

Dipyridamole/ASA Shortage

Quick Take:

- Address and aggressively manage modifiable risk factors
- Pharmacological alternatives include:
 - Clopidogrel 75 mg PO once daily, or
 - ASA 81-325 mg PO once daily
- For those who are on dipyridamole/ASA because of stroke while taking ASA monotherapy, clopidogrel seems the logical choice; however, if clopidogrel is not an option, return to ASA monotherapy

TABLE 1: CANADIAN SUPPLIERS OF DIPYRIDAMOLE/ASA¹

Product	Strength Dipyridamole/ASA	DIN	Manufacturer
Taro-Dipyridamole/ASA	200 mg/25 mg	02471051	TAR
Aggrenox® Discontinued Feb 2020	200 mg/25 mg	02242119	BOE

BACKGROUND

Since the discontinuation of Aggrenox® in February 2020, only 1 product of dipyridamole/ASA (Taro Pharmaceuticals) remains on the Canadian market; Taro has experienced a manufacturing disruption and the product is expected to be shorted until 15 May 2020.²

HEALTH CANADA-APPROVED INDICATION OF DIPYRIDAMOLE/ASA³

- Prevention of stroke in patients who have had a previous stroke or a transient ischemic attack (TIA)

MANAGEMENT OPTIONS

Address Modifiable Risk Factors of Stroke/TIA

The following modifiable risk factors should be addressed and aggressively managed in all patients:⁴⁻⁷

- Lifestyle:
 - diet (particularly sodium intake)
 - physical activity
 - tobacco use
 - alcohol use
 - recreational drug use (e.g., cocaine, amphetamines)
- Blood pressure
- Diabetes mellitus
- Dyslipidemia

For more details, see [Thrombosis Canada clinical guidelines](#) – stroke: secondary prevention.

Pharmacological Alternatives^{4,6,8,9}

Aside from dipyridamole/ASA, 2 other agents are used for the secondary prevention of stroke and TIA:

- Clopidogrel 75 mg PO once daily, or
- ASA 81-325 mg PO once daily

Notes:

- Dipyridamole/ASA and clopidogrel have similar efficacy¹⁰
- ASA monotherapy is somewhat less effective when compared to clopidogrel or dipyridamole/ASA¹⁰ but is more effective than placebo and is considered an appropriate option for secondary stroke prevention^{4,5,8,9}

A common scenario that may be seen in practice is patients who were switched to dipyridamole/ASA after experiencing a stroke or TIA while taking ASA monotherapy. This is considered “treatment failure” or “breakthrough stroke/TIA.”

- Potential reasons for breakthrough include:⁸
 - ASA resistance – may be largely accounted for by **non-adherence**
 - explore if non-adherence may have contributed to breakthrough
 - emphasize the importance of adherence and offer suggestions, if appropriate
 - **poor control of modifiable risk factors**
 - see above and address any gaps
 - reduced absorption of enteric-coated ASA
 - evidence suggests the bioavailability of enteric-coated ASA products may be reduced in some patients¹¹
 - **use non-enteric-coated ASA**
 - inadequate dose in patients weighing >70 kg
 - some data indicate low-dose ASA in secondary stroke prevention is less effective at reducing major cardiovascular events in patients weighing >70 kg compared to those weighing <70 kg¹²
 - other data have shown a trend toward decreased effectiveness of low-dose ASA in patients weighing >70 kg, although not statistically significant¹³
 - while a dose-dependent relationship is not clear from available data, it is **reasonable to recommend ASA 325 mg daily for patients who have experienced breakthrough** on low-dose ASA and who are not at high risk of bleeding
 - alternate mechanisms of stroke such as cardioembolic (e.g., atrial fibrillation)
 - this should have been assessed at time of breakthrough and, if deemed a stroke by mechanism other than ischemic noncardioembolic, the patient should have been switched to appropriate antithrombotic treatment
 - non-modifiable risk factors (e.g., age)
- Management:
 - switch to clopidogrel
 - if clopidogrel not an option, return to ASA monotherapy
 - patient likely switched because some experts recommend switching to either clopidogrel or dipyridamole/ASA in the event of breakthrough while on ASA;⁵ however, it is not known if switching to a different agent improves outcomes compared to remaining on ASA^{5,9}
 - ASA monotherapy is more effective than placebo,¹⁰ so patient will benefit

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