Trends in oral solid dosage forms: Review of 2023 EMA approvals

Background

This document is an overview of NCEs approved by the European Medicines Agency in 2023 as oral solid dosage forms and provides an insight into current formulation development strategies. The primary data source is the EPAR documentation, which can be found on the EMA website.

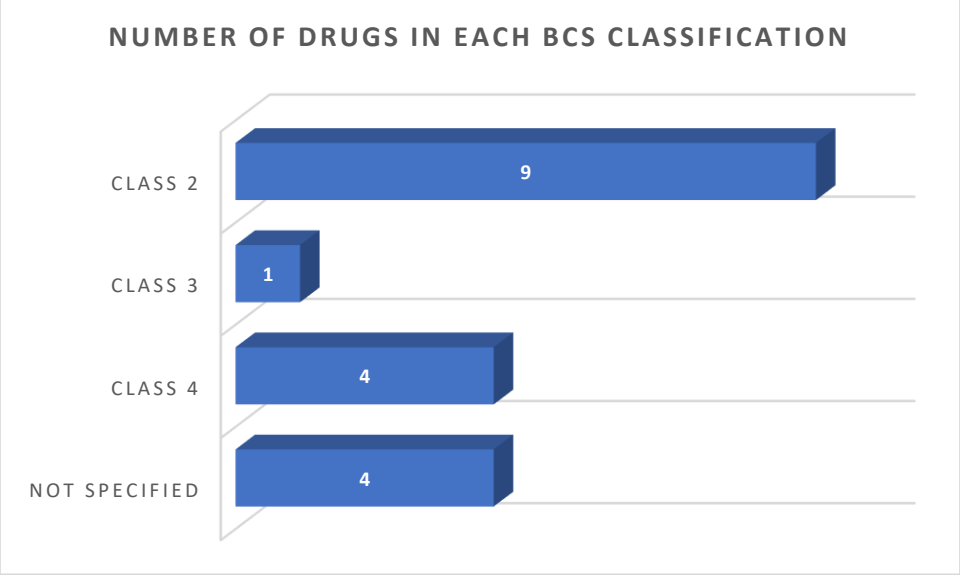
Nineteen of the NCEs approved by the EMA in 2023 were in the form of orally administered solid dosage forms; these comprised seventeen products containing a single active agent and one combination product. One approval was for a paediatric formulation of a drug already licenced for use in adults (dabrafenib): the paediatric form was an orodispersible tablet - this drug substance and dosage form is excluded from the review.

Drug Substance

Eight of the eighteen NCEs which are the subject of this review were in the form of salts: Dihydrochloride (3); tosylate (1); citrate (1); mesylate (1); arginine (1); and sodium (1);

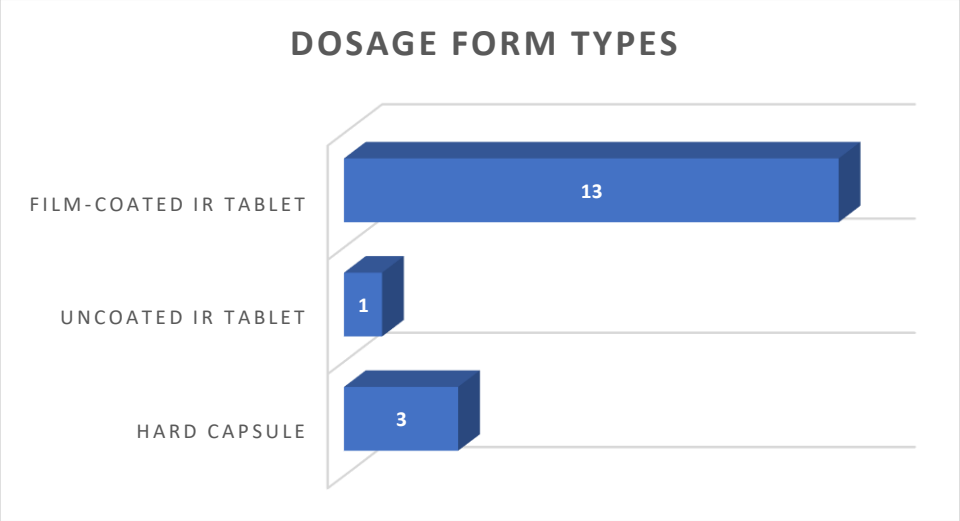
The average molecular weight (non-salt form) was 426 g/mol (range 228-634).

