Trends in oral solid dosage forms:
Review of 2020 & 2021 EMA approvals

Background

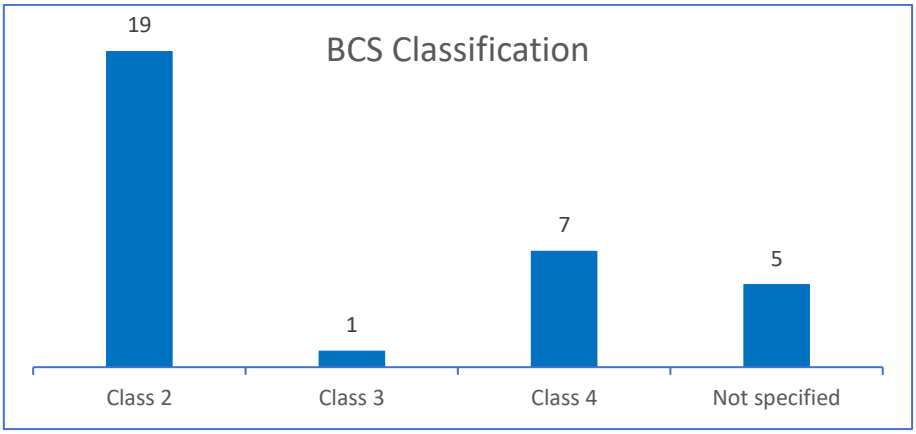
This post is the latest in an occasional review of EMA product approvals and is intended to provide an insight into current formulation development strategies being adopted for orally administered NCEs. Approvals in 2020 and 2021 are described.

Thirty-two of the new medicines approved by the EMA in 2020 & 2021 were orally administered solid dosage forms containing a single NCE; these medicines are the subject of this review. Any combination products containing NCEs are excluded.

Drug Substance

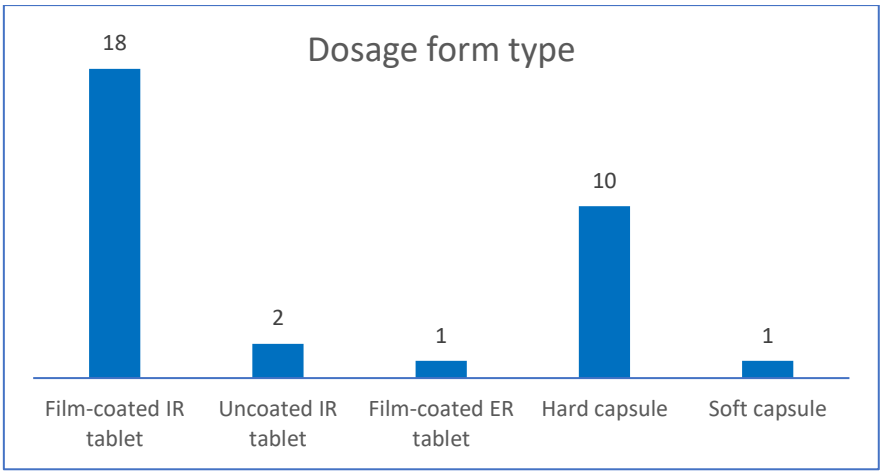
Seven of the NCEs are in the form of salts, namely hydrochloride (x2), maleate (x2), hydrogen sulfate, tromethamine, and choline. Two NCEs are monohydrates. Tucatinib (Tukysa®) API is manufactured as the crystalline hemiethanolate but is converted to the amorphous nonsolvate during drug product manufacture.

At least 60% of the NCEs are categorised as BCS Class 2 (low solubility, high permeability).



