not recommended in the authorised product information (Summary of Product Characteristics and Package Leaflet, SmPC/PL). In addition, the paper states that a justified portion of home-dwelling older people should be able to break the tablets by hand without any relevant pain or discomfort and that the company should develop and justify a test method for this purpose. Both reflections clearly bridge real-world clinical practice with regulatory expectations. More research into this domain is needed, eg, on the question of which patient characteristics predominantly determine their ability to break tablets by hand.[23]

4 | ENTERAL FEEDING TUBES

Feeding tubes are commonly used in patients who are unable to safely swallow food or drink by mouth or who are experiencing difficulties taking the necessary daily caloric intake. This commonly relates to people who are seriously ill or suffering from swallowing disorders or to patients at both ends of the life span.[24,25] Where administration of a drug product through a tube is the only or the preferred route of administration, there is a need for adequate information to support or alternatively disprove this administration procedure.[26,27] Where such information is missing in the SmPC/PL, healthcare professionals have to rely on the best available scientific information and knowledge (eg, professional handbooks, literature, company helpdesk) and develop their own procedure. When product-specific characteristics related to drug stability, bioavailability, adhesion to enteral feed tube wall and

the effect of prior mixing with food or drink are not available, patients might be exposed to a risk for adverse outcomes whereas such risk could (easily) have been avoided by adequate information in the SmPC/PL.

Currently, the administration of drug products through an enteral feeding tube has only been studied for a small number of drugs. For example, on 21 October 2018, a search in the database of the Dutch regulatory authorities (https://www.geneesmiddeleninformatiebank.nl/en/) for nasal tube anywhere in the SmPC resulted in three relevant hits and none for the word gastrostomy. In addition, a search in the EMA database for human medicines, authorised, European Public Assessment Report (EPAR) resulted in 109 hits for nasal tube and 19 for gastrostomy. Thus, there is urgent need to close this information gap.

In 2014, the European guideline on paediatric drug development stated that companies should realise that drugs may need to be administered to children through a feeding tube.[28] The guideline requires companies to address the feasibility of administration of a drug product through a feeding tube where this would be the main route of administration or a very likely option, and to include the relevant instructions (or warnings) in the SmPC/PL. Aspects to be addressed during drug development included dose recovery, the dosing volume, particle size, viscosity, chemical compatibility with the tube material, the risk of physical blockage and the volumes for tube rinsing. The reflections on enteral drug administration in older people in the draft reflection paper for older people are very similar to the guidance already adopted for children.[10,28]

Acknowledging an urgent need for further information on the administration of drug products through a feeding tube for patients at both ends of the life span, and acknowledging that a question and answer (Q&A) document generally requires less time for development than a full reflection paper or guideline, in 2018 the EMA published a Q&A on the minimum data requirements for oral immediate products to be administered through feeding tubes to patients of any age. This Q&A focuses on the ease of administration and chemical compatibility. For example, it addresses the ease of administration by pushing the plunger with reasonable finger effort, or how the product can be modified, eg, diluted with water to ease the administration process. The Q&A states that repeat use in vitro studies should be performed and that studies should mimic the intended clinical practice, including use with commonly used materials (eg, polyurethane, polyvinylchloride and silicone). It also states that in the normal case, leachable and extractable studies are not needed on the basis of a short transient contact time between the product and the tube material. The Q&A emphasises that it is not necessary to consider all types of combinations of tubes, doses, flush volumes etc as a bracketing and/or worst-case approach is considered sufficient.[29]

5 | MEDICATION MANAGEMENT

Older people may encounter therapeutic complexities, including difficulties opening medication packages or remembering when to take which product from the overall medication regimen.[30] To undertake daily activities outside home, they may also need to transport medicines with them on a daily basis or for emerging situations. Multicompartment compliance aids (MCAs), also referred to as pill boxes, are commonly used to mitigate such practical medication problems. Filling the MCA compartments may be the responsibility of the patient, a lay or professional caregiver or the pharmacy.[31] Since there are numerous MCAs on the market their ease of opening and ability to protect products against moisture, oxygen and light significantly varies. The same applies to multiple drug dispensing systems (MDDs).[32]