The BCS Classification was disclosed for fourteen of the eighteen NCEs; they were predominantly Class 2 (low solubility, high permeability).



Dosage form types

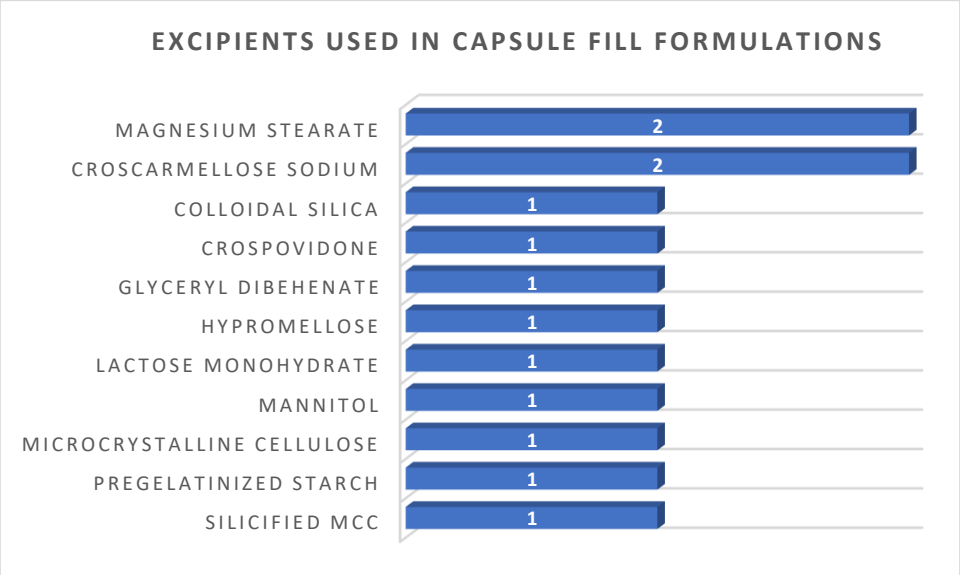
Film-coated immediate release tablets were the principal dosage form. In addition, there was one uncoated immediate release tablet and three hard capsule formulations.



Excipients

- ***Capsules***

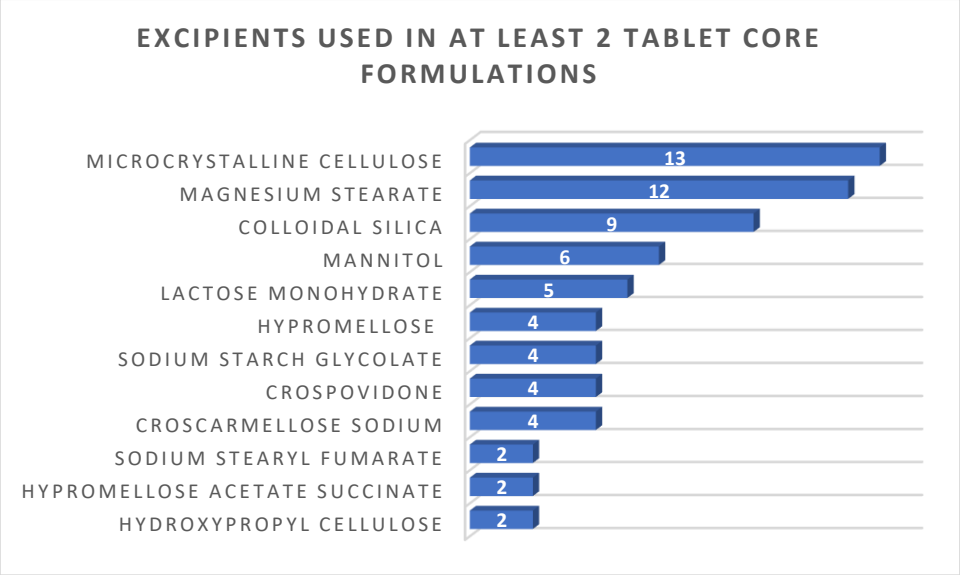
Excipients appearing in the capsule fill formulations are displayed below. Two of the three capsule products used a hypromellose shell and the third product used a gelatin shell.



