

THE PRESCRIBE AWARDS FOR 2020

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2020 Prescrire Drug Awards

Every month, in the New Products section of our French edition, *Prescrire's* Editorial Staff single out, among the plethora of new products, those worth adding to one's list of useful treatment options or worth using instead of other products, while also pointing out which medicines are best avoided. This is achieved by systematically analysing the evaluation data available on new drugs, existing drugs authorised for different clinical situations, and new forms or new dose strengths of existing drugs. Occasionally, a previously analysed drug is re-examined "with more follow-up", when more recent data justify reassessing its harm-benefit balance.

Prescrire's multidisciplinary team has been analysing drugs for 40 years, free from influence from the health industry or institutions. We ensure our independence by the fact that *Prescrire* is funded exclusively by its subscribers, carrying no paid advertising in either the French or the English edition, and receiving no grants or subsidies of any kind.

The 2020 Prescrire Drug Awards are based on the analyses published in the "New Products" section of our French edition in 2020. These awards recognise products that represent a therapeutic advance, in that they offer better efficacy than existing treatments, provoke less frequent or less severe adverse effects (provided they also have similar efficacy), or enable a drug with a favourable harm-benefit balance to be used more safely or easily.

A Pilule d'Or for 2020!

One new product examined in 2020 represents a major therapeutic advance worthy of a Pilule d'Or (Golden Pill Award), six years after it was last awarded. Two products earned a place on the 2020 Honours List. None made the "Noteworthy" list.

Ebola vaccine rVSV-Zebov in an outbreak of Ebola virus disease: markedly reduces the incidence of this often fatal infection

Ebola virus disease is a serious infection. Most outbreaks have occurred in Africa, killing 30% to 90% of infected patients, depending on the outbreak. Death occurs in a context of generalised haemorrhage and multiorgan failure. Prevention is based mainly on strict hygiene and protective measures for anyone likely to have been in contact with infected patients, including healthcare professionals. Treatment is mainly symptomatic.

Ebola vaccine rVSV-Zebov is a live attenuated vaccine based on vesicular stomatitis virus (VSV), engineered (rVSV) to express a protein from Zaire Ebola virus (Zebov).

The evaluation data show that, during an outbreak of Zaire Ebola virus disease, vaccination protects at least two-thirds of persons who have potentially been in contact with infected patients, and that its protective effect starts from day 10 after vaccination. Its harms are acceptable, given the severity of this disease, and include adverse effects common to all vaccines, as well as joint and skin disorders. Ervebo[®] was awarded the Pilule d'Or on the basis of these data.

A number of risks and unknowns must be taken into account, however. For example, although vesicular stomatitis virus is not generally pathogenic in humans, it has been found in certain body fluids of vaccinees, which raises the possibility that they could transmit this virus to other people. *Ebola vaccine rVSV-Zebov* is a live vaccine that has not been evaluated in immunocompromised individuals, and the consequences of infection with the vaccine virus in this situation are unknown. In addition, a threefold risk of miscarriage was reported in women who became pregnant during the 2 months after vaccination. Compliance with the vaccine's storage conditions (between -80°C and -60°C) is challenging and complicates its use in many countries. The duration of the vaccine's protective effect is unknown. Finally, vaccination does not eliminate the need for strict protective and hygiene measures around patients infected with Ebola virus.

Fexinidazole in sleeping sickness due to *Trypanosoma brucei gambiense*: effective, and more convenient than standard treatments

Human African trypanosomiasis (or sleeping sickness) is caused by a parasite of the genus *Trypanosoma*, usually *T. brucei gambiense*. This disease is endemic in many countries in sub-Saharan Africa. It typically affects people living in rural or periurban areas.

If left untreated, the disease is usually fatal within 2 to 3 years on average from the start of infection with *T. brucei gambiense*. The disease progresses through two stages: the early haemolymphatic stage, characterised by recurrent fever, joint pain, muscle pain and fatigue, followed by the advanced meningoencephalitic stage, during which the parasites infect the central nervous system, causing neuropsychiatric disorders that almost always progress to coma and death.

Cure rates with *pentamidine* or *nifurtimox* + *eflornithine* combination therapy (NECT), depending on the

disease stage, exceed 95%. But these treatments require daily injections or infusions for 7 days, administered in a healthcare facility, which limits access to these treatments in regions with limited health infrastructure, some of which are also affected by armed conflict.

Fexinidazole is an antiparasitic drug for oral use. After 10 days of treatment, its cure rate exceeds 90% at both stages of the disease. Its adverse effects are acceptable when weighed against this level of efficacy: nausea, vomiting, neuropsychiatric disorders, and QT prolongation. *Fexinidazole* Winthrop[®] earned a place on the Honours List in the 2020 Prescribe Drug Awards because of *fexinidazole*'s positive harm-benefit balance and because the availability of an oral treatment for this disease represents a clear practical advance for patients.

However, NECT remains the first-choice treatment for patients with the most advanced forms of the disease and who have access to this treatment, as it is probably slightly more effective in this situation.

Tafamidis in transthyretin amyloid cardiomyopathy: reduction in mortality

Transthyretin amyloidosis is a rare, fatal disease that generally presents between 30 and 50 years of age. Patients have a life expectancy of about ten years after diagnosis. This disorder is caused by instability of the protein transthyretin and leads to amyloid deposits in a range of organs. The clinical signs vary depending on the organs affected, but include cardiac disorders (heart failure, thrombosis and conduction disturbances).

Tafamidis is a drug that binds to and appears to stabilise transthyretin. In a placebo-controlled trial in 441 patients with symptomatic transthyretin amyloid cardiomyopathy, mortality after 30 months of treatment was lower in the *tafamidis* group: 30% versus 43% in the placebo group. One limitation of these results is that they remain to be confirmed in at least one other trial, conducted by a different team.

The benefits of *tafamidis* must be weighed against its harms: infections and gastrointestinal, ocular and probably hepatic disorders. Uncertainty remains over the optimum daily dose. Nevertheless, the magnitude of the effect observed led *Prescribe* to place Vyndaqel[®] on the Honours List of the 2020 Prescribe Drug Awards.

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2020 Pilule d'Or/Golden Pill

The Pilule d'Or (Golden Pill) is granted to drugs that represent a major therapeutic advance in a field in which no treatment was previously available.

• ERVEBO[®] (*Ebola vaccine rVSV-Zebov*) MSD

For active immunisation of individuals 18 years of age or older to protect against Ebola virus disease caused by Zaire Ebola virus (Prescribe Int n° 223).

2020 Honours List

Drugs included on the Honours List constitute a clear advance for some patients compared with existing therapeutic options, albeit with limitations. Those on this year's list, in alphabetical order, are:

• FEXINIDAZOLE WINTHROP[®] (*fexinidazole*) Sanofi Aventis

For human African trypanosomiasis (sleeping sickness) due to *Trypanosoma brucei gambiense* (Prescribe Int n° 221).

• VYNDAQEL[®] (*tafamidis*) Pfizer

For adults with transthyretin amyloid cardiomyopathy (Prescribe Int n° 222).