Generally, MCAs and MDDs contain tablets and capsules outside their original packaging. Normally, MCAs are filled with products to be used in the next week, although they may also contain medication for any unforeseen future use. MDDs, however, may be filled with tablets and capsules that should be used at a specific date and time up to a month after filling. The use of MCAs and MDDs is generally based on the assumption that their use is in the best interest of the patient and that they sufficiently protect tablets and capsules against environmental conditions at room temperature for a short period of time. However, healthcare professionals also realise this may not be true, eg, dabigatran,[33] and mistakes may be made.[34] A clear call for further information regarding the stability of medicines to ensure safe and effective use of MCAs was published in 2015.[35]

To support well-informed decision making by patients and healthcare professionals, the draft reflection paper encourages companies to study the stability of drug products that are likely to be used by older people for short periods of time outside their original package in an open dish study and to summarise the results in the SmPC/PL. This approach would support users with information on the minimum/maximum product stability in any packaging and thus provide guidance on the acceptability of a specific MCA or MDD for storage within a specific temperature range and over a defined period of time.

6 | FUTURE WORK

The EU regulatory system is based on directives and regulations which are further detailed in guidelines, reflection papers etc to support the marketing of products with a positive benefit to risk. As guidelines and reflection papers normally have a prospective approach,[12,36] practical problems with marketed (old) products cannot be fully solved by new guidelines or reflection papers. This raises the question to all stakeholder parties (authorities, industry, academia, healthcare professionals, patients etc) of how the medication safety and efficacy of marketed products can be further optimised. Information from healthcare professionals, caregivers and patients on practical medication problems and (near) medication incidents can help industry and authorities to reconsider the senior-friendliness of new and marketed products, the urgency of any changes to the drug product design and the need for new regulatory provisions.[37] Information

from other stakeholder parties on the emerging issues of medication safety and efficacy in an increasing older population are important also, eg, appropriate and useful strategies to address a problem, ie. heuristics, information technology.[38,39]

7 | CONCLUSION

The increased longevity, age and multimorbidity of European and other patient populations worldwide requires continuous re-evaluation of existing regulatory provisions and/or the development of new provisions to realise the best attainable standard of public health. Currently, the necessity to better address older peoples needs in prescribing, drug development, dispensing and use is increasingly acknowledged as another essential factor to achieve desired health outcomes.[6,9] As part of EMA efforts, a reflection paper on the pharmaceutical development of medicines for use in the older people has been developed. The draft reflections point out the most evident critical aspects that should be considered in the future drug development of products likely to be used by older patients. It is important that all stakeholder parties, including medical doctors, nurses, pharmacists and HTA experts understand what the reflection paper tries to achieve and how they can help in optimising the paper to foster medication safety and older peoples quality of life. Moreover, the reflections reveal the inevitable need for transdisciplinary collaboration of a wide group of stakeholder parties in the development of meaningful and practical regulatory provisions to ensure adequate drug product quality, safety and efficacy for the evolving older patient population.

COMPETING INTERESTS

All authors are EMA experts. Nevertheless, this manuscript should be considered as personal work.

DATA AVAILABILITY STATEMENT

Not applicable.