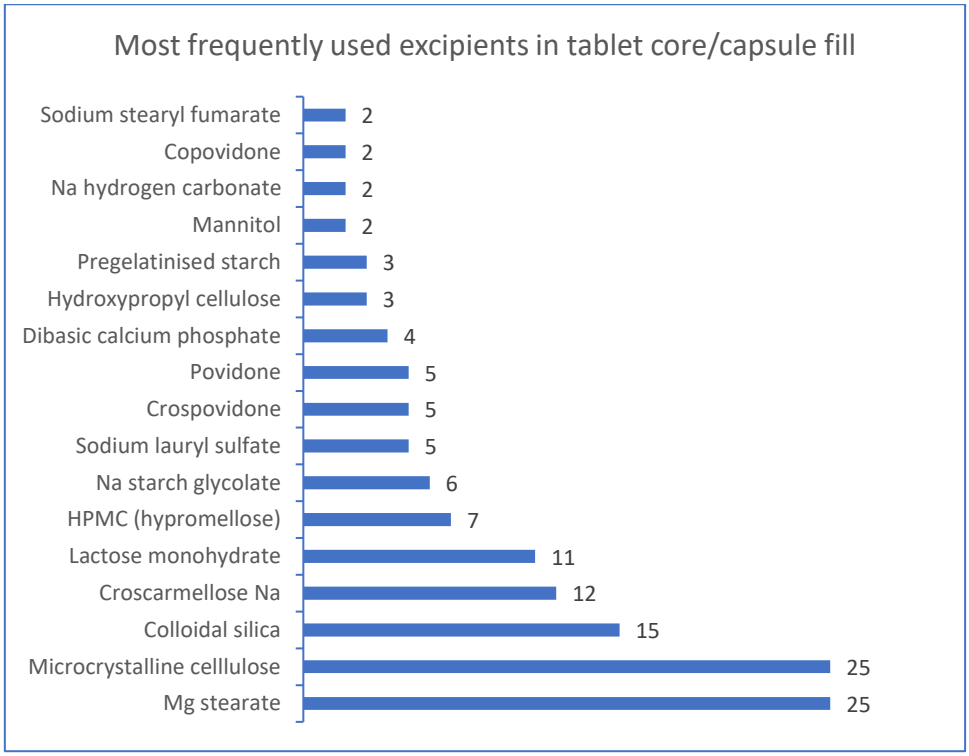
Tablets vs. Capsules

Unsurprisingly, immediate-release (IR) tablets are the predominant dosage form. There is one extended-release (ER) tablet. Around one-third of the approvals are hard capsules. One product is a softgel.



Excipients

Excipients appearing in two or more of the formulations are presented in the chart below; any film coating ingredients are excluded. Microcrystalline cellulose and magnesium stearate are found in 80% of the products.



The following excipients appear in only one product: citric acid, mannitol, hydroxypropyl cellulose/low-substituted hydroxypropyl cellulose, pregelatinized starch, dibasic calcium phosphate, vitamin E TPGS, macrogol 4000, macrogolglycerol hydroxystearate, α-tocopherol (used in the softgel formulation), microcrystalline cellulose (MCC) spheres, tartaric acid, anhydrous lactose, talc, fumaric acid, sodium chloride, potassium chloride, and silicified microcrystalline cellulose.

Six of the ten hard capsule formulations use gelatin shells and the remainder use HPMC shells.

The tablet film coatings are based on HPMC (9 products), PVA (9 products) or PVA-PEG graft copolymer (1 product).