MCC = microcrystalline cellulose

- ***Tablets***

Excipients appearing in two or more of the tablet core formulations are presented in the chart below.

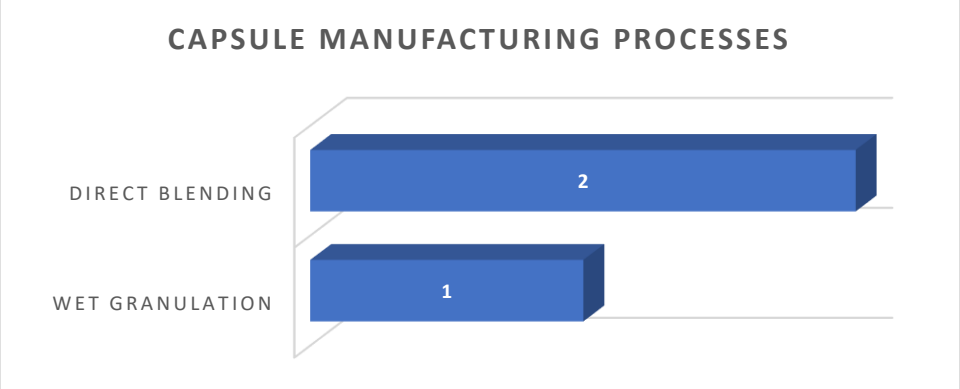


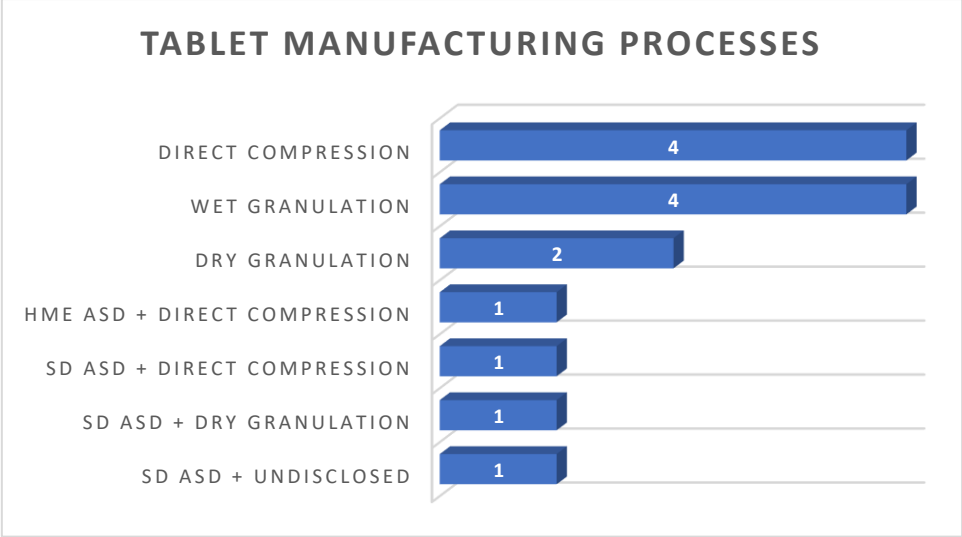
The following excipients appear in only one product: anhydrous lactose, maize starch, hydroxypropyl-β-cyclodextrin, polyvinylpyrrolidone/vinyl acetate copolymer, propyl gallate, silicified microcrystalline cellulose, sodium chloride, sodium lauryl sulfate and vitamin E TPGS.

The tablet film coatings are based on hypromellose (seven products) and polyvinyl alcohol (six products).

Manufacturing processes

Capsule and tablet manufacturing processes are summarised in the charts below.





HME = hot-melt extrusion; SD – spray-dried

As can be seen above, four tablets contained drug in the form of an amorphous solid dispersion (ASD). Three of the NCEs were BCS Class 2 and one was BCS Class 4. The ASDs were manufactured as follows:

- Two products: API spray-dried with hypromellose acetate succinate
- One product: API spray-dried with hydroxypropyl-β-cyclodextrin
- One product: Hot-melt extrusion using polyvinylpyrrolidone-vinyl acetate copolymer and a solution of API in vitamin E TPGS

Comments

As might be anticipated, the majority of the NCEs were BCS Class 2; three of these were formulated as ASDs to enhance solubility. ASDs aside, the dosage forms could be considered conventional in terms of manufacturing processes and excipient choice.