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REFERENCES

1. Anderson LA, Prohaska TR. Fostering engagement and independence: opportunities and challenges for an aging society. *Health Educ Behav*. 2014;41(1 Suppl):5S-9S.
2. Vladeck BC. Economic and policy implications of improving longevity. *J Am Ger Soc*. 2005;53(9 Suppl):S304-S307.
3. Wouterse B, Huisman M, Meijboom BR, Deeg DJ, Polder JJ. The effect of trends in health and longevity on health services use by older adults. *BMC Health Serv Res*. 2015;15(1):574.
4. Rechel B, Grundy E, Robine JM, et al. Ageing in the European Union. *Lancet*. 2013;381(9874):1312-1322.
5. Stegemann S, Baeyens JP, Becker R, et al. Design of pharmaceutical products to meet future patient needs requires modification of current development paradigms and business models. *Z Gerontol Geriatr*. 2014;47(4):285-287.
6. Cerreta F, Eichler HG, Rasi G. Drug policy for an aging population the European Medicines Agencys geriatric medicines strategy. *N Engl J Med*. 2012;367(21):1972-1974.
7. European Medicines Agency. Concept paper on the need for a reflection paper on quality aspects of medicines for older people. Available at https://www.ema.europa.eu/en/documents/scientific-guideline/concept-paper-need-reflection-paper-quality-aspects-medicines-older-people-first-version_en.pdf 2013; Accessed 28 September 2019.
8. Van Riet-Nales DA, Hussain N, Sundberg KA, et al. Regulatory incentives to ensure better medicines for older people: from ICH E7 to the EMA reflection paper on quality aspects. *Int J Pharm*. 2016;512(2):343-351.
9. Beard JR, Officer A, de Carvalho IA, et al. The world report on ageing and health: a policy framework for healthy ageing. *Lancet*. 2016;387(10033):2145-2154.
10. European Medicines Agency. Reflection paper on the pharmaceutical development of medicines for use in the older population (draft). Available at: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-pharmaceutical-development-medicines-use-older-population-first-version_en.pdf; Accessed 28 May 2020.
11. European Medicines Agency. Guideline on pharmaceutical development of medicines for paediatric use Rev 1 (draft). 2013. Available at https://www.ema.europa.eu/en/documents/scientific-guideline/draft-guideline-pharmaceutical-development-medicines-paediatric-use_en.pdf; Accessed 28 September 2019.
12. European Medicines Agency. Procedure for European Union Guidelines and related documents within the pharmaceutical legislative framework. 2009. Available at https://www.ema.europa.eu/en/documents/scientific-guideline/procedure-european-union-guidelines-related-documents-within-pharmaceutical-legislative-framework_en.pdf; Accessed 28 May 2020.
13. Van Riet-Nales DA, Doeve ME, Nicia AE, et al. The accuracy, precision and sustainability of different techniques for tablet subdivision: breaking by hand and the use of tablet splitters or a kitchen knife. *Int J Pharm*. 2014;466(1-2):44-51.
14. Freeman MK, White W, Iranikhah M. Tablet splitting: a review of weight and content uniformity. *Consult Pharm*. 2012;27(5):341-352.
15. Wilczynski S, Koprowski R, Duda P, Banys A, Blonska-Fajfrowska B. Microtomographic studies of subdivision of modified-release tablets. *Int J Pharm*. 2016;511(2):899-912.
16. Hodel EM, Kaur H, Terlouw DJ. Stability of dihydroartemisinin-piperaquine tablet halves during prolonged storage under tropical conditions. *Am J Trop Med Hyg*. 2017;96(2):338-340.
17. Douroumis D. Practical approaches of taste masking technologies in oral solid forms. *Expert Opin Drug Deliv*. 2007;4(4):417-426.
18. Gracia-Vásquez SL, González-Barranco P, Camacho-Mora IA, González-Santiago O, Vázquez-Rodrguez SA. Medications that should not be crushed. *Medicina Universitaria*. 2017;75:50-63.
19. Jongbloed-de Hoon M, Colbers A, Velthoven-Graafland K, et al. Brief report: pharmacokinetics of crushed Elvitegravir combination tablet given with or without enteral nutrition. *J Acquir Immune Defic Syndr*. 2017;74(5):571-574.
20. Wells KA, Losin WG. In vitro stability, potency, and dissolution of duloxetine enteric-coated pellets after exposure to applesauce, apple juice, and chocolate pudding. *Clin Ther*. 2008;30(7):1300-1308.
21. Arruabarrena J, Coello J, Maspoch S. Raman spectroscopy as a complementary tool to assess the content uniformity of dosage units in break-scored warfarin tablets. *Int J Pharm*. 2014;465(1-2):299-305.
22. Abu-Geras D, Hadziomerovic D, Leau A, et al. Accuracy of tablet splitting and liquid measurements: an examination of who, what and how. *J Pharm Pharmacol*. 2017;69(5):603-612.

