# Daclatasvir PK Fact Sheet



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## Details

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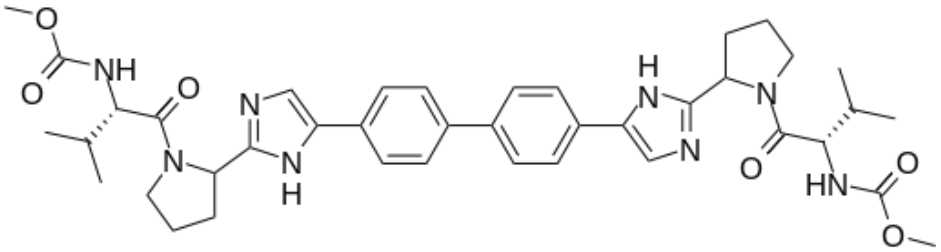
| *Generic Name* | Daclatasvir |
| *Trade Name* | Daklinza® |
| *Class* | NS5A replication complex inhibitor |
| *Molecular Weight* | 739 (812 as dihydrochloride) |
| *Structure* |  |

## Summary of Key Pharmacokinetic Parameters

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| *Linearity/non-linearity* | Pharmacokinetics increased in a largely dose-proportional manner from 1 to 100 mg, though exposures overlapped between 60 and 100 mg [1]. |
| *Steady State* | Steady state was achieved after 4 days of once daily administration. |
| *Plasma Half life* | 12-15 h |
| *Cmax* | 1534 ng/ml (60 mg once daily) |
| *Cmin* | 232 ng/ml (60 mg once daily) |
| *AUC* | 14122 ng.h/ml (60 mg once daily) |
| *Interindividual Variation* | ~20-40% (60 mg once daily, 14 days, n=4) [1] |
| *Bioavailability* | 67% |
| *Absorption* | In healthy subjects, administration of daclatasvir 60 mg tablet after a high-fat meal decreased daclatasvir Cmax and AUC by 28% and 23%, respectively, compared with fasting conditions. Administration after a light meal resulted in no reduction in daclatasvir exposure. |
| *Protein Binding* | >99% |
| *Volume of Distribution* | 47 L |
| *CSF:Plasma ratio* | Not studied |
| *Semen:Plasma ratio* | Not studied |
| *Renal Clearance* | Minimal (6.6% of total daily dose) |
| *Renal Impairment* | The pharmacokinetics of daclatasvir (60 mg single oral dose) were studied in non-HCV infected subjects with renal impairment. Daclatasvir unbound AUC was estimated to be 18%, 39% and 51% higher for subjects with creatinine clearance (CLcr) values of 60, 30 and 15 ml/min, respectively, relative to subjects with normal renal function. Subjects with end-stage renal disease requiring haemodialysis had a 27% increase in daclatasvir AUC and a 20% increase in unbound AUC compared to subjects with normal renal function. |
| *Hepatic Impairment* | The pharmacokinetics of daclatasvir (30 mg single oral dose) were studied in non-HCV infected subjects with mild (Child-Pugh A), moderate (Child-Pugh B), and severe (Child-Pugh C) hepatic impairment compared with unimpaired subjects. Cmax and AUC of total daclatasvir (free and protein-bound) were lower in subjects with hepatic impairment; however, hepatic |

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impairment did not have a clinically significant effect on the free drug concentrations of daclatasvir.

## Metabolism and Distribution

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| *Metabolised by* | CYP3A4 |
| *Inducer of* | Very weak inducer of CYP3A4<br>(no dose adjustment of coadministered CYP3A4 substrates necessary) |
| *Inhibitor of* | P-gp, OATP1B1/B3, BCRP.<br>Does not inhibit CYP3A4 [2], or CYPs 1A2, 2B6, 2C8, 2C9, 2C19, and 2D6 in vitro. |
| *Transported by* | P-gp |

## References

*Unless otherwise stated (see below), information is from:*
Daklinza® Summary of Product Characteristics, Bristol-Myers Squibb *(discontinued).*
Daklinza® US Prescribing Information, Bristol-Myers Squibb Co.

1. Nettles RE, *et al*. 2011, *Hepatology*, 54(6):1956-1965.
2. Amblard F, *et al*. 2013, *Bioorg Med Chem Lett*, 23: 2031-2034.

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