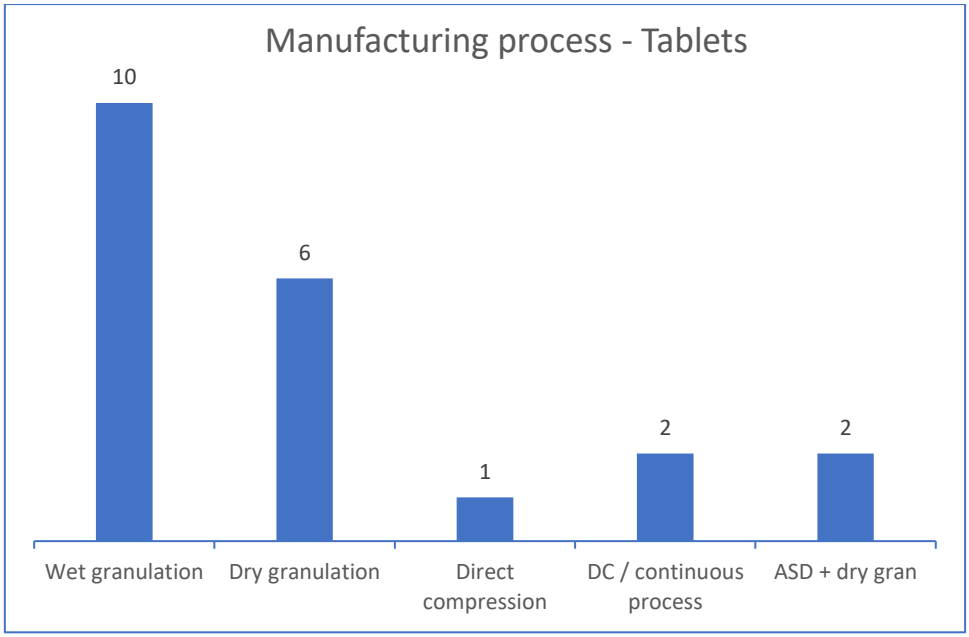
Amorphous solid dispersion (ASD)

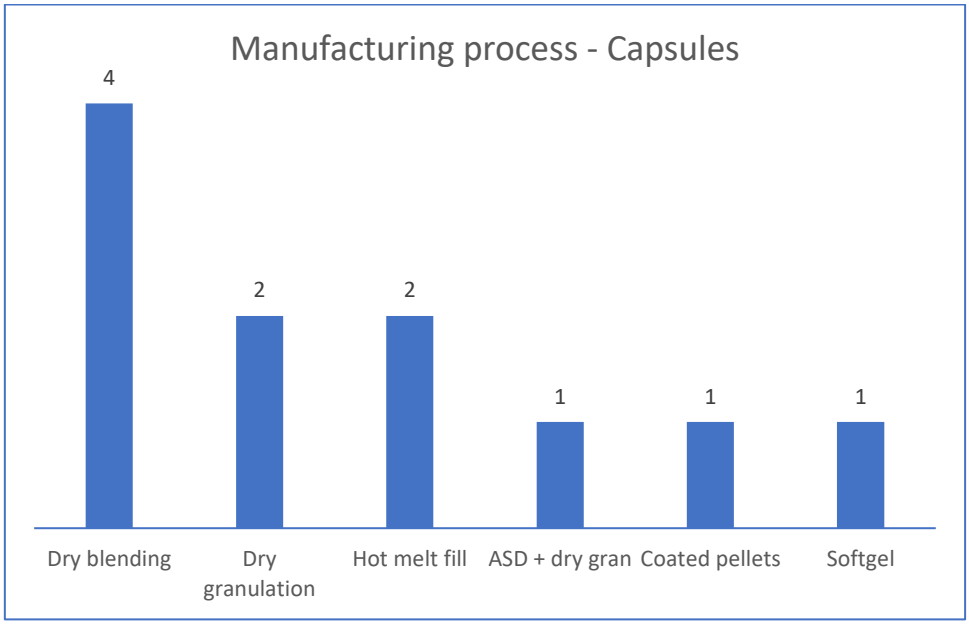
Two tablets (Tukysa®, Qinlock®) and one capsule (Gavreto®) contain drug in the form of a spray-dried ASD; the stabilising polymers are copovidone, HPMCAS and HPMC, respectively.

Manufacturing process

For tablets, the majority are produced by granulation processes. The tablet cores for two Pfizer products (Cibinqo® and Daurismo®) are made by direct compression using a continuous process.

For one of the capsule products (Bylvay®), drug is layered onto MCC spheres; the finished product can be swallowed whole or the capsule contents can be sprinkled onto food.





Comments

The oral solid NCE formulations approved during 2020 and 2021 are predominantly conventional in nature. In three of the products the drug substance was converted into an amorphous intermediate by spray drying. Continuous manufacturing continues to occupy a niche.