23. Van Riet-Nales D, Donkerbroek L, Nicia A, Oussoren C, de Boer A, van den Bemt B. The development of a test battery to assess the hand-eye functions relevant in predicting easy and accurate tablet subdivision in older people: a pilot study. *Br J Clin Pharmacol*. 2020;86(10):1969-1981. https://doi.org/10.1111/bcp.14201
24. Jukic PN, Gagliardi C, Fagnani D, Venturini C, Orlandoni P. Home enteral nutrition therapy: difficulties, satisfactions and support needs of caregivers assisting older patients. *Clin Nutr*. 2017;36(4):1062-1067.
25. Kozeniecki M, Fritzshall R. Enteral nutrition for adults in the hospital setting. *Nutr Clin Pract*. 2015;30(5):634-651.
26. Kurien M, Penny H, Sanders DS. Impact of direct drug delivery via gastric access devices. *Expert Opin Drug Deliv*. 2015;12(3):455-463.
27. Stegemann S. Drug administration via enteral tubing: an unresolved but increasing challenge. *Expert Opin Drug Deliv*. 2015;12(2):159-161.
28. European Medicines Agency. Guideline on pharmaceutical development of medicines for paediatric use (revision 2). Available at https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-pharmaceutical-development-medicines-paediatric-use_en.pdf 2013; Accessed 18 September 2018.
29. European Medicines Agency. Administration of oral immediate release medicinal products through enteral feeding tubes. Available at https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-guidelines/qa-quality/quality-medicines-questions-answers-part-2 2018; Accessed 18 September 2019.
30. Notenboom K, Beers E, van Riet-Nales DA, et al. Practical problems with medication use that older people experience: a qualitative study. *J Am Geriatr Soc*. 2014;62(12):2339-2344.
31. Howell EH, Senapati A, Hsich E, Gorodeski EZ. Medication self-management skills and cognitive impairment in older adults hospitalized for heart failure: a cross-sectional study. *SAGE Open Medicine*. 2017;5:2050312117700301. https://doi.org/10.1177/2050312117700301
32. Mertens BJ, Kwint HF, van Marum RJ, Bouvy ML. Are multidose drug dispensing systems initiated for the appropriate patients? *Eur J Clin Pharmacol*. 2018;74(9):1159-1164.
33. Robertson SG, Glass BD. Stability of repackaged dabigatran etexilate capsules in dose administration aids. *Eur J Hosp Pharm*. 2018;25(e2):e93-e97.
34. Gilmartin-Thomas JF, Smith F, Wolfe R, Jani Y. A comparison of medication administration errors from original medication packaging and multi-compartment compliance aids in care homes: a prospective observational study. *Int J Nurs Stud*. 2017;72:15-23.
35. Gilmartin JF, Raimi-Abraham BT, Jani Y, Smith F, Orlu-Gul M. Taking the guesswork out of supplying multicompartment compliance aids: do pharmacists require further guidance on medication stability? *Ing J Pharm Pract*. 2015;23(5):367-369.
36. European Medicines Agency. Status of EMEA scientific guidelines and European Pharmacopoeia monographs and chapters in the regulatory framework applicable to medicinal products. Available at https://www.ema.europa.eu/en/documents/scientific-guideline/status-emea-scientific-guidelines-european-pharmacopoeia-monographs-chapters-regulatory-framework_en.pdf. 2008; Accessed 18 September 2019.
37. Karapinar arkit F, Van den Bemt PMLA, Sadik M, Van Soest B, Knol W, et al. Opportunities for changes in the drug product design to enhance medication safety in older people: evaluation of a national public portal for medication incidents. *Br J Clin Pharmacol*. 2020;86(10):1946-1957. https://doi.org/10.1111/bcp.14392
38. Feufel MA, Rauwolf G, Meier FC, Karapinar-arkit F, Heibges M. Heuristics for designing user-centric drug products: lessons learned from human factors and ergonomics. *Br J Clin Pharmacol*. 2020;86(10):1989-1999. https://doi.org/10.1111/bcp.14134
39. Eggerth A, Hayn D, Schreier G. Medication management needs information and communications technology-based approaches, including telehealth and artificial intelligence. *Br J Clin Pharmacol*. 2020;86(10):2000-2007. https://doi.org/10.1111/bcp.